

48th CONGRESS OF THE INTERNATIONAL SOCIETY OF PAEDIATRIC ONCOLOGY (SIOP)

DUBLIN, IRELAND, OCTOBER 19–22, 2016, SIOP ABSTRACTS

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ABSTRACTS

SIOP ABSTRACTS

SIOP AWARD SESSION

O-001 | Addition of FLT3 Inhibitor Lestaurtinib to Post-Induction Chemotherapy does not Improve Outcomes in MLL-Rearranged Infant Acute Lymphoblastic Leukemia (ALL): AALL0631, A Children's Oncology Group Study

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Background/Objectives: Infants with MLL-rearranged (MLL-r) ALL have a poor outcome. MLL-r ALL overexpresses FLT3, and the FLT3 inhibitor lestaurtinib potentiates chemotherapy-induced cytotoxicity in preclinical models. The primary objective of AALL0631 was to determine if the addition of lestaurtinib to post-induction chemotherapy would improve outcome for infants with MLL-r ALL.

Design/Methods: Post-induction risk groups were defined by age and MLL status: high risk (HR) <90 days, MLL-r; intermediate risk (IR) ≥90 days, MLL-r; standard risk (SR) any age, MLL-germline (MLL-g). SR patients received standard chemotherapy (Arm A) including extended maintenance for 24 months of total therapy. IR and HR patients received intensified chemotherapy ± lestaurtinib (given enterally, twice daily, starting the day after completion of each intensive chemotherapy block). The study had two sequential phases: a safety/activity (S/A) phase, which determined a safe and biologically active dose of lestaurtinib to be 5 and 4.25 mg/kg/day for IR and HR patients, respectively; and an efficacy phase to determine the relative efficacy of chemotherapy only (Arm B) versus chemotherapy + lestaurtinib (Arm C). Event free survival (EFS) was determined from end-induction and compared for IR/HR patients treated with Arm B versus Arm C; EFS was determined from enrollment for SR patients treated with Arm A.

Results: For all IR/HR patients, 3-year EFS was 37% for Arm B (n=54) versus 37% for Arm C (n=67; p=0.90). For IR patients, 3-year EFS was 46% for Arm B (n=44) versus 41% for Arm C (n=52, p=0.59). For HR patients, 3-year EFS was 0% for Arm B (n=10) versus 20% for Arm C (n=15, p=0.25). For SR patients treated with Arm A, the 3-year EFS was 87% (n=64).

Conclusion: The addition of lestaurtinib to post-induction chemotherapy did not improve outcome for infants with MLL-r ALL. Infants with MLL-g ALL had a favorable outcome with therapy that included a prolonged maintenance phase.

O-002 | Results of ACNS0331: Phase III Trial of Involved-Field Radiotherapy (IFRT) and Low Dose Craniospinal Irradiation (LD-CSI) in Average-Risk Medulloblastoma: A Report from Children's Oncology Group

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Background/Objectives: Conventional therapy for average-risk medulloblastoma is standard dose CSI (SD-CSI) to 23.4Gy and posterior fossa radiotherapy (PFRT) to 54Gy with cisplatin/cyclophosphamide based chemotherapy.

Design/Methods: This trial tests whether a 5.4Gy reduction in the CSI dose (18Gy, LD-CSI) in patients 3-7y and a reduction in boost volume (IFRT) in patients 3-21y receiving chemotherapy results in non-inferior event free survival (EFS) or overall survival (OS).

Results: Of 549 children enrolled, 464 were eligible and without central review findings of excess disease and were randomized to PFRT (237) or IFRT (227). Of those, 226 were 3-7y and randomized to SD-CSI (110) or LD-CSI (116). With median follow-up of 6.1 years, there was a significant difference in EFS between patients with excess residual disease as determined at central review, compared to the remaining eligible patients (p=0.054, two-sided log-rank test; p=0.027, one-sided log-rank test). The 5 year OS in PFRT and IFRT is 84.8%±2.8% and 84.7%±2.8%, respectively. The 5 year EFS in PFRT and IFRT is 80.5%±3.1% and 82.4%±3.0%, respectively. The predetermined hazard ratio (HR) limit to determine inferiority for EFS was 1.6 and the observed 94% upper confidence limit of HR was 1.3. Therefore, IFRT is deemed non-inferior to PFRT. The 5 year OS in SD-CSI and LD-CSI is 85.3%±3.9% and 78.2%±4.6%, respectively. The 5 year EFS in SD-CSI and LD-CSI is 82.1%±4.3% and 71.4%±5.1%, respectively. The predetermined HR limit for EFS to determine inferiority was 1.6 and the observed 80% upper confidence limit of HR was 1.9. Therefore, LD-CSI is deemed inferior to SD-CSI.

Conclusion: For average-risk patients, these data support decreasing radiation volume to the primary site. However, decreasing CSI dose to 18Gy may increase risk of recurrence and is not recommended. Pretreatment imaging review may avoid enrollment of inappropriate patients in these trials.

O-003 | Is Intensive Chemotherapy for Childhood Acute Lymphoblastic Leukemia Feasible in a Low-Middle Income Country? The Guatemala Experience

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Background/Objectives: UNOP (Unidad Nacional de Oncología Pediátrica) is the only paediatric hemato-oncology center in Guatemala and implemented a slightly modified ALL IC-BFM protocol to determine the feasibility and efficacy of therapy, despite the obstacles to treat acute lymphoblastic leukaemia (ALL) in a low-middle income country (LMIC).

Design/Methods: Patients aged 1-17 years were treated according to a modified ALL IC-BFM 2002 protocol including intensive polychemotherapy blocks for high-risk patients. Risk classification was based on age, white blood cell count, immunophenotype, genetics (available for a subgroup only), and early response to therapy.

Results: From July 2007 to June 2014, 787 patients were treated: 160 standard-risk (SR), 450 intermediate-risk (IR) and 177 high-risk (HR). Disease features at diagnosis were median age 6.9 years (range 1-17.8), 56.8% male, 55.2% malnutrition, 15% WBC count ≥ 100,000, 5.8% T-ALL lineage, 12.5% CNS 3 and 0.3% of hypodiploidy. Out of 281 patients investigated, 7.1% were positive for BCR/ABL, 2.8% for MLL/AF4, and 7.5% for ETV6/RUNX1.

Induction death rate was 6.6%; 92.9% of patients experienced morphological remission. During the first complete remission death or treatment abandonment occurred in 4.8% and 2.6% of the patients, respectively. With a median observation time of 3.6 years and abandonment considered an event, the 5-year event-free survival (EFS) and overall survival estimates were 56.2% (SE = 2.1%) and 64.1% (SE=2.1%), respectively, with a 5-year cumulative incidence of relapse of 28.9% (SE = 0.4%). By risk group, the 5-year EFS were 71.1% (SE = 4.5%) in the SR group, 58.2% (SE = 2.9%) in the IR group, and 38.4% (SE=4.0%) in the HR group.

Conclusion: A well-organized center in a LMIC can provide intensive treatment for ALL and substantially reduce abandonment. Outcomes remain suboptimal due to late diagnosis, early deaths, and a high relapse rate, which may have a genetic basis. Earlier diagnosis, better management of complications, and better knowledge of ALL will improve outcomes.

O-004 | Progressive Paediatric Solid Tumours other than Bone-Sarcomas Benefit from Metronomic Chemotherapy: A Subgroup Analysis from a Double Blind Placebo Controlled Randomized Study

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Background/Objectives: Oral metronomic chemotherapy is often used with scepticism in progressive paediatric solid malignancies in the palliative setting. In the first randomised controlled trial of metronomic chemotherapy conducted by our group in these patients, no signif-

icant benefit in progression free survival or overall survival was reported in entire cohort. We here report the subgroup analysis of paediatric bone sarcomas versus other diagnoses.

Design/Methods: We conducted the double-blind, parallel design, placebo-controlled randomised study in primary extracranial, non-haematopoietic, paediatric solid malignancies who had progressed after at least 2 lines of chemotherapy with no further curative options. One group received best supportive care and placebo while other received best supportive care along with a 4-drug antiangiogenic metronomic regimen of Thalidomide, Celecoxib, and alternating cycles of Etoposide and Cyclophosphamide. Clinical and imaging assessment was done at baseline, 9 weeks (or earlier if progressed), 18 weeks and at 27 weeks. Primary end point was PFS.

Results: From Oct 2013-Dec 2015, we screened 123 and enrolled 108 patients. 52 were randomised to placebo group and 56 to metronomic group. This included Ewing sarcoma (34), Osteosarcomas (38), neuroblastomas (10), esthesioneuroblastoma (2), soft tissue sarcoma (6), rhabdomyosarcoma (9), retinoblastoma (3), others (5). At median follow-up of 4 months, patients with bone sarcomas (Ewing + Osteosarcoma) (n=72), did not show a significant difference between metronomic and placebo arms in median PFS (48 days vs 49 days) [HR=0.98(95%CI 0.58-1.52), p=0.79] or median OS (79 days vs 110 days) [HR=1.05 (95%CI 0.64-1.73), p=0.83]. In the non-bone sarcoma cohort (n=36), however, the metronomic arm was significantly better compared to placebo in terms of median PFS (62days vs 40 days) [HR=0.39 (95%CI 0.18-0.81), p=0.01] as well as median OS (95 days vs 59 days) [HR=0.42 (95%CI 0.19-0.92), p=0.03].

Conclusion: Metronomic chemotherapy improves PFS and OS in progressive paediatric solid tumours other than bone sarcomas. NCT01858571.

O-005 | Biomarkers Accurately Predict Cytokine Release Syndrome (CRS) after Chimeric Antigen Receptor (CAR) T Cell Therapy for Acute Lymphoblastic Leukemia (ALL)

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Background/Objectives: Chimeric antigen receptor (CAR)-modified T cells with anti-CD19 specificity are a highly effective novel immune therapy for relapsed/refractory hematologic malignancies. Dramatic responses with complete remission rates as high as 90% have been reported in patients with relapsed/refractory ALL treated with CTL019 (Maude et al., NEJM 2014). Cytokine release syndrome (CRS) is the most significant and life-threatening toxicity.

Design/Methods: To improve understanding of and develop predictive models for CRS, we measured 43 cytokines and clinical biomarkers serially in 39 children and 12 adults treated with CTL019.

Results: We found peak levels of 24 cytokines, including IFN γ , IL6, sIL2R α , sgp130, and sIL6R, during the first month after CTL019 infusion were highly associated with severe (life-threatening) CRS. We found the pattern of hypercytokinemia in patients with severe CRS mirrored the same pattern seen in patients with hemophagocytic syndrome/macrophage activation syndrome. The elevation of IL6, sIL6R, and sgp130 in patients with severe CRS along with the pronounced response to the IL6R inhibitor tocilizumab, establishes the novel observation that IL6 trans-signaling is clinically and biologically relevant.

We measured cytokines in the first 3 days after infusion and before patients developed severe CRS. Using regression modeling, we could accurately predict which patients would develop severe CRS before they became critically ill with a signature composed of three cytokines: IFN γ , sgp130, and IL1RA. These results were validated in an independent cohort of patients. Changes in serum biochemical markers, including C-reactive protein and ferritin, were associated with CRS but failed to predict development of severe CRS.

Conclusion: These comprehensive profiling data provide novel insights into CRS biology, and importantly represent the first data that can accurately predict which patients have a high probability of becoming critically ill. These data have direct therapeutic relevance and may guide future cytokine directed therapy.

O-006 | The Inform Personalized Medicine Program for High-Risk Paediatric Cancer Patients

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Background/Objectives: Relapses from high-risk tumours pose a major clinical challenge in paediatric oncology. The German INFORM registry (Individualized therapy For Relapsed Malignancies) addresses this problem using an integrated next-generation sequencing approach to rapidly identify patient-specific therapeutic targets in real time in all treatment centres of the German Society of Pediatric Oncology and Haematology.

Design/Methods: Whole-exome, low-coverage whole-genome and RNA sequencing is complemented with microarray-based expression and DNA methylation profiling. Identified alter-

ations are discussed and prioritized in a standardized fashion according to biological significance and potential druggability in a weekly board. Potential therapeutic drug targets and follow-up data are deposited in a central database. The treating oncologist can use the molecular information for clinical decision making.

Results: To date, tumours from 166 patients have been profiled with a median turnaround time of 21 days. Entities included brain tumours, sarcomas, leukaemias, neuroblastomas and a small group of rare high-risk entities. In 10/166 cases our molecular classification did not confirm the histological diagnosis, including secondary high-grade gliomas thought to be medulloblastoma relapses in 4 cases. In 102/166 (61%) patients we identified high-confidence druggable alterations. E.g., we identified a INPP5D(SHIP1):ABL1 fusion in a relapsed B-ALL, a hypermutation phenotype in a BRAFV600E-positive glioma and ALK aberrations in several neuroblastomas and in an atypical infantile glioma. Tyrosine kinases, the PI3K/mTOR pathway, MAPK pathway and cell-cycle regulators were commonly affected. The molecular information was used for (experimental) therapies as decided by the treating oncologist in a considerable number of cases.

Conclusion: Comprehensive profiling of relapsed paediatric high-risk malignancies is feasible in a clinically meaningful timeframe, and provides valuable diagnostic information and possible therapeutic targets. In 2016 the INFORM program will be extended to several other countries. A series of biomarker driven phase I/II (combination) trials with targeted compounds is planned to start recruitment in Q1 2017.

FREE PAPERS SESSION 1: EARLY PHASE CLINICAL TRIALS

O-007 | Phase I Study to Evaluate Dose, Safety and Tolerability of the Polo-Like Kinase Inhibitor Volasertib in Paediatric Patients with Acute Leukaemia and Advanced Solid Tumours

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Background/Objectives: Volasertib is a selective and potent cell cycle kinase inhibitor that induces mitotic arrest and apoptosis by targeting polo-like kinase (PLK). Results from the first paediatric volasertib study are presented.

Design/Methods: Volasertib dose escalation (3+3 design) was performed in two age groups (1: 2 to <12 years, 2: 12 to <18 years) to determine the maximum tolerated doses (MTD) in paediatric oncology patients who failed prior therapy. The MTD was assessed based on dose limiting toxicities (DLTs) in course 1.

Results: Twelve patients in group 1 (doses 200, 250, 300 mg/m²) and ten patients in group 2 (doses 200, 250 mg/m²) were treated. The most frequently reported adverse events (AEs; occurring in >20% of patients) were thrombocytopenia, febrile neutropenia, vomiting, anaemia, nausea, neutropenia, abdominal pain, headache and increased liver enzymes. The AE profile in both age groups was comparable. In group 1, no DLTs were reported and dose escalation was stopped at 300 mg/m² based on data monitoring committee recommendation. In group 2, DLTs were reported in two patients (250 mg/m²): intracranial haemorrhage in the context of grade 4 thrombocytopenia (patient with leukaemia), and febrile neutropenia, grade 4 thrombocytopenia and gastrointestinal haemorrhage (patient with osteosarcoma). The MTD was determined at 200 mg/m². In this heavily pretreated patient population, stable disease (for up to 28 courses) was the best overall response, including transient reduction of blasts in 4/7 leukaemia patients and reduction of tumour markers in a neuroblastoma patient.

Conclusion: Volasertib tolerable doses and safety in paediatric patients were determined. Reported AEs were mostly expected from the antimitotic mode of action. Preliminary signs of antitumour/antileukemic activity were observed. Based on these results a study was recently initiated investigating volasertib (dose finding) combined with standard chemotherapy in children with relapsed/refractory acute myeloid leukaemia.

O-008 | Rapiri Phase I Study Associating Rapamycin and Irinotecan in Children with Refractory Malignant Solid Tumors: Good Tolerance and Promising Results in Brain Tumors and Sarcomas

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Background/Objectives: Intratumor hypoxia is considered as a key factor in tumour cell resistance to therapies, as well as a biomarker of poor prognosis in several paediatric cancers. In preclinical setting, rapamycin, a mTOR inhibitor, associated with irinotecan, a HIF-1 α inhibitor, were able to induce tumour cell apoptosis in paediatric models. Therefore, a RAPIRI phase I study, combining rapamycin and irinotecan was proposed to children with refractory solid tumors.

Design/Methods: 42 eligible children were enrolled using a 3+3 design to determine the maximum tolerated dose (MTD) of rapamycin and irinotecan association. Rapamycin was administered once daily in a 28-day cycle associated with intravenous infusion of irinotecan at D1 and D15. A dose escalation scheme was included 10 levels, where rapamycin was administered from 1 to 2.5 mg/m² and irinotecan from 125 to 240 mg/m². Toxicity and pharmacokinetics were characterized. Response evaluation was performed at 2 cycles.

Results: 1/6 patients experienced dose limiting toxicity at 3 different levels, but, finally, dose escalation was achieved until level 10. No MTD was determined. Mostly, toxicities were mild to moderate and systematically reversible. PK analyses were able to determine a range of efficient concentrations linked to tumors responses, which were assessable in 32 patients. 14 brain tumors were analyzed: 1 ependymoma and 1 ATRT had a partial response (PR) and 6 (2 medulloblastomas, 1 PNET, 1 ependymoma and 1 high grade glioma) were in stable disease (SD). Three osteosarcomas and 3 Ewing sarcomas were also evaluable: 2/6 patients were in partial response and 1 in stable disease.

Conclusion: As no MTD was established, we might suggest a recommended dose of 125 mg/m² for irinotecan and 1.5 mg/m² for rapamycin based on PK and toxicity analyses. With the relative promising results in brain tumors, the phase II study will focus first on those cancers.

O-009 | Efficacy of Crizotinib in ALK+, MET+ or ROS1+ Advanced Paediatric Malignancies: Results of the Acse Phase II Trial

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Background/Objectives: Alterations of crizotinib targets ALK, MET, ROS1 are found in a wide range of adult and paediatric cancers. Crizotinib is approved for the treatment of alk+ NSCLC but not developed in Europe for children. To avoid off-label use and allow for a nationwide safe access to crizotinib for adult and paediatric patients with ALK+, MET+ or ROS1+ tumors, the French National Cancer Institute (INCa) launched the AcSe program, funding both access to tumour molecular diagnosis and an exploratory multi-tumour phase II trial.

Design/Methods: Molecular diagnosis was performed in 28 INCa molecular genetics centers by FISH assay or sequencing, as well as through pangenomic tumour profiling. After failure of standard treatment, patients with an ALK+, MET+ or ROS1+ malignancy received crizotinib 280 mg/m² BID (165 mg/m² BID for anaplastic large cell lymphoma [ALCL]) in capsules or oral solution. Responses were assessed every 8 weeks using RECIST v1.1.

Results: From 08/2013 to 08/2015, 17/107 paediatric tumors were positive, including: 7/49 neuroblastomas (4 ALK-mutated, 2 ALK-amplified, 1 ALK-translocated and mutated), 2/3 inflammatory myofibroblastic tumors [IMT] (1 ALK-translocated, 1 ROS1-translocated), 3/16 malignant gliomas (2 MET-amplified, MET-translocated), 5/39 other cancers (3 ALK-translocated, 1 ROS1-translocated, 1 MET-amplified).

Twelve patients were enrolled: median age 9 years [3–17], 66% boys. Six patients are still on treatment (2 for >12 months); 6 have stopped crizotinib (4 PD, 1 doctor's decision, 1 patient's decision). Among 11 evaluable patients, best responses were 1 CR (ALCL), 4 PR (2 ROS1-translocated IMT, ALCL, ROS1-translocated meningioma), 2 SD (ALK-translocated mesothelioma, MET-amplified glioma), 4 PD (2 ALK-mutated neuroblastoma, MET-translocated glioma, MET-amplified xanthoastrocytoma).

Crizotinib was well tolerated with a majority of AE grade 1: elevated transaminases, vomiting, fatigue. There were five grade 3 AEs: QTc prolongation, nausea, loss of appetite, anemia, ALT increased.

Conclusion: Responses and clinical benefit with crizotinib were demonstrated in children with ALK+, MET+ and ROS1+ tumors.

O-010 | Phase 2 Study of Cabazitaxel in Paediatric Patients with Recurrent or Refractory High Grade Glioma or Diffuse Intrinsic Pontine Glioma: A Poetic Group Study

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Background/Objectives: Cabazitaxel is a novel taxane with demonstrated penetration across the blood-brain barrier, making it a potential therapy for brain tumors. Through the Pediatric Oncology Experimental Therapeutics Investigators' Consortium (POETIC), a phase 1 study established the MTD of cabazitaxel at 30 mg/m² in paediatric patients with relapsed or refractory solid tumors, including brain tumors. This phase 2 study evaluated the effectiveness of cabazitaxel in paediatric patients with recurrent high-grade glioma (HGG) or diffuse intrinsic pontine glioma (DIPG).

Design/Methods: Patients with recurrent, measurable HGG or DIPG were enrolled and treated with cabazitaxel at 30 mg/m² IV once every 3 weeks with tumour assessment every 9 weeks. Patients remained on drug if they had no evidence of progressive disease or unacceptable toxicity. Efficacy was based on objective response as defined by modified RANO criteria. If two objective responses were seen in the first 10 evaluable patients, an additional 19 patients would be enrolled.

Results: Sixteen patients (8 with HGG and 8 with DIPG; median age 9.5; range 3 to 16) were enrolled at 8 POETIC and 3 non-POETIC institutions. Eleven of 16 patients were evaluable for tumour assessment. Five patients were withdrawn: 4 due to an AE (3 for anaphylaxis; 1 for increased ALT and AST) and 1 for parental request. All remaining 11 patients progressed within 4 cycles of treatment. No objective responses were observed and the study was closed for futility.

Conclusion: Cabazitaxel, as a single agent, did not show efficacy in the treatment of paediatric HGG or DIPG. Further studies in other brain tumors are being considered.

FREE PAPERS SESSION 2: LYMPHOMA - HODGKIN

O-011 | Parenthood in 817 Male Patients Treated for Hodgkin Lymphoma During Childhood and Adolescence

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Background/Objectives: It is well known that alkylating agents like procarbazine (PCZ) and cyclophosphamide (CP) can affect testicular function.

Little is known about parenthood in men treated with chemo- and radiotherapy for Hodgkin Lymphoma (HL) during childhood and adolescence.

Design/Methods: Frequency of parenthood was documented in 817 male survivors < 18 years at diagnosis. They were treated between June 19, 1978 and July 18, 1995 in five HL treatment studies DAL-HD 78 to DAL-HD 90. Their median age at last follow-up was 32.6 years (range 12.3 - 51.9 years).

Results: 632 pts. in CCR with had a long-term follow-up > 5years, 135 (21.4%) had children. Compared to the German population (GP) significant differences in parenthood were documented in patients > 30 years only when they received PCZ. Parenthood was similar to the GP in patients not receiving PCZ. Nine predictors of parenthood were evaluated. To assess their relative effects on parenthood, we used multivariable Cox regression analyses. Of the nine variables, only the cumulative dose of PCZ had a significant influence on parenthood. Using the group without procarbazine as the reference group, the hazard ratio (HR) is 0.83 for the group receiving two cycles of PCZ (95% CI 0.68–1.0) (p=0.05), 0.83 (0.72–0.96) (p=0.01) for patients receiving four and 0.76 (0.68 – 0.84) (p=0.0001) for patients receiving six to eight cycles of PCZ. The remaining eight variables or their subgroups had no significant effect.

Conclusion: A significant and dose dependent effect of procarbazine on parenthood was documented in male pts. treated for HL during childhood and adolescence, an effect not demonstrated in female patients treated with the same five HL-protocols (Lancet Oncol. 2015; 16: 667–75).

O-012 | Post-Treatment PET-CT Rather than Interim PET-CT Using Deauville Criteria Predicts Outcome in Paediatric Hodgkin Lymphoma: A Prospective Study Comparing PET-CT Versus Conventional Imaging

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Background/Objectives: Data about significance of [¹⁸F]-FDG positron emission tomography (PET) at interim assessment and end of treatment in paediatric Hodgkin lymphoma (HL) are limited.

Design/Methods: Patients (≤ 18 years) with HL were prospectively evaluated with contrast-enhanced computed tomography (CECT) and PET combined with low-dose CT (PET-CT) at baseline, post 2 cycles of chemotherapy and post completion of treatment. Revised international working group criteria (RIW) and Deauville (DA) five point-scale for response assessment by PET-CT were used. All patients received ABVD chemotherapy along with involved field

radiotherapy (25 Gy) for early stage (IA, IB and IIA) and advanced stage (IIB-IV) with bulky disease.

Results: Of the 57 enrolled patients, median follow-up was 81.6 months (range: 11-97.5 months). Treatment decisions were based on CECT. At baseline, PET-CT vs CECT identified 67 more disease sites; 23 patients (40.3%) were upstaged and of them in 9 patients (39%) upstaging would have affected treatment decision; notably none of these patients relapsed. Specificity of interim PET-CT based on RIW (61.5%) and DA (91.4%) criteria for predicting relapse was higher than CECT (40.3%) ($p=0.02$ and $p<0.0001$ respectively). EFS based on interim PET-CT response (positive vs. negative scan: 93.3 ± 4.1 vs. 89.6 ± 3.8 ; $p=0.44$) and CECT (CR vs. No CR: 90.6 ± 4.6 vs. 91.1 ± 3.6 ; $p=0.99$) was insignificant. Specificity and PPV of post-treatment PET-CT (DA) was 95.7%, 33.3% vs. 76.4% and 7.6% by CECT ($p=0.004$ and $p=0.001$ respectively). Post-treatment PET-CT (DA) showed significantly inferior OS in patients with positive scan vs. negative scan (66.4 ± 22.5 vs. 94.5 ± 2.0 , $p=0.029$).

Conclusion: Interim PET-CT has better specificity and use of DA criteria further improves it. Escalation of therapy based on interim PET in paediatric HL needs further conclusive evidence to justify its use. Post-treatment PET-CT (DA) predicts OS and has better specificity and PPV in comparison to conventional imaging.

O-013 | The Impact of HIV Infection on Overall Survival in Children with Hodgkin Lymphoma in South Africa

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Background/Objectives: South Africa is home to the world's largest epidemic, with 5.6 million people living with HIV (17.3 per cent). The national roll-out of antiretroviral medication has improved survival of children with HIV. We aimed to determine how HIV infection impacted on Hodgkin Lymphoma (HL) management.

Design/Methods: A retrospective study was conducted to determine survival rates and prognostic factors in South African children with HL, and a sub-analysis was performed of children with HIV. Descriptive statistics, Kaplan-Meier survival curves, Cox regression model, analysis of variance and Pearson's chi square test were employed.

Results: Of 294 children with HL identified between January 2000 and December 2010, 29 were HIV positive (9.9%). There was no significant difference between the HIV positive and HIV negative cohorts with regard to age, stage, B symptoms or histology. Only nine patients (30%) were receiving antiretroviral therapy at the time of diagnosis with HL, and seven of these showed viral suppression. The overall survival for the entire cohort was 79% while that for the HIV positive children was 44.2% ($p = 0.001$, hazard ratio = 3.84). Causes of death in the HIV positive group included relapsed/refractory disease (7/14), second malignancy (1/14), infection (5/14) and unknown causes (1/14). HIV infection was an independent risk factor for poor survival on multivariate analysis ($p = 0.018$).

Conclusion: Children with HIV have a much higher chance of dying if diagnosed with HL due to opportunistic and nosocomial infections, and relapsed/refractory disease. HIV infection is an independent risk factor for poor prognosis in children with HL but it is as yet unclear whether this is associated with socioeconomic conditions. This study does not confirm an increased incidence of HL in HIV positive South African children. Particular attention should be paid to the HIV positive subset of children with HL to lower treatment-related mortality and risk-stratify accurately.

O-014 | Ruxolitinib, A JAK1/JAK2 Inhibitor, Significantly Prolongs Survival in Both Primary Mediastinal B-Cell Lymphoma & Hodgkin Lymphoma Xenograft NSG Mouse Model: A Potential Targeted Adjuvant Therapy

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Background/Objectives: Primary mediastinal B-cell lymphoma (PMBL) and Hodgkin lymphoma (HL) are common malignancies among adolescents and young adults, and share similar molecular features (Rosenwald et al., *JEM*, 2003). Frequent gains of chromosome 9p exhibit higher Janus Kinase 2 (JAK2) transcript levels with increased JAK2 activity (Bentz et al., *Genes Chromosomes Cancer*, 2001), suggesting aberrant activity of JAK2/STAT pathways, which may in part play an important role in the pathogenesis of HL and PMBL. Ruxolitinib is a potent and selective JAK1/JAK2 inhibitor against myeloproliferative neoplasms that consistently exhibits dysregulation of the JAK1/JAK2 pathway, including those MPNs with a JAK2^{V617F} mutation.

We investigated the efficacy of ruxolitinib in PMBL and HL cells xenografted into NSG mice.

Design/Methods: Cell proliferation and apoptosis analysis were assessed using MTS and Caspase-3/7 assay (Promega), respectively. Karpas-1106P PMBL and L428 HL cells were sub-

cutaneously injected into NSG mice (6-8wks old) and ruxolitinib was administered by oral gavage (generously provided by Incyte Corporation, Wilmington, DE, USA) for 21 days. Tumour progression was monitored by bioluminescent imaging and survival rates were analyzed by the Kaplan-Meier method.

Results: We observed that ruxolitinib significantly inhibited cell proliferation ($p<0.05$), and significantly increased programmed cell death ($p<0.05$) against both Karpas-1106P and L-428 cells. We also observed that ruxolitinib significantly decreased tumour progression in PMBL ($p<0.05$) and HL ($p<0.05$) xenografted NSG mice vs control. Importantly, ruxolitinib (45.0mg/kg) significantly improved survival in PMBL ($p<0.0001$) and HL ($p=0.0001$) xenograft NSG mice compared to control.

Conclusion: Ruxolitinib showed significant anti-proliferative effects and ruxolitinib significantly prolonged survival in PMBL and HL xenografted NSG mice. Ruxolitinib may be a potential targeted adjuvant agent in the treatment of PMBL and HL.

FREE PAPERS SESSION 3: AML

O-015 | Prognostic Scoring Systems Validated for CML in Adult's, Correlate Poorly with Survival in Paediatric Patients Treated with Imatinib

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Background/Objectives: Recent reports have questioned the applicability of the adult prognostic scores to CML in children. The aim was to investigate the predictability of the three scoring systems (Sokal, Hasford, Eutos) for survival in children.

Design/Methods: It is a retrospective, single-center study of children diagnosed with CML over a 12-year period (2004-2015). Patients were treated with imatinib. The scores were derived from: <http://bloodref.com/myeloid/cml/sokal-hasford>. The log-rank test (Mantel-Cox) was utilized to quantify differences in survival probabilities. The monitoring with cytogenetics/RQ-PCR was infrequent and at varying intervals. Hence, the scores could not be correlated with the monitoring tools. Patients who presented in accelerated/blast crisis and those who abandoned treatment were excluded.

Results: Fifty-two children were diagnosed with CML. The median age was 9.8-years (range: 2-13). Nine were excluded: accelerated/blast crisis-4, non-compliance-5. No patient received a 2nd generation TKI or a bone marrow transplant, due to restricted finances/accessibility. Further discussion will be on patients diagnosed in chronic phase who were compliant ($n=43$). The median follow-up was 39-months (range: 1-137). Seven (16%) patients died after progressing to blast crisis at a median duration of 9-months (range: 4-38) from diagnosis. The 10-year OS/EFS was $80.5\pm 6.8\%$. As per Eutos, Hasford and Sokal scores, 58%, 35%, and 51% patients were categorized as low-risk, and 42%, 9%, and 14% as high-risk, respectively. By Hasford and Sokal scores, 56% and 35% patients were categorized as intermediate-risk, respectively. The 10-year EFS/OS of patients in low, intermediate and high-risk Sokal category was $85.7\pm 7.6\%$, $77\pm 12\%$ and $50\pm 35\%$, respectively ($p=0.88$). EFS/OS in low and intermediate Hasford category was $86.7\pm 8.8\%$ and $80.7\pm 8.9\%$ ($p=0.58$) and in low and high-risk Eutos was $87\pm 7\%$ and $72.2\pm 12.1\%$, respectively ($p=0.51$).

Conclusion: Sokal, Hasford or Eutos scores were not predictive of survival in children (<13 years) with CML. A larger cohort is desirable to derive a scoring system that would be applicable to children.

O-016 | Shorter Remission Telomere Length Predicts Delayed Neutrophil Count Recovery after Acute Myeloid Leukemia Therapy: A Report from the Children's Oncology Group

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Background/Objectives: Suboptimal outcomes for children with acute myeloid leukaemia (AML) necessitate maximally intensive therapy. However, adverse events, such as prolonged periods of profound myelosuppression, contribute to AML treatment-related mortality. Telomeres, the repetitive DNA-protein structures at chromosome ends, influence cellular replicative capacity in that critically short telomeres can induce cell senescence or apoptosis. Our objective was to evaluate the impact of remission telomere length upon duration of post-therapy neutropenia in a paediatric AML cohort.

Design/Methods: Subjects were diagnosed with *de novo* AML, enrolled on Children's Oncology Group study AAML0531, and included those with ($n=53$) and without ($n=62$) significantly delayed neutrophil recovery following chemotherapy. We used quantitative PCR to measure telomere content (TC), a validated proxy for telomere length, from remission bone marrow samples obtained after the second induction chemotherapy course.

Results: Less TC was significantly associated with prolonged neutropenia after the fourth ($p<0.001$) and fifth chemotherapy courses ($p=0.002$). Cox regression adjusting for age at diagnosis confirmed that TC remained independently predictive of time to recovery of absolute neutrophil count (ANC) for both the fourth and fifth courses ($p=0.002$ and $p=0.009$, respectively). DNA from subjects was analyzed for germline mutations in four telomere maintenance

genes associated with telomere biology disorders. Sequence analysis revealed no enrichment of rare or novel variants in the delayed recovery group.

Conclusion: Less telomere content at end of AML induction is associated with reduced capacity for hematopoietic reconstitution independently of age, and may identify those at highest risk for markedly delayed bone marrow recovery. This association is not related to differences in host factors, telomere maintenance gene variants, AML disease characteristics, or therapeutic exposures. By ascertaining remission telomere length early in AML therapy, patients at highest risk for prolonged neutropenia are potential candidates for augmented supportive care and therapeutic modifications, with the goal of minimizing therapy-related toxicities such as infectious complications.

O-017 | Tracking Residual Disease and Subclonal Heterogeneity in Paediatric AML using Extremely Sensitive Error Corrected Sequencing

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Background/Objectives: Acute myeloid leukaemia (AML) is an oligoclonal disease, and chemotherapy can select for resistant subclones that proliferate as refractory or relapsed disease. Unlike ALL, AML does not have clonal cell surface markers that can be easily used for disease monitoring. The current gold standard for assessment of minimal residual disease is multi-parameter flow cytometry (MPFC) with a sensitivity of 0.001. However, over 30% of children with MPFC-negative MRD still relapse, highlighting the need for more sensitive MRD strategies. The clinical use of next-generation sequencing (NGS) for MRD has been thwarted by the high error rate of 0.005-0.01 by these platforms. We have developed an error-corrected next-generation sequencing (ECS) strategy with a lower limit of detection of 0.0001 and retrospectively applied ECS to paediatric *de novo* AML at the time of diagnosis and end of induction 1.

Design/Methods: We have developed a panel of 90 genes frequently mutated in AML and applied ECS to characterize all mutations occurring at 0.0001 or greater in children with *de novo* AML participating in the Children's Oncology Group TARGET project or the AAML1031 study. Sequencing was performed at the Genome Technology Access Center at Washington University in St. Louis. Bioinformatics and validation of called mutations via droplet digital PCR was performed in the Druley lab.

Results: We find that each patient harbors multiple "targetable" subclones at the time of diagnosis, and ECS can track each of these mutations with greater sensitivity than MPFC, suggesting that ECS could be used to assess MRD.

Conclusion: ECS improves the sensitivity of NGS by two orders of magnitude and can be a cost-effective tool for MRD and to characterize all subclones present at the time of AML diagnosis. With this capability, personalized, gene-based therapy could be utilized to avoid the outgrowth of resistant subclones to non-specific therapy.

O-018 | The Integrated Immunological Signature of Refractory Cytopenia of Childhood (RCC)

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Background/Objectives: Clinical and laboratory evidence suggest a T-cell mediated pathophysiology of MDS-Refractory Cytopenia of Childhood (RCC), as illustrated by the presence of minor paroxysmal nocturnal haemoglobinuria (PNH) clones, T cell receptor (TCR) β -chain variable (V β) domain (TCRV β) skewing, and aberrant immunophenotypes. It is however still unknown to what extend these immune phenomena concomitantly occur in low-grade paediatric MDS.

Design/Methods: We evaluated the presence of minor PNH clones, TCRV β skewing and immunophenotypic aberrancies in a unique, international prospectively included cohort of 72 patients with RCC, in search for a recurrent integrated immunological signature.

Results: Small PNH clones were apparent in 31 cases (43%), TCRV β skewing in 30 cases (42%), and B cell-immunophenotypic aberrancies in 43 cases (60%). In only 9 patients (13%) all these three were present. Two parameters were present in 25 patients (35%), and 27 patients (38%) displayed only 1 parameter. In 11 patients (15%) none of the three characteristics was present.

Only the presence of a small PNH clone (>0.1%) was correlated with response to IST (88% PNH+ versus 40% of PNH- patients responded at six months, respectively, $P=0.038$). However, from the current study, we could not predict the strongest predictable value of combined parameters, with respect to response on immunosuppressive therapy (IST) in patients with RCC, as only 23 patients were treated with IST.

Conclusion: We conclude that patients with RCC frequently show immunological aberrancies, but that the immunological signature is rather heterogeneous. Future studies in extended RCC series are required to build prediction models for response to immunosuppressive therapy.

FREE PAPERS SESSION 4: GLIAL TUMOURS

O-019 | Hypermutation, Neoantigen Formation and Immune Checkpoint Inhibition for Childhood Biallelic Mismatch Repair Deficient Cancers

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Background/Objectives: Biallelic mismatch repair deficiency (bMMRD) is an aggressive cancer predisposition syndrome resulting in rapid onset of various childhood malignancies and patients rarely reach adulthood. These children harbor homozygous germline mutations in mismatch repair genes, resulting in a systemic loss of replication repair. We have previously shown that secondary somatic loss of polymerase (POLE and POLD) proofreading result in exceptionally high mutation burden. Evidence suggests that high mutation and neoantigen loads are associated with response to immune checkpoint inhibitors (ICIs).

Design/Methods: We performed exome sequencing and neoantigen prediction on 42 bMMRD cancers and compared to childhood and adult neoplasms. Immune checkpoint inhibitors were offered to bMMRD patients with recurrent tumors.

Results: While bMMRD brain tumors demonstrate the highest mutation loads (mean 17,740+/-7703), all other high-grade tumors were hypermutant (mean 1589+/-1043). bMMRD GBM harbored mean neoantigen load 7-16 times higher than immunoresponsive adult tumors ($p=0.00001$). Strikingly, mutation load varies dramatically between primary and recurrent cancers and is related to prior therapy. Spatial and temporal sampling of individual bMMRD tumors revealed large variations in mutation load and neoantigen landscape.

Based on these preclinical data, bMMRD patients with recurrent cancers are being treated with ICIs with encouraging clinical and radiological responses.

Conclusion: This report is the first to delineate the mutable nature of the neoantigen landscape in cancers where new mutations are constantly arising due to lack of replication repair. The encouraging responses of recurrent cancers to ICIs can inform treatment for other hypermutant cancers arising from primary (genetic predisposition) or secondary mismatch repair deficiency.

O-020 | The Genetic Characteristics of Paediatric Low Grade Gliomas

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Background/Objectives: Pediatric low-grade gliomas (PLGG) are the most common childhood brain tumour. Recently, alterations of the RAS/MAPK pathway have been identified as the major driver of PLGG however little is known about prevalence of specific lesions and prognostic implications.

Design/Methods: We undertook a population based study of all PLGG diagnosed within 1985-2015. Detection of BRAF-V600E, BRAF fusions, FGFR1-TACC1 and MYBL1 was performed using QX200™ Droplet Digital™ PCR and NanoString technologies. Molecular results were correlated with pathology, demographics and outcome.

Results: Full clinical and molecular data are available on 351 patients. The most frequent alteration in PLGG was BRAF-KIAA1549 (38%), followed by BRAF-V600E (14%), FGFR1-TACC1 (3%) and MYBL1 (1%) leaving 44% PLGG with unknown alterations. Among BRAF-KIAA1549 variants most prevalent was 16-9 (58%), followed by 15-9 (28%) and 16-11 (9.5%). The distribution of each alteration varied depending on pathology and tumour location. Specifically, the 15-9 fusion was predominantly found in hemispheric and spinal PLGG, whereas 16-9 was characteristic for cerebellar pilocytic astrocytoma. In addition to the high prevalence of BRAF-KIAA1549 in pilocytic astrocytoma (73%), it was found also in glioglioma (13%) and diffuse astrocytoma (10%). BRAF-V600E was most frequently found in pleomorphic xanthoastrocytoma, ganglioglioma and diffuse astrocytoma. MYBL1 was most prevalent in diffuse astrocytoma and exclusive to the hemispheres. Ten years PFS were 50.3% and 19.4% for BRAF fused and BRAF mutated tumors respectively ($p=0.0001$). Moreover, 15 years OS revealed 94.5%, and 67% for BRAF fused and BRAF mutated tumors respectively ($p=0.026$). Sub-group analysis revealed no significant difference in PFS and OS among patients with BRAF-KIAA1549 fusion variants. All patients with FGFR1-TACC1 and MYBL1 are still alive.

Conclusion: While a significant number of PLGG still require further molecular analysis, the common RAS/MAPK alterations are related to tumour location and impact survival in these patients. Biopsy and molecular analysis is required to tailor therapy for children with non-NF1 PLGG.

O-021 | Dose-Finding Study of Vinblastine in Combination with Nilotinib in Patients with Refractory or Recurrent Low-Grade Glioma: Results of the Itcc/Siope-Brain Vinilo Phase I Trial (NCT01887522)

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Background/Objectives: New rescue regimens are needed for refractory/recurrent low-grade glioma (LGG). Nilotinib has potential synergistic effects with vinblastine against angiogenesis and tumour cell growth as well as immunostimulatory properties.

Design/Methods: This phase I trial aimed at determining the recommended doses of VBL and NIL in combination for phase II trials (RP2D) using a dual agent model-based method (Wang & Ivanova, Biometrics 2005). Nilotinib was given orally twice-daily (planned BID doses: 115, 230 & 350 mg/m²) in combination with VBL weekly injections (planned doses: 3, 4, 5 & 6 mg/m²), for a maximum of twelve 28-day cycles. 35 patients were enrolled across 4 dose levels: 3 + 115, 3 + 230, 4 + 230, and 3 + 350. 10/35 had NF1. Patients had received a median of 3 prior treatment lines (1-10).

Results: Dose limiting toxicity (DLT) consisted in hematotoxicity in 3, skin toxicity in 2, and hypertension complicated with seizure in 1. Identified RP2D: 3 mg/m² weekly for VBL + 230 mg/m² BID for NIL (estimated probability of DLT = 18%). Thirteen patients completed the 12 cycles and 1 is still on treatment; 3 stopped therapy due to toxicity (none at the RP2D), and 18 due to disease progression. Seven patients (2 with NF1) had a radiological response. The 12-month PFS was 45% (95%CI, 30-61%). Effective levels of nilotinib were achievable at steady state.

Conclusion: Efficacy of the VINILO combination at the RP2D will be evaluated in a randomized Phase II comparing this regimen to VBL alone.

(Study sponsored by INCa-PHRC, I4M charity and Novartis).

O-022 | Early Ependymoma Outcomes from the Paediatric Proton Consortium Registry

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Background/Objectives: The Pediatric Proton Consortium Registry (PPCR) tracks patterns of care and outcomes of children treated with proton therapy at the major United States paediatric centers. The purpose of this study is to present the early results of the ependymoma cohort.

Design/Methods: Between September 2012 and June 2015, 113 children with intracranial ependymoma were treated across 6 proton centers in the United States participating in the PPCR. The basis of this report is 56 of these children with non-metastatic grade 2 or 3 tumors treated curative-intent focal proton therapy (PT) who had follow-up available. The median age was 3.9 years old (range 0.1-21.2). The cohort included 35 males; 41 patients were white, 4 black, 3 Asian, and 8 unknown or other race. Thirty-eight tumors were infratentorial and 18 were supratentorial. Thirty-four tumors were grade 3 and 22 were grade 2. Forty, 7, and 9 patients underwent gross total, near total, and subtotal resection, respectively, prior to radiation. Twenty-nine patients received 59.4 Gy(RBE), 23 received 54 Gy(RBE) and 4 received 55.8 Gy(RBE). The majority (49/56) were treated with passively scattered PT. Eleven patients were enrolled on the Children's Oncology Group study ACNS0831.

Results: With a median follow-up of 1.2 years (range, 0.1-3.0), local control is 91% and progression free survival is 88%. There are 3 isolated local recurrences, 2 metastatic recurrences, and 2 patients with simultaneous local and metastatic recurrence. Overall survival is 95%. One patient died of local progression, one patient died of metastatic progression, and one patient died of hypernatremia due to uncontrolled diabetes insipidus. One patient (1.8%) developed symptomatic brain necrosis which stabilized following steroid management. Ten patients (18%) have developed hearing deficits. No patients have developed vision loss or vasculopathy.

Conclusion: This multi-institutional, prospective outcome study demonstrates the early efficacy and feasibility of proton therapy for paediatric ependymoma.

O-023 | Long-Term Health Related Quality of Life (HRQOL) and School Functioning among Children Treated with Proton Therapy for Intracranial Ependymoma at Age ≤ 3 Years

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Background/Objectives: The purpose of this analysis is to report the health related quality of life (HRQOL) among survivors who received proton therapy (PRT) for ependymoma at a very young age.

Design/Methods: Twenty-two children with intracranial ependymoma who received PRT at age ≤ 3 years and had no evidence of recurrent disease participated in a cross-sectional HRQOL study. HRQOL was assessed at follow-up by child self-report (CSR, age ≥ 5) and parent proxy-

report (PPR, age 2+) using the PedsQL Core and Brain Tumour Modules, and school data questionnaires.

Results: Median age was 2.8 years (1.0-3.9) at treatment and 7.2 years (4.3-17.0) at HRQOL assessment (median follow-up 4.9 years (2.0-13.7)); 18 had infratentorial tumors: 4 supratentorial; 8 required EVD or shunt for hydrocephalus; 6 required a gastric-tube; 10 received chemotherapy; median PRT dose was 54 Gy (RBE). Mean CSR and PPR HRQOL scores were: total core (77.4 and 72.1), physical (84.8 and 74.3), emotional (71.0 and 71.1), social (77.9 and 73.0), school (71.4 and 68.4), psychosocial (73.4 and 70.8), and cognitive (75.0 and 70.6). CSR scores for treated children were lower in emotional (p=0.018) and psychosocial (p=0.069) functioning compared with healthy controls, but total core (p=0.422), physical (p=0.132), social (p=0.146), and school (p=0.306) scores were similar. The requirement for a gastric-tube or EVD/shunt, or higher mean hypothalamus and pituitary dose were associated with lower CSR and PPR HRQOL scores. Chemotherapy was also associated with lower CSR HRQOL scores. Ninety-five percent of children functioned in a regular classroom, 57% used an IEP, 43% a classroom aid, and 14% an outside tutor.

Conclusion: Children treated with proton therapy for ependymoma at a very young age report HRQOL scores similar to healthy controls in multiple HRQOL domains. Increasing dose to the hypothalamic-pituitary axis, chemotherapy use, and gastric-tube or ventricular drain/shunt correlated with lower HRQOL scores.

O-024 | Disseminated Low-Grade Glioma in Children and Adolescents- A Twenty Year Single Service Retrospective Analysis of Treatment Modality and Outcomes

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Background/Objectives: Low-grade gliomas in children usually have an indolent clinical course and the outcome both in terms of survival and morbidity is good for most patients. As disseminated disease is rare, there is a paucity of data on the incidence, clinical characteristics, tumour behaviour, and treatment outcomes.

Design/Methods: We conducted a retrospective analysis of children and adolescents with disseminated LGG (either at presentation or relapse) treated between 2003 and 2005 at two London Hospitals - Great Ormond Street Hospital and University College Hospital. Data collected included: patient demographics, tumour histology, genetic mutations, treatment modalities and outcomes both in terms of mortality and morbidity.

Results: Of 295 children diagnosed with LGG during this period, 34 had disseminated disease either at diagnosis or recurrence; 7/34 also had type 1 neurofibromatosis. Four of the 34 also had the BRAF translocation. Pilocytic astrocytoma was the predominant histological subtype and comprised 44% [n=15] of the cohort. The most common location of the primary was the posterior fossa (29%). Twenty-one patients [62%] had disseminated disease at diagnosis. Chemotherapy was the most common primary treatment modality [50%]. Treatment response after initial treatment was: stable disease or partial response - 59% [n=20], progressive disease 41% [n=14]. Median follow up for the cohort was 35 months [range, 1 day - 125 months]. Transformation to a high-grade glioma occurred in four children. Twenty-four patients are currently alive, one was lost to follow up and nine have died. All but one death was due to disease progression. There were no factors identified that appeared to be associated with disseminated disease.

Conclusion: Patients with disseminated low grade gliomas have poorer prognosis and survival. Although treatment modalities for disseminated LGG are multi-modal, prospective studies are needed to determine the true incidence and optimal treatment.

FREE PAPERS SESSION 5: FACTORS EFFECTING CANCER CAUSATION AND OUTCOME

O-025 | Health Conditions Associated with Metabolic Syndrome after Cancer at a Young Age: A Nationwide Register-Based Study

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Background/Objectives: Childhood cancer survivors are at risk for developing metabolic syndrome (MetS), which subsequently leads to cardiovascular morbidity and excess mortality. Our aim was to investigate the purchases of medications associated with MetS among 7,551 early onset cancer patients compared to siblings.

Design/Methods: Our nationwide Finnish population-based registry study analyzed the drug purchase of medication among early onset cancer patients diagnosed with cancer below the age of 35 years between 1994 and 2004 compared to siblings by linkage to the drug purchase registry, allowing for a maximal follow-up of 18 years.

Results: The hazard ratios (HRs) for purchasing antihypertensives and diabetes drugs were higher after both childhood (HR 4.6, 95% CI 3.1-7.0; HR 3.0, 95%CI 1.5-6.1) and young adulthood (YA) cancer (HR 1.5, 95%CI 1.3-1.8; HR 1.6, 95%CI 1.1-2.2) compared to siblings. The

HRs for purchasing lipid-lowering drugs were elevated both after childhood (HR 4.3, 95%CI 0.9-19.5) and YA cancer (HR 1.6, 95%CI 1.04-2.5), but only reached significance in YA cancer patients. Among specific cancer diagnosis groups, highest HR values for antihypertensives were found in childhood acute lymphoblastic leukaemia (ALL) (HR 6.1, 95%CI 3.7-10.3) and bone tumour (HR 4.3, 95%CI 1.9-9.4), and YA ALL (HR 4.8, 95%CI 3.1-7.0) and acute myeloid leukaemia (AML) (HR 3.4, 95%CI 2.5-5.1) patients. Moreover, childhood ALL (HR 6.3, 95%CI 2.7-14.8), AML (HR 7.6, 95%CI 1.9-24.5) and central nervous system (CNS)-tumour (HR 3.5, 95%CI 1.3-9.2) and YA ALL (HR 3.7, 95%CI 1.2-9.5) patients showed the strongest likelihood of purchasing diabetes drugs compared to siblings.

Conclusion: The purchase of medications associated with MetS was increased after early onset cancer and highly dependent on the age at cancer diagnosis and the cancer diagnosis.

Prevention strategies are imperative for reducing potentially life-threatening cardiovascular complications after early onset cancer.

O-026 | Costs for Childhood Cancer Care Prior to and in the Year after Diagnosis: A Population-Based Study in Ontario and British Columbia, Canada

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Background/Objectives: Childhood cancer presents unique issues regarding treatment, late effects, and long-term survival, but few studies have reported costs. Child-specific costs are useful for economic evaluation and planning care. Costs may vary across different healthcare jurisdictions.

Design/Methods: Patients diagnosed with cancer at ages 91 days to 14 years between 1995-2009 were identified from British Columbia (BC) and Ontario (ON) cancer registries. Data were linked with clinical and administrative healthcare databases. Total resource-specific costs (CAD 2012) during 90 days pre-diagnosis and one year post-diagnosis were estimated for patients with leukaemia, lymphoma, central nervous system (CNS), and "other" cancers.

Results: Patients ($N_{ON}=4,396$; $N_{BC}=1,441$), had mean ages of 6_{ON} and 7_{BC} years at diagnosis; $36_{ON}\%$ and $33_{BC}\%$ had leukaemia, $21_{ON}\%$ and $23_{BC}\%$ CNS tumours, $10_{ON}\%$ and $10_{BC}\%$ lymphoma, $33_{ON}\%$ and $34_{BC}\%$ other cancers, and $93.5_{ON}\%$ versus $93.2_{BC}\%$ survived ≥ 1 year. Pre-diagnosis mean total cost for all patients was \$6,316 and \$2,491 for ON and BC, respectively. Costs were highest for patients with CNS tumours (\$7,843) in Ontario and for lymphoma (\$3,490) in BC. Post-diagnosis mean total cost was \$137,693 (\$134,820 ≥ 1 ; \$173,202 < 1) in Ontario and \$90,760 (\$89,317 ≥ 1 ; \$109,305 < 1) in BC. Inpatient hospitalizations represented $>75\%$ and $>72\%$ of all costs.

Conclusion: First-year childhood cancer costs are higher than those reported in adult studies. Total costs were lower in BC than Ontario; however, similar trends were found in both (higher costs for patients who survived < 1 year and hospitalization as the largest driver of costs). Future work will estimate net cancer-attributable costs and long-term costs, including treatment complications and subsequent malignancies, for both provinces. The difference in pre-diagnosis costs between provinces will be further investigated.

O-027 | Cancer Treatment and Sex: are Boys and Girls Treated the Same?

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Background/Objectives: Sex differences in childhood cancer survival have been documented, but less is known on sex differences in treatment among children were not previously reported. This paper aims to explore sex differences in survival as well as in treatment among childhood cancer patients in Ireland.

Design/Methods: Data were extracted from the National Cancer Registry Ireland on patients under 20 years who were diagnosed with invasive cancer between 1994-2012 ($n=3,704$). Data include information on sex, age, type of cancer, stage, survival and treatment. We analyzed gender differences in survival and treatment for the following cancers: Acute Lymphoblastic Leukaemia (ALL); Acute Myeloid Leukaemia (AML); Hodgkin Lymphoma (HL); Non-Hodgkin Lymphoma (NHL); Astrocytoma; Medulloblastoma; Neuroblastoma; and other cancers of the Central Nervous System (CNS). Survival was estimated using Kaplan-Meier survival estimates, and gender differences in treatment were analyzed using models of relative risk.

Results: We found evidence for gender differences in cancer treatment in Ireland across a number of cancers: Girls were less likely to receive radiotherapy for ALL (RR 0.54; CI 0.36-0.79); they were less likely to receive a surgery for HL (RR 0.57; CI 0.30-1.04), astrocytoma (RR 0.87; CI 0.75-1.01) and for other CNS cancers (RR 0.76; CI 0.60-0.96); they and were more likely to receive chemotherapy for HL (RR 1.13; CI 1.04-1.25) and less likely to receive chemotherapy for NHL (RR 0.91; CI 1.03).

Conclusion: Treatment protocols do not specify different treatment by sex, yet we found statistically significant differences across five different types of treatment. These findings may suggest that different approaches are used for treating girls and boys although the reason behind it is not well documented. Our findings call for further research in the area.

The study was funded by the Irish Cancer Society.

O-028 | Disparities in Paediatric Leukemia Incidence and Survival: A Population-Based Cancer Registry Analysis Comparing Thailand and the United States

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Background/Objectives: Pediatric leukaemia incidence and survival varies worldwide due to differences in population risk factors and access to diagnosis and treatment. We analyzed acute lymphoblastic (ALL) and acute myeloid (AML) leukaemia incidence and survival trends in children age 0-19 years from 1990-2011 in Thailand. We compared these results to United States (US) data.

Design/Methods: We extracted paediatric leukaemia cases from five provincial population-based cancer registries in Thailand ($n=1,245$). Cases from the US were obtained from the Surveillance, Epidemiology, and End Results program ($n=6,738$). We computed age-standardized incidence rates (ASIR) and relative survival and estimated survival functions using the Kaplan-Meier method. We used jointpoint regression to analyze incidence and survival trends and estimate annual percent changes.

Results: While the ALL ASIR was lower in Thailand compared to the US (21.1 vs. 31.2 cases per million), the AML ASIR was 7.7 cases per million in both countries. The proportion of ALL and AML diagnosed in Thailand was 60% and 23%, respectively, vs. 75% and 19% in the US ($p<0.001$). ALL incidence increased annually by 1.5% in Thailand ($p=0.015$) and 0.9% in the US ($p=0.003$). AML incidence increased annually by 2.3% in Thailand ($p=0.047$) while it remained constant in the US. Five-year survival significantly improved in Thailand between the two periods from 1990-2000 and 2001-2011 for both AML (19% to 29%, $p=0.009$) and ALL (45% to 55%, $p=0.001$). ALL and AML five-year survival was 86% and 54% in the US. ALL survival increased annually by 1.5% in Thailand ($p=0.022$) and 0.7% in the US ($p<0.001$). While AML survival increased annually by 1.8% in the US ($p<0.001$), no trend was identified in Thailand.

Conclusion: Our results warrant investigating novel population risk factors for paediatric leukaemia, especially AML, in Thailand, and identifying diagnostic and treatment disparities to address the survival gap between Thailand and the US.

O-029 | Childhood Cancer: Survival in Argentina. Report from the National Paediatric Cancer Registry, ROHA Net. 2000-2009

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Background/Objectives: Information on the epidemiology of childhood cancer is mandatory for the planning of health-care policies. The Argentine National Paediatric Cancer Registry (ROHA), is a hospital-based registry with national coverage active since 2000. The aim of the current study was to analyze the five-year survival of children diagnosed with cancer in Argentina during 2000-2009 by major morphological subgroup.

Design/Methods: Newly diagnosed paediatric cancer cases are registered in the ROHA (estimated coverage is 93% of the country's cases). Five-year overall survival was estimated using Kaplan-Meier methods.

Results: Between 2000 and 2009, a total of 10,181 new cancer diagnoses in children aged under 15 years were reported to the registry. Five-year overall survival (95% CI) for all cancers was 61.7% (60.7; 62.7). Specific five-year survival for the most common morphological types was: leukaemias 60.1% (58.6; 61.7), lymphomas and related neoplasms 73.7% (71.2; 76.1), brain neoplasms 43.8% (41.4; 46.3), soft tissue sarcomas 44.5% (40.3; 48.6), neuroblastomas 46.9% (43.1; 50.7), renal tumors 72.7% (68.3; 76.6), and malignant bone tumors 38.9% (34.5; 43.2).

Conclusion: Sixty-one percent of children diagnosed with cancer in Argentina survived at least five years after diagnosis. Even though this figure is lower than what has been reported for more developed countries, survival patterns by type are quite similar. Improving these results remains a challenge for our health-care system.

O-030 | High Yield of Causative Mutations by Whole Exome Sequencing in Selected Individuals with Childhood Cancer

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Background/Objectives: Childhood cancer predisposition shows extensive genetic heterogeneity with currently over 100 predisposing conditions described and likely many to be identified. Recognition of genetic predisposition in a child with cancer may lead to better treatment choices and surveillance options.

Design/Methods: We applied whole exome sequencing on germline DNA of children and their parents. These children were diagnosed with cancer and had at least one of the following features: intellectual disability (ID) or congenital anomalies, adult type of cancer, a family history for childhood cancer or multiple primary malignancies. All included cases remained undiagnosed after consultation by a clinical geneticist and often multiple genetic tests.

Results: Analysis of the 45 included patients resulted in a high yield of causative mutations. Five patients carried mutations in the known cancer genes *TP53*, *DICER1* (n=3) and *ETV6*. In five children, exome sequencing revealed syndromes that likely contributed to their malignancy (*EP300* based Rubinstein Taybi syndrome in a girl with AML; *EZH2* based Weaver syndrome in a boy with Burkitt lymphoma, *PHF6* based Borjeson-Forsman-Lehmann syndrome in a boy with a low grade glioma and in two boys with ALL *ARID1A* based Coffin Siris syndrome and *ACTB* based Baraitser Winter syndrome). In addition, we identified several novel candidate genes for childhood cancer. For instance, in a girl with lymphoma and congenital anomalies of the kidney (CAKUT) and uterus a *de novo* mutation in *E4F1* (p.Arg90*) was found, which could explain both conditions. *E4F1* is a binding partner of *HNF1β*, a gene known to be involved in CAKUT. In addition, *E4F1* is a key posttranslational regulator of *TP53*.

Conclusion: Our study shows the value of exome sequencing in the field of childhood cancer predisposition, both to facilitate the diagnosis of known syndromes as well as to trace novel genes involved in cancer susceptibility.

FREE PAPERS SESSION 6: ALL-GENOMICS

O-031 | High Throughput Sequencing as a Measure of Early Response to Therapy in Childhood ALL

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Background/Objectives: Early response to induction chemotherapy is a significant prognostic factor in the outcome of children with acute lymphoblastic leukaemia (ALL). High throughput sequencing (HTS) technologies of rearranged immune receptor (TCR and Ig) genes raise the possibility of a more accurate, sensitive, and standardizable approach to determination of early response to therapy. We investigated whether an HTS assay would quantify residual disease at end of induction therapy for children with ALL and be of prognostic value.

Design/Methods: We assessed 480 patients enrolled on Children's Oncology Group (COG) clinical trials AALL0331 and AALL0232 who had minimal residual disease at day 29 (end of induction) of less than 0.1% using traditional flow cytometric methods. High throughput sequencing of CDR3 regions of IGH and TCRG was performed on all samples. Diagnostic dominant clonal CDR3 sequences were searched for in the corresponding matched d29 sample.

Results: The assays defined the dominant clonal sequences in 93% of the patients. Seventy per cent of this subgroup was found to have residual disease (based on assay of a maximum of one million cells with a limit of detection of approximately 1/1,000,000) present at d29. Sixty per cent of the residual disease detected by HTS was reported as MRD negative by mpFC. Using an MRD cutoff of 10⁻⁴, HTS defined a correlation with event-free survival (p=0.0003). For the "standard risk" patients, being MRD positive by the HTS assay correlated with outcome (p=0.02). A correlation was noted between poorer outcome and a "germline" or only TCRG rearranged genotype (p=0.04).

Conclusion: We have studied a 480 patient cohort for which mpFC, HTS, and outcome data available. HTS is an accurate and standardized assay whose increased sensitivity compares well to mpFC, identifies a subgroup of patients with a very low risk of relapse and is thus relevant to determination of patient outcome.

O-032 | Minimal Residual Disease Monitoring Using Minor-BCR-ABL1 Genomic Breakpoint in Childhood Acute Lymphoblastic Leukemia Identifies a Subgroup with Distinct Biology and a Very Poor Prognosis

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Background/Objectives: We showed previously that two standard targets used for minimal residual disease (MRD) monitoring in childhood BCR-ABL1+ ALL (immunoglobulin/T-cell receptor (IG/TR) rearrangements and the BCR-ABL1 transcript quantification) correlate poorly in some patients. Here we established MRD monitoring based on patient-specific genomic (intronic) BCR-ABL1 breakpoint sequence and compared MRD levels obtained from different approaches.

Design/Methods: The BCR-ABL1 genomic breakpoints of 35 minor-BCR-ABL1+ ALL were found using multiplex long-distance PCR. The patient-specific intronic fusion sequences (BCR-ABL1-DNA) were used for MRD quantification in 386 bone marrow samples and compared with IG/TR and BCR-ABL1 transcript levels. Moreover, BCR-ABL1 was detected by FISH in sorted cell subpopulations.

Results: Analysis confirmed poor correlation between IG/TR and BCR-ABL1 transcript (correlation coefficient R=0.70). Moreover, also the two DNA-based methods (IG/TR vs. BCR-ABL1-DNA) correlated poorly (R=0.69) with 21% of samples BCR-ABL1-positive (up to 10e-1) and IG/TR-negative. While the correlation was excellent in some patients, others had several subsequent samples with poor correlation (>1 log difference). BCR-ABL1-DNA quantification had the best predictive value for overall survival (p=0.0003 at week+12 of treatment). Sorting experiments confirmed BCR-ABL1 presence outside the lymphoid blast population (myeloid/T/non-malignant B-cells) in non-correlating patients while only B-lymphoid blasts were affected in patients with good correlation. Patients with BCR-ABL1 higher than IG/TR by more than 1 log at the end of induction (day+33) had significantly worse outcome (2 years OS 84+/-9% (n=21) vs. 28+/-23% (n=6); p=0.004).

Conclusion: BCR-ABL1-DNA quantification probably provides the most accurate measurement of leukaemic burden and has the highest predictive value. The poorer outcome of patients with BCR-ABL1 higher than IG/TR possibly reflects multilineage involvement, suggesting, that some minor-BCR-ABL1+ ALL are in fact CML identified in a lymphoid blast crisis. These cases might be candidates for long-term tyrosine kinase inhibitors treatment, early SCT or alternative approaches.

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O-033 | BCR/ABL1 Point Mutations are Uncommon in Children with Ph+ Acute Lymphoblastic Leukemia Receiving Dasatinib Plus Multiagent Chemotherapy: A Report from Children's Oncology Group Trial AALL0622

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Background/Objectives: The addition of tyrosine kinase inhibitors (TKI) such as imatinib or dasatinib to the treatment of children and young adults with Ph+ ALL has greatly improved outcome compared to historical controls. Point mutations in the ABL1 kinase play a role in treatment response and relapse, and are reported in as many as 60% of adult patients receiving hyper-CVAD plus TKI (Ravandi, Blood, 116(12):2070-7, 2010).

Design/Methods: COG AALL0622 tested the safety and feasibility of adding dasatinib to the same intensified chemotherapy backbone that was combined with imatinib in COG AALL0031. BCR/ABL1 mutation status was analyzed by next generation sequencing (MolecularMD) from samples obtained at diagnosis and relapse/progression with limit of detection at 1-5%.

Results: Eleven out of 15 patients with marrow relapse (73%) had mutation data at baseline and at progression/relapse. One patient was identified with a Q252H mutation at diagnosis and T315I at relapse; both mutations are associated with dasatinib resistance and neither alteration was detected at the opposite time-point. Another patient was identified with E189K at the time of disease progression, which is not thought to confer resistance to dasatinib. Thus, 1 of 11 subjects had a kinase domain mutation at baseline and two subjects had a mutation at progression/relapse. Combined with previously published data from COG AALL0031 (1 of 9 imatinib-treated subjects with BCR-ABL1 mutations at relapse: Chang et al, BJH 157: 507-510, 2012), only 3 / 20 (15%) paediatric patients with Ph+ ALL treated with intensive chemotherapy plus TKI had a BCR-ABL1 mutation present at relapse. The mutation was associated with TKI resistance in only 2 patients (10%).

Conclusion: The majority of treatment failures in children, in contrast to adults, are not due to failure of TK inhibition. Because the chemotherapy backbone used is maximally intensive, relapse prevention should focus on the introduction of additional novel agents (eg. monoclonal antibodies).

O-034 | Recurrent MEF2D Fusions Define a New Subtype of Acute Lymphoblastic Leukemia Associated with Older Age at Diagnosis and Poor Outcome

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Background/Objectives: Chromosomal rearrangements are initiating events in the pathogenesis of acute lymphoblastic leukaemia (ALL) and are widely used to stratify disease risk and direct therapy, but many ALL cases lack a known rearrangement, particularly in older individuals. The goal of this study was to perform RNA sequencing to identify new chromosomal rearrangements in ALL.

Design/Methods: we performed transcriptome sequencing of 579 cases of B-ALL enrolled on the Children's Oncology Group (COG) trials including AALL0232 (N=221), AALL0331 (N=72), AALL0932 (N=61), AALL1131 (N=93), P9901 (N=1), and adults with B-ALL enrolled on various non-COG protocols (N=138). Rearrangements were confirmed by RT-PCR, fluorescence in situ hybridization, and functional effects assessed in vitro.

Results: We identified rearrangements between *MEF2D* (myocyte enhancer factor 2D) and five partner genes (*BCL9*, *CSF1R*, *DAZAP1*, *HNRNPUL1* and *SS18*) in 22 B progenitor ALL cases, the most common of which was *MEF2D-BCL9*. Each resulted in expression of chimeric fusion proteins with the N-terminus of *MEF2D* juxtaposed to the C-terminus of the partner gene. *MEF2D* cases had a high frequency of Ras pathway mutations. With the exception of the *MEF2D-CSF1R* case, which was Ph-like, *MEF2D*-rearranged ALL was characterized by a gene expression profile exhibiting overexpression of HDAC9. *MEF2D*-rearranged cases also exhibited a, distinct immunophenotype (CD10w/-, CD38+), DNA copy number alterations at the sites of rearrangement, older age of diagnosis (median 16.6 years), and poor outcome (five year event free survival 61.7% ±15.6%).

Conclusion: *MEF2D*-rearranged ALL represents a distinct form of high-risk leukaemia enriched in adolescents and young adults, for which new therapeutic approaches such as histone deacetylase inhibitors should be explored.

O-035 | The Genomic Landscape of T-Lineage Acute Lymphoblastic Leukemia

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Background/Objectives: Comprehensive studies examining the genomic landscape of T-lineage ALL are lacking, but are important to identify all oncogenic drivers.

Design/Methods: We performed transcriptome sequencing, exome sequencing and DNA copy number analysis for 264 cases of T-ALL studied on the Children's Oncology Group AALL0434 study. Cases with immunophenotypic data (N=189), included 19 early T-cell precursor (ETP) cases, 24 near-ETP (with normal CD5 expression) and 146 Non-ETP cases.

Results: 176 driver genes were identified including *NOTCH1* (n=194, 73%), *FBXW7* (n=64, 24%), *PHF6* (n=50, 19%), *PTEN* (n=37, 14%), *USP7* (n=32, 12%), *DNM2* (n=29, 11%) and *BCL11B* (n=27, 10%). New mutations included *CCND3* (n=15, 6%), *MYB* (n=13, 5%), *CTCF* (n=13, 5%), *MED12* (n=7, 3%), *USP9X* (n=7, 3%), *SMARCA4* (n=7, 3%) and *CREBBP* (n=6, 2%).

The following pathways to be most frequently mutated: cell cycle/tumour suppression (N=225; *CDKN2A/B* (n=206), *CDKN1B* (n=35), *RBI1* (n=28)); *NOTCH1/FBXW7* (n=212), *P13K-AKT* (n=130), *JAK-STAT* (n=99) and *Ras* (n=51). We identified a high frequency of mutations in transcriptional regulators in 222 cases, including 108 cases with mutations in a core regulatory complex comprising *TAL1* (n=51), *MYB* (n=45), *RUNX1* (n=18) and *GATA3* (n=13). In 90 of these 108 cases (83%), only a single mutation was present in any of the four genes, consistent with a central role of this complex in leukemogenesis. Epigenetic alterations were identified in 178 cases, including *PHF6* (n=63), *SMARCA4* (n=23), *KDM6A* (n=22) and *EZH2* (n=18), and new deletions and mutations in *KMT2A* (MLL; n=11).

Conclusion: These findings provide the first comprehensive landscape of genomic alterations in T-ALL and have provided new insights into the genes and pathways mutated in this disease, their interaction, and the nature of clonal heterogeneity in T-ALL.

O-036 | CRLF2 Over-Expression is a Poor Prognostic Marker in Children with High Risk T-Cell Acute Lymphoblastic Leukemia

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Background/Objectives: Although introduction of risk-adapted therapy improved their prognosis, paediatric T acute lymphoblastic leukaemia (T-ALL) patients still have a worse outcome compared to B-Cell Precursor (BCP)-ALL patients and they could greatly benefit from the identification of new prognostic markers.

Alteration of Cytokine Receptor-like Factor 2 (*CRLF2*) gene, a hallmark correlated with poor outcome in BCP-ALL, has not been reported in T-ALL. However, aberrations in *IL7Rα*, that heterodimerizes with *CRLF2* to form the receptor for thymic stromal lymphopoietin (TSLP), have been described. This observation prompted us to investigate if *CRLF2* could also be affected in T-ALL.

Design/Methods: We analyzed *CRLF2* expression in 212 T-ALL paediatric patients enrolled in the AIEOP-BFM ALL 2000 study in Italian (AIEOP) and German (BFM-G) centers.

Results: Seventeen out of 120 (14.2%) AIEOP patients presented *CRLF2* mRNA expression 5 times higher than the median (*CRLF2-high*); they had a significantly inferior event-free survival (EFS) (41.2%±11.9 vs. 68.9%±4.6, p=0.006) and overall survival (47.1%±12.1 vs. 73.8%±4.3, p=0.009) and an increased cumulative incidence of relapse/resistance (CIR) (52.9%±12.1 vs. 26.2%±4.3, Hazard ratio=2.84, p=0.007) compared to *CRLF2-low* patients. The prognostic value of *CRLF2* over-expression was validated in the BFM-G cohort. Cox model analysis showed that patients with *CRLF2-high* expression had a 2.5-fold increased risk of relapse. Interestingly, *CRLF2* over-expression was associated with poor prognosis in the high risk (HR) subgroup where *CRLF2-high* patients were more frequently allocated.

Interestingly, although in T-ALL the *CRLF2* protein was localized mainly in the cytoplasm, in *CRLF2-high* blasts we found a trend towards a stronger TSLP-induced pSTAT5 response, sensitive to the JAK inhibitor Ruxolitinib. Moreover, gene set enrichment analysis showed an inverse correlation between the expression of *CRLF2* and of cell cycle regulators.

Conclusion: *CRLF2* over-expression is a poor prognostic marker identifying a subset of HR T-ALL patients that could benefit from alternative therapy, potentially targeting *CRLF2* pathway.

FREE PAPERS SESSION 7: LATE EFFECTS (FERTILITY/ENDOCRINE)

O-037 | Effect of Cranial Irradiation and Alkylating Agent Chemotherapy on Sperm Concentration of Survivors of Childhood ALL: A Report from the St. Jude Lifetime Cohort Study

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Background/Objectives: The independent impact of low dose cranial irradiation (CRT) used in childhood acute lymphoblastic leukaemia (ALL) for prevention or treatment of central nervous system disease on sperm concentration has not been evaluated previously using multivariable modeling.

Design/Methods: We performed semen analyses in 71.8% (173/241) of adult survivors of paediatric ALL who participated in SJLIFE and had received alkylating agent chemotherapy with or without CRT. Cumulative alkylating agent treatment was quantified using the cyclophosphamide equivalent dose (CED). Log-binomial regression models were used to examine associations between demographic and exposure variables and oligo- or azoospermia. Variables with p < 0.1 in univariate models were included in the multivariable model.

Results: Eighty-two survivors received no CRT, 62 >0-<20Gy CRT and 29 ≥20-<26Gy CRT. 62(35.8%) were normospermic, 46(26.6%) were oligospermic (sperm concentration <15 million/mL) and 65(37.6%) were azoospermic. In univariate analyses, neither CRT>0-<20Gy (Relative risk (RR)=0.99,95% confidence interval (CI),0.77-1.28,p=0.95) nor CRT ≥20-<26Gy (RR=1.09,95% CI,0.81-1.46,p=0.58) compared to CRT=0 was statistically significant. In multivariable models, risk of oligo- or azoospermia was increased for those who were 5-9 years of age at diagnosis (compared to 0-4 years of age) (RR=1.30, 95% CI,1.05 to 1.61), treated with CED= 8-12 g/m² (RR=2.06(95% CI,1.08-3.94), or CED≥12 g/m² (RR=2.12 (95% CI,1.09, 4.12), but not with CED=4-8 grams/m² (RR=1.42(95% CI,0.70-2.89, p=0.33), compared to >0-4 grams/m².

Conclusion: Treatment with <26Gy CRT did not increase the risk of oligo- or azoospermia in adult survivors of paediatric ALL. Treatment with a cumulative CED>8 g/m² increases the risk of oligo- and azoospermia. Those who were 5-9 years of age at diagnosis were also at increased risk. These findings can be used to counsel adult survivors of paediatric ALL and newly diagnosed patients and their families, and to guide the design of future ALL treatment protocols.

O-038 | Effect of Cancer and its Treatment on Ovarian Function Markers in Long-Term Female Survivors of Childhood Cancer

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Background/Objectives: This study aimed to investigate which chemotherapeutic agents and radiation body sites are dose-dependently associated with ovarian function markers in female childhood cancer survivors (CCSs).

Design/Methods: The study is part of the DCOG LATER-VEVO study, a nationwide retrospective cohort study on female fertility of Dutch 5-year CCSs. The control group consisted of sisters of survivors and females from the general population. Study measurements included filling out a questionnaire, providing a blood sample for hormonal analyses (AMH and FSH levels), and undergoing a transvaginal ultrasonic evaluation of the ovaries (antral follicle count, AFC).

Results: Of the 1,166 CCSs and 836 controls participating in the study, 629 (54%) and 432 (52%), respectively, provided a blood sample and/or underwent an ultrasound measurement. CCSs were at increased risk of having low (<0.5 µg/l) AMH levels, low AFC (≤5 follicles), and elevated (≥10 U/L) FSH levels (OR (95% CI) 9.5 (3.5-25.8), 3.6 (1.4-8.8), 8.7 (2.7-27.9), respectively). Moreover, in a multivariable model, corrected for attained age, BMI, smoking, use of contraceptives, and time since treatment, significant negative dose-effect relations were found for AMH and AFC for the following treatment modalities: cyclophosphamide (p for trend=0.04 and 0.05, respectively), procarbazine (p trend <0.001 and 0.01, respectively), radiation to the lower abdomen or pelvis (p trend <0.001 and 0.003), and total body irradiation (TBI) (p trend=0.04 and <0.001, respectively). Moreover, for FSH a significant positive dose-effect relation was found for procarbazine, abdominal/pelvic radiation, and TBI (all p trend <0.001).

Conclusion: CCSs treated with cyclophosphamide, procarbazine, lower abdominal/pelvic radiation, or TBI are at risk of a reduced ovarian function, with higher doses leading to low AMH and AFC values and elevated FSH levels. These results should be taken into account when counseling female CCSs, as well as female patients who are about to undergo anti-cancer therapy, regarding their future reproductive potential.

O-039 | Clinical and Genetic Predictors of Impaired Fertility in Female Survivors of Childhood Cancer

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Background/Objectives: An important late effect among females who survive childhood cancer is treatment-related ovarian damage and impaired fertility. While chemotherapy and radiation therapy are associated with impaired fertility, few other risk factors have been identified. Furthermore, little is known about the role of genetic susceptibility to these late effects. As Anti-Müllerian Hormone (AMH) is a demonstrated marker of ovarian reserve, our objective was to identify clinical and genetic predictors of AMH levels in these patients.

Design/Methods: Female survivors of childhood cancer (n=181) were recruited from the Texas Children's Cancer Center Long-Term Survivor Program (LTSP). AMH (ng/mL) was measured using an enzyme-linked immunosorbent assay. Information on age at diagnosis and enrollment, race, ethnicity, cancer diagnosis, pelvic radiation, and use of alkylating agents was abstracted from medical records. The following single nucleotide polymorphisms (SNPs) were selected based on known or suspected function: *AMHR2* rs2002555; *CYP2C9*4* rs56165452; *CYP2C19*2* rs4244285; and *CYP2C19*3* rs4986893. SNPs were genotyped using TaqMan assays. Linear regression was used to determine the association between selected factors and AMH levels (log₁₀[AMH+1]).

Results: The mean age at LTSP enrollment was 12.4 years. The most common cancer diagnosis was acute lymphoblastic leukaemia (47.2%), and a substantial proportion of the population was Hispanic (41.0%). The following variables were significantly associated with lower AMH levels: pelvic radiation (beta=-0.61, P<0.001) and treatment with alkylating agents (beta=-0.09, P=0.04). Enrollment age was associated with higher AMH levels (beta=0.01, P=0.04). Hispanic ethnicity was marginally associated with lower AMH levels (beta=-0.08, P=0.08). There were no significant genetic associations.

Conclusion: Our results confirm previous associations of treatment-related factors and ovarian damage, while suggesting a potential association between Hispanic ethnicity and ovarian damage. While the SNPs evaluated were not predictive of AMH levels, more work is needed to explain why some patients experience impaired fertility, while others do not, despite similar therapy.

O-040 | Routine Thyroid Ultrasound Surveillance in Survivors of Hodgkin Disease (HD) and Central Nervous System (CNS) Tumors Following Radiation Exposure: to do or not to do?

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Background/Objectives: Long-term survivors (LTS) of childhood cancer who have received mantle and craniospinal radiation (XRT) are at an increased risk for thyroid dysfunction and carcinomas. The need for routine thyroid surveillance with ultrasound (RTS) following XRT remains controversial. We have performed RTS since 2003 and report our results to date in two of the highest risk populations: 46 LTS of HD and 43 LTS of CNS tumors diagnosed between 1976-2010 (HD) and 1987-2007 (CNS).

Design/Methods: RTS begins five years post diagnosis upon entering the LTS clinic. Intervals for follow up scans depend on the results of the primary screening. LTS with abnormal findings including persistent, increasing or large solitary nodules or cysts are followed with repeat scans and frequently with biopsy (bx).

Results: Nineteen of 46 LTS of HD had abnormal thyroid ultrasounds of which 10/19 had a bx resulting in: malignant carcinomas (3); benign changes (7). Twenty of 43 LTS of CNS tumors had abnormal ultrasounds of which 11/20 had a bx resulting in: malignant or pre-malignant carcinomas (6); benign changes (5). In total, thirty nine of 89 LTS (44%) had abnormalities detected of which 21 (54%) had a bx performed. Nine of 21 (42%) had a malignancy or pre-malignancy detected requiring further intervention. Of all patients with an abnormal ultrasound, only one with HD and three with CNS tumors had an initially normal study.

Conclusion: LTS of mantle and craniospinal XRT are at high risk for developing abnormalities of the thyroid detected by ultrasound as early as five years post diagnosis. Although the overall malignancy / pre-malignancy rate was low, for those with an abnormal thyroid ultrasound for which a bx was recommended the rate was substantial at 42%. Based on these findings RTS should be considered for LTS at high risk based on prior XRT exposure.

O-041 | Decreased Risk of Hypothyroidism after Craniospinal Irradiation (CSI) with Proton Therapy (PRT) in Patients with Medulloblastoma

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Background/Objectives: Children with medulloblastoma often develop endocrine deficiencies following CSI. CSI with PRT has the potential to decrease the risk of hypothyroidism. We aimed to compare the incidence of hypothyroidism in patients with medulloblastoma treated with photon or PRT.

Design/Methods: Patients with medulloblastoma who received CSI as initial therapy at a single institution from 1997-2014 were retrospectively reviewed. Ninety-six patients (54 photon, 42 PRT) who had baseline and follow-up thyroid studies were analyzed. We used logistic regression analyses to compare risk for any, primary, and central hypothyroidism. Dosimetry for all proton patients was compared to historical controls.

Results: At a median follow up of 6.7 years (4.9 yrs in PRT and 10.3 yrs in photon), 33/96 (34%) developed hypothyroidism (median time: 3.5 years). Hypothyroidism developed in 25/54 (46%) patients who received photon therapy vs 8/42 (19%) in the PRT group (p=0.005). Primary hypothyroidism developed in 15/96 (16%) patients, including 12/54 (29%) receiving photons and 3/42 (10%) with PRT (p=0.04). Central hypothyroidism developed in 17/96 (18%) of patients, including 13/54 (24%) with photons and 4/42 (10%) with PRT (p=0.064). On multivariable analysis, adjusting for risk group, CSI dose, age, and gender PRT was independently associated with decreased risk for any (p=0.002), primary (p=0.02), and central (p=0.02) hypothyroidism. Standard-risk disease was associated with a decreased risk for any (p=0.01), and central (p=0.004) hypothyroidism independent of other factors. Median doses in the proton group include 26.5 Gray (Gy) (range 23.6-59.3) to the hypothalamus, 25.9 Gy (range 23.6-56.5) to the pituitary, and 0.195 Gy (range 0.003-8.7) to the thyroid. These doses are significantly lower than historical control groups treated with conventional radiation therapy.

Conclusion: CSI with PRT reduces primary and central hypothyroidism with reduced doses to the thyroid, pituitary, and hypothalamus.

O-042 | Changes in Body Mass Index in Long Term Survivors of Childhood Acute Lymphoblastic Leukemia Treated Without Cranial Radiation and with Reduced Glucocorticoid Therapy

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Background/Objectives: Cranial radiation and glucocorticoids are associated with an increase in BMI z-score in survivors of childhood acute lymphoblastic leukaemia (ALL). We aimed to investigate the impact of a contemporary treatment protocol that omitted prophylactic cranial radiation and glucocorticoids from the maintenance phase on longitudinal BMI z-score in children with ALL.

Design/Methods: We performed a retrospective audit of heights and weights and BMI z-scores from diagnosis to seven years after diagnosis of 196 children with standard and medium risk ALL. These patients were treated on a protocol without cranial radiation and with no glucocorticoids administered during maintenance treatment.

Results: A non-significant increase in BMI z-score occurred after the induction phase containing prednisone; [Estimated Marginal Mean (EMM) 0.42, $P=0.220$], with a return to pre-treatment levels during intensification (0.37, $P=0.347$) and consolidation treatment (0.29, $P=0.779$). There was a significant increase in the EMM BMI z-score during re-induction containing dexamethasone (0.98, $P<0.0001$). This increase persisted throughout the intensification (0.87, $P<0.0001$) and maintenance phase (0.82, $P<0.0001$) and remained higher up to seven years after diagnosis (0.78, $P=0.006$). A linear mixed model identified significant associations between a higher BMI z-score and male sex, higher BMI z-score at diagnosis and lower socioeconomic status, (all $P<0.0001$).

Conclusion: Children who did not receive cranial radiation and no glucocorticoids during maintenance are at increased risk of treatment-related increases in BMI z-score. The predominant increase occurred during re-induction containing dexamethasone and persisted long-term. Interventions to prevent cardiometabolic complications are needed.

FREE PAPERS SESSION 8: SUPPORTIVE/PALLIATIVE CARE

O-043 | Nutritional Status at Diagnosis Predicts Long Term Survival in Children and Adolescents with Cancer in Central America

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Background/Objectives: In 2012 we reported that more than 60% of children with cancer in Central America were severely malnourished at diagnosis and that malnutrition was associated with higher rates of abandonment of therapy and death (Eur J Cancer 2012; 48: 243-252). With a median follow up now of 8.6 years we examine the relationship of nutritional status at diagnosis to long term survival.

Design/Methods: The original cohort of 1,790 patients, enrolled from October 2004 to September 2007, were followed up until October 2015. Initial nutritional status was defined by a combination of arm anthropometry and serum albumin, and categorized as adequately nourished, moderately malnourished and severely malnourished. The three main clinical categories were acute lymphoblastic leukaemia (ALL), lymphomas and solid tumours, the latter two subdivided into stage 4 or metastatic disease and all others. Correlations between overall and event-free survival (OS and EFS) and nutritional status on each clinical category, were made by means of Kaplan-Meier survival curves, log-rank tests and Cox regression models adjusted for tumours severity.

Results: Nutritional status at diagnosis was unrelated to long term survival in patients with ALL ($p=0.275$) but correlated with survival in those with lymphomas (especially in those severely malnourished, $p=0.013$) and solid tumours ($p<0.0001$).

Cox regression model on survival, adjusted for grade, in patients with lymphomas showed that both lymphoma severity (grade 4 vs others HR=1.73, $p=0.042$) and nutritional status (severely malnourished vs others HR=2.15, $p=0.012$) increased the risk of event. Same results were obtained in patients with solid tumours adjusted for extent of tumour (metastatic tumours vs no metastatic HR=1.62, $p=0.001$; severely malnourished vs others HR=2.13, $p<0.0001$).

Conclusion: Nutritional status at diagnosis is unrelated to long term survival in patients with ALL in Central America, but malnourished patients with lymphomas and solid tumours have poorer survival rates related to the extent of disease and treatment-related mortality.

O-044 | Nutritional Ignorance and Restrictions among Families of Children with Cancer: A Cross-Sectional Study of 700 Families

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Background/Objectives: Malnutrition is common and worsens outcomes among children with cancer. Ignorance and cultural restrictions represent important modifiable causes of malnutrition. No prior studies have explored these factors in this population.

Design/Methods: All untreated patients with cancer aged ≤ 18 years presenting at a paediatric oncology clinic were recruited. Families were asked nine questions about nutritional knowledge (correct answers combined into "Knowledge score") and twelve questions about food restrictions (Number of restrictions combined into "Restriction score"). Knowledge questions tested ability to achieve good nutrition with cheap, common foods. Restriction questions assessed cultural beliefs causing restriction of foods during illness. Secondary outcomes included nutritional status and possible socio-demographic causes of nutritional ignorance.

Results: Seven hundred patients were included with median age 9 years. Poverty (53.4% below poverty line) and illiteracy (16.5% and 37.1% of fathers and mothers) were common. Mean knowledge score was 4.2 ± 1.8 . A link between nutrition and cancer survival was understood by most families (96.4%). Most perceived expensive foods like fruits and juices to be nutritionally superior to milk (57.3%), eggs (55.7%), or cereals (59.1%). Commercial foods were considered more nutritious than homemade foods (71.6%). Median restriction score was 2 (range 0-11). Restriction of protein and energy rich foods such as meats (40.7%), oils (29.4%), eggs (29.1%), sugar/jaggery (23.4%), and cereals/pulses (11.6%) was frequent. Low knowledge scores were associated with rural background, poverty, and illiteracy ($P<0.001$ for all). Knowledge score < 4

was associated with both low weight (OR 1.53, $P=0.007$) and low height (OR 1.62, $P=0.003$). Restriction score > 2 was associated with low weight (OR 1.35, $P=0.049$) but not low height.

Conclusion: This first study of its kind shows that nutritional ignorance and harmful restrictions are common among families of children with cancer. Directed educational interventions may thus represent a way to indirectly improve cancer outcomes in these patients.

O-045 | Children Undergoing Hematopoietic Stem Cell Transplantation More Frequently Die in Hospital or PICU with Shorter End of Life Care Than Those Dying at Home

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Background/Objectives: Transplant related mortality (TRM) and malignancy relapse means paediatric transplant (HSCT) centres should provide palliative and end of life care (PC/ELC). Treatment exclusively aimed at cure may lead to unrealistic expectations and impede appropriate PC/ELC.

Design/Methods: We undertook a retrospective analysis of place of death, timing and communication around ELC in our unit. Children dying after HSCT between January 2011 and December 2015 were included. Unit data base and clinical case notes were used to obtain epidemiological data, clinical details, place and cause of death. Time from medical discussion with parents/child about "no possibility of cure", withdrawal of life-saving support and time to death was documented.

Results: A total of 55 from 245 transplanted children (23%) died, 37 boys and 18 girls median age 6y10m (range 0.5-17y). Deaths varied per year: avg. admission/yr $n=34$ (range 20-44) avg. deaths 10/yr (range 2-17). In 33 children with malignant disease, cause of death was relapse in 9 (27%) and TRM in 24 (73%). Thirteen (39%) died at home, 18% ($n=6$) in HSCT unit and 43% ($n=14$) in PICU. In children with non-malignant disease ($n=22$), 2 died from progressive disease (9%), TRM accounting for the remainder. One patient died at home, 55% ($n=12$) dying in PICU and 9 (41%) dying in hospital. For children dying at home ELC discussion was initiated at mean 1 month before death (range 3dy-3mo). Children were admitted to PICU median of 14 days before death (range 1-49) with ELC discussion initiated at mean 18 hours before death (range $< 1 - 120$).

Conclusion: In children undergoing HSCT, deaths are mainly hospital/PICU based. Children with relapsed malignancies are more likely to die at home, with ELC discussion introduced weeks before death, contrasting to PICU where discussion occurred shortly before death. We show ELC/PC in paediatric HSCT needs improvement especially for admissions to PICU.

O-046 | Efficacy and Safety of Palonosetron Versus Ondansetron in Prevention of Chemotherapy Induced Nausea and Vomiting (CINV) in Children

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Background/Objectives: Palonosetron, being a long acting antiemetic, is potentially more effective, cheaper and convenient antiemetic for prevention of CINV. We compared efficacy and safety of PG(palonosetron+dexamethasone) with OG(ondansetron+dexamethasone) in prevention of CINV in children receiving moderately(MEC) and highly emetogenic chemotherapy(HEC).

Design/Methods: A prospective single center non-blinded randomized controlled trial was done among children (3-17 years) with cancer receiving first cycle of chemotherapy. Sample size was calculated to give 20% superiority of palonosetron versus ondansetron based on published data on adult patients. Children with brain tumours and comorbidity causing vomiting were excluded. Dose of palonosetron was 5 mcg/kg single dose for 72 hours. Outcome variables (nausea, vomiting, adverse effects, and need of rescue antiemetics) were statistically tested with chi square test.

Results: Two hundred children (mean age 8 years, male:female=1.8:1) were randomized to allocate study groups. Demographic data, diagnosis, chemotherapy schedules and drug cost of antiemetics were comparable among study groups. Zero emesis in acute(< 24 hours), delayed(24-120 hours) and overall phase(0-120 hours) was observed in 88%, 88% and 81% of cases respectively for PG versus 84%, 79% and 72% respectively for OG($P=0.42$, 0.09 and 0.21 respectively). Complete response rate (no nausea and no vomiting) in acute, delayed and overall phase was 87%, 86% and 79% respectively for PG versus 81%, 72% and 65% respectively for OG($P=0.25$, 0.015 and 0.03 respectively). Rescue antiemetics(metoclopramide and/or lorazepam) were used in 5 children in PG versus 4 children in OG($P=0.73$). The efficacy of the 2 drugs was same when analyzed separately for MEC or HEC. Side effects were mild (constipation, abdominal pain and headache) and comparable among both the groups.

Conclusion: Efficacy, safety and drug cost of palonosetron(5 mcg/kg) was comparable with ondansetron but due to less frequent dosing, palonosetron was more suitable for busy health care facilities. Prevention of nausea in delayed phase was better with palonosetron.

O-047 | Voriconazole Plasma Levels, its Determinants, and its Impact on Outcome of Invasive Fungal Infections in Children with Cancer: A Prospective Study

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Background/Objectives: Voriconazole plasma levels, its determinants (age, dose, route, generic formulations, and concomitant drugs) and impact of levels on outcome of invasive fungal infections(IFI) was evaluated.

Design/Methods: We prospectively studied 256 consecutive children (<19 years) given voriconazole either for prophylaxis (N=154) or treatment (N=102) of IFI between August 2008 and February 2016 as per the recommended doses. IFI diagnosis and clinical outcome evaluation were based on EORTC mycoses study group definitions. The therapeutic range was defined as 1–6 µg/ml.

Results: A total of 458 levels were analysed at steady-state [75 on intravenous and 181 on oral doses]. Significant inter- and inpatient variability in levels was observed and 46% of patients required dose adjustment. 53% of children achieved an adequate trough level initially and 61% achieved after therapeutic drug monitoring (TDM)-based dose adjustments. A significant correlation between dose and trough levels was observed in patients less than 11 years (Spearman's rank correlation coefficient =0.18, $P < 0.03$). A significant relationship was established between plasma levels above normal range and liver toxicity ($P=0.03$). On IV to oral switch, 25% children had drop in the serum levels to subtherapeutic levels. No impact of gender, steroids usage, and use of generic formulations was observed on levels or outcome. Children with level <1 µg/ml were more likely to have treatment failure at week 6 compared to children with >1 µg/ml (failure, 20.4% vs. 2.1%; $P < 0.001$). 26% children with suboptimal trough levels at 12 hours post voriconazole showed optimal levels at 8 hours suggesting early plasma clearance and need for frequent dosing.

Conclusion: Our study confirms the large variability in voriconazole plasma levels necessitating higher than recommended doses in young children, and a trend to non-linear pharmacokinetics in older patients. A significant relationship between voriconazole trough level >1 µg/ml and outcomes as well as some adverse events was confirmed justifying its TDM especially in young children.

O-048 | Improved Inpatient Outcomes Following Implementation of a Paediatric Early Warning Score (PEWS) in a Resource-Limited Paediatric Oncology Hospital

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Background/Objectives: Hospitalized paediatric oncology patients are at high risk for clinical decline and mortality, particularly in resource-limited settings. Pediatric Early Warning Scores (PEWS) are nursing-administered clinical assessment tools used to aid with early identification of deterioration; however, these scores have never been studied in oncology patients in resource-limited settings. We describe the effects of implementing PEWS at Unidad Nacional de Oncología Pediátrica (UNOP), a paediatric oncology hospital in Guatemala.

Design/Methods: In 2014, a multidisciplinary team implemented a modified PEWS tool at UNOP to improve the quality of care for hospitalized patients. This study compares inpatient outcomes in the year before (2013) and after (2015) PEWS implementation. We evaluated the frequency of unplanned PICU transfer, PICU outcomes, and inpatient toxic deaths between these two periods using retrospective chart review. T-tests, Wilcoxon two-sample tests, and Fisher's exact test were used to compare the two periods.

Results: In the period before and after PEWS implementation, UNOP had 1701 and 2280 inpatient admissions, respectively. The frequency of unplanned PICU transfer among these hospitalized patients decreased significantly after PEWS implementation (157 vs 130 unplanned PICU transfers, 9.2% vs 5.7%, $p < 0.001$), with no increase in inpatient toxic deaths (3.7% before vs 2.6% after, $p=0.27$). There was a decrease in PICU utilization (1376 to 1088 ICU-patient days/year, 21% decrease), and total hospital length of stay (LOS) (mean 38 days before vs 32 days after, $p=0.04$) for unplanned inpatient PICU transfers following PEWS implementation. There were no significant changes in severity of illness on PICU admission or PICU mortality.

Conclusion: Implementation of PEWS in this resource-limited paediatric oncology hospital resulted in decreased inpatient deterioration events, decreased PICU utilization, and shorter hospital LOS. This work demonstrates that PEWS is a feasible, low-cost, and effective quality improvement measure to improve hospital care for children with cancer in hospitals of all resource levels.

FREE PAPERS SESSION 9: PPO

O-049 | The Impact of Growth Hormone Deficiency on Neurocognitive Function in Adult Survivors of Childhood Acute Lymphoblastic Leukemia Treated with Cranial Radiation

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Background/Objectives: Long-term survivors of childhood acute lymphoblastic leukaemia (ALL) treated with cranial radiation therapy (CRT) are at risk for neurocognitive problems.

CRT is also associated with growth hormone deficiency (GHD). We examined the unique contribution of GHD to neurocognitive problems in survivors of ALL treated with CRT.

Design/Methods: Adult survivors of ALL treated with CRT (N=571 [49% female]; mean age=37.4, range: 19.4-62.2) completed a battery of neurocognitive tests (attention, memory, processing speed, executive function), and self-reported neurobehavioral symptoms. Performances were converted to age-adjusted standard scores ($\mu=0$, $\sigma=1.0$) based on normative data. GHD was defined as previous diagnosis of GHD or plasma IGF-1 < -2.0 z-score for sex and age at the time of neurocognitive assessment. Multivariable linear regression models were used to examine the effects of GHD and relevant covariates.

Results: Of the 571 survivors, 298 (52%) had GHD, 97 (17%) had hypothyroidism and 150 (26%) had hypogonadism. Survivors with GHD versus those without GHD demonstrated lower performance on measures of vocabulary ($p=0.02$), processing speed ($p=0.04$), cognitive flexibility ($p=0.01$), and verbal fluency ($p=0.001$), and reported more symptoms of task inefficiency ($p=0.04$) and emotional dysregulation ($p=0.02$). In multivariable models adjusting for gender, age at diagnosis, CRT, and intrathecal and high-dose intravenous methotrexate, GHD was associated with a 19% lower verbal fluency z-score ($p=0.04$) and a 19% higher score for symptoms of emotional dysregulation ($p=0.06$). Hypothyroidism was associated with a 25% lower score for verbal fluency ($p=0.05$), and a 38% higher score for symptoms of poor task efficiency ($p=0.03$). CRT was associated with 27-99% higher z-scores across all neurocognitive tests (all $p < 0.01$), but was not associated with self-reported symptoms.

Conclusion: Adult survivors of childhood ALL treated with CRT are at risk for GHD, which may have a modest impact on neurocognitive and neurobehavioral problems beyond that associated with primary neurotoxic treatment exposures.

O-050 | Importance of Baseline Data for Children Receiving Cranial Proton Radiation Therapy

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Background/Objectives: Pediatric brain tumour patients (PBTP) present for radiation therapy with pre-existing developmental and medical histories independent of tumour treatment. With focus on possible late effects of proton radiation therapy (PRT) insufficient attention has been paid to pre-existing conditions. This study describes a cohort of PBTP prior to PRT and a cohort of PBTP 2 to 5 years post PRT.

Design/Methods: PBTP scheduled for PRT receive neuropsychological evaluations (expansion of COG ALTE07C1) prior to PRT, and yearly post-PRT as standard of care. Parents/patients consent to a Proton Data Registry.

Results: At baseline, of 121 PBTP (age 2 to 31, M=11.21 years, SD=5.85; 60% male; RT dose M=5400cGy, range=3000-6000cGy), 23% (28 patients) presented with at least 1 pre-morbid condition including ASD, ADHD, Language Disorders, Learning Disability, and Mood (anxiety/depression/bipolar) Disorders, as well as non-credible effort on assessment (data removed from analysis). PBTP demonstrated average IQ, processing speed, attention, inhibition, verbal and visual memory, planning, and adaptive functioning, with low average visual motor ability. When dividing cohort by presence of pre-morbid conditions, the pre-existing condition cohort had significantly worse verbal memory $F(1,73)=12.80$, $p=.001$, $\eta^2=.15$, processing speed $F(1,55)=7.36$, $p<.01$, $\eta^2=.12$, adaptive functioning $F(1,78)=10.40$, $p<.01$, $\eta^2=.12$, and IQ $F(1,95)=4.04$, $p<.05$, $\eta^2=.04$. A cohort ($n=26$; age 4-22, M=11.73, SD=4.75; 73% male), 19% with pre-morbid conditions, at 2-5 years post PRT (M=3.11, SD=.95) demonstrated average IQ, attention, inhibition, verbal and visual memory, and planning, with low average visual motor ability, processing speed, and adaptive functioning. There were no group differences.

Conclusion: It is essential to document pre-PRT abilities and developmental and behavioral factors to understand the potential impact of cranial PRT on PBTP. Those with pre-existing conditions have weaker performance at baseline. Future studies will further examine whether PRT exacerbates pre-existing conditions, and if those with pre-existing conditions respond differently to PRT.

O-051 | The Difficulty of Measuring Executive Functioning in Patients Treated for Paediatric Cerebellar Tumors

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Background/Objectives: The current study aimed to analyze tests measuring executive functioning and behavioral aspects in patients treated for paediatric cerebellar tumors and to identify risk factors influencing their performance. Additionally, the administered measures were compared in terms of their validity to detect executive dysfunctioning.

Design/Methods: In total, a group of 27 patients (8-16 years) treated for a paediatric cerebellar tumour was assessed with three different executive functioning measures: the Behavioral Rating Inventory for Executive Functioning (BRIEF), the Trail Making Test (TMT) and the Wisconsin Card Sorting Test (WCST). Furthermore, the Strength and Difficulties Questionnaire (SDQ) was administered. Subsequently, test results of the patients were contrasted against the normative samples of these tests using one sampled t-tests. The role of the risk factors (tumour histology, treatment type, age at diagnosis, time since diagnosis) was analyzed via correlations. To examine whether the different instruments detected the same patients as impaired, cross-tables were used.

Results: The data indicate that the investigated patients suffered from impairments in executive functioning. Especially impacted were flexibility in thinking, launching initiative, concept formation and problem solving. Behavior was affected in peer relationships and in dealing with emotional problems. Patients with a high-grade tumour were more impaired in executive functioning and showed more behavioral problems than patients with a low-grade tumour. It can be concluded that the different test instruments did not detect the same patients as impaired, with the behavior rating (BRIEF) showing the fewest amount of detections.

Conclusion: This study did not only demonstrate that paediatric cerebellar tumors and associated risk factors have a substantial impact on executive functioning, but also that it is vital to assess it with differentiated diagnostic methods, especially since neurological impairments are not always visible on a behavioral level.

O-052 | Predictors of Posttraumatic Stress Symptoms in Parents of Children Newly Diagnosed with Cancer

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Background/Objectives: Obstacles faced by parents of children newly diagnosed with cancer, including learning how to navigate the healthcare system and communicate with doctors, can elevate risk for negative health outcomes and psychological outcomes. Specifically, research has shown a high prevalence of posttraumatic stress symptoms (PTSS) among these caregivers. Rumination, parents' repetitive thinking about problems, such as managing their child's illness, is a strong predictor of PTSS, but factors influencing rumination are not well-established in this population. To better understand the impact of parents' challenges, the present study examined the relationship between parents' difficulties with obtaining healthcare for their child, rumination, and PTSS following a paediatric cancer diagnosis.

Design/Methods: Caregivers (N = 40, M_{age} = 38.15, SD = 8.14) of children with cancer completed the Impact of Events Scale-Revised (IES-R), a measure of PTSS, Barriers to Care Questionnaire (BCQ), and Ruminative Responses Scale (RRS) as part of an ongoing study. The BCQ Skills subscale assessed parents' problems associated with their child's care and treatment, including knowing "how the health care system works".

Results: The bootstrapped (specified: 5,000) regression analysis was significant $F(2, 37) = 31.24, p < .001$. BCQ Skills and rumination predicted 62.80% of the variance in parent PTSS. Skills had an indirect effect on PTSS through rumination, point estimate = $-.31, 95\% CI [-0.64, -.06]$, with a large effect size, $\kappa^2 = .37$. There was no direct effect of Skills on PTSS, when controlling for rumination, point estimate = $-.29, 95\% CI [-0.67, .09]$.

Conclusion: Skills for competently navigating healthcare are associated with greater rumination and increased PTSS among caregivers of children newly diagnosed with cancer. Targeting parents' skills and maladaptive thought patterns through a standard of clinical care may reduce risk for PTSS and other negative psychological outcomes, but further research examining these skills and other barriers to care is necessary.

O-053 | Contribution of Neurocognitive Function to Academic Outcomes in Paediatric Cancer: A Latent Class Analysis

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Background/Objectives: One characteristic possibly placing survivors of paediatric cancer at increased risk for academic and psychosocial challenges is poor neurocognitive functioning (e.g., attention, memory). This study aimed to identify the impact of neurocognitive functioning on impairments in academic and psychosocial domains using latent class analysis. We further examined the contribution of identified risk factors (age at diagnosis, cancer type, treatment) on outcomes class.

Design/Methods: 118 paediatric oncology patients (M age = 11.4, 37.3% female; 48.3% African American; M time since diagnosis = 3.7 years) completed neuropsychological evaluations at a university medical center from February 2004 to March 2015. Cancer diagnoses included leukaemia, lymphoma, solid tumors, brain tumour, neurocutaneous syndromes and other cancers. Patients received chemotherapy (60.2%), radiation (29.6%), or surgery only (20.4%). Neurocognitive, academic, and behavioral/emotional functioning were examined using well-validated measures. Discreet, homogeneous subgroups (latent classes) of patients were identified using latent profile analysis. Demographic and medical factors were evaluated as predictors of class membership using multinomial regressions.

Results: The average latent class probabilities for a 3-class model indicated satisfactory class separation (range: .00-.17) and homogeneity (range: .83-.93). Class differences were observed across all academic and neurocognitive domains. Class 1 (Standard Scores: 62 to 87) displayed a pattern of impaired performance relative to the other classes and standard norms. No significant Class differences were observed with respect to behavioral/emotional functioning. Class membership was predicted by age at diagnosis ($p=.02$), gender ($p=.005$), and ethnicity ($p=.001$) but not cancer diagnosis or treatment modality ($ps > .17$).

Conclusion: The heterogeneous paediatric cancer population of this study could be grouped based on varying neurocognitive profiles. Only demographics and age at diagnosis predicted class in this study. Consistent with recent psychosocial guidelines, routine neurocognitive monitoring is warranted to identify children at risk for poor academic outcomes. Early and preventative cognitive and academic intervention trials targeting at-risk individuals are needed.

O-054 | Attendance to Follow-Up Care in Survivors of Adolescence and Young Adult Cancer: Implementation of the Theory of Planned Behaviour

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Background/Objectives: Attendance to follow-up care in survivors of adolescence and young adult (AYA) cancer is important to monitor their health and detect late effects early.

The aim was to study whether the theory of planned behaviour (TPB) applies to follow-up care in AYA cancer survivors: we aimed to investigate predictors of the intention to attend follow-up care, and whether the intention is associated with the actual attendance of care.

Design/Methods: We conducted a questionnaire survey in AYA cancer survivors diagnosed between 1990 and 2005 at age 16-25 years, registered in the Cancer Registry Zurich and Zug, Switzerland and who had survived at least 5 years.

We applied linear regression models to investigate predictors (attitudes, subjective social norms and perceived behavioural control) of the intention to attend follow-up care and logistic regression models to study the association between the intention and the actual attendance.

Results: Of 389 contacted survivors, 160 (41.1%) returned the questionnaire. Of these, 98 (61.3%) were male, their mean age was 34.0 years, mean age at diagnosis was 21.6 years and mean time since diagnosis 12.4 years. Ninety-four survivors (58.8%) indicated to attend follow-up care.

Survivors reported positive attitudes regarding follow-up care, perceived moderate supportive subjective social norms, and reported to feel in control of attending follow-up care.

After adjusting for relevant socio-demographic and cancer-related characteristics, we found positive attitudes (Coeff.=0.63;95% CI:0.28-0.98) and supportive subjective social norms (Coeff.=0.61;95% CI:0.45-0.76) towards follow-up care to be significant predictors of the intention to attend follow-up care. In contrast, perceived behavioural control was not associated with intention.

The intention was positively associated with the self-reported actual attendance of care (OR=2.5,95% CI:1.8-3.3).

Conclusion: Promoting positive attitudes and highlighting supportive social norms towards the attendance to follow-up care might help to improve the attendance in survivors of AYA cancer.

FREE PAPERS SESSION 10: STEM CELL TRANSPLANTATION/IMMUNOLOGY

O-055 | Regulation of Cytokine Release and Anti-Burkitt Lymphoma (BL) Effects of Anti-CD20 Car Modified Expanded Natural Killer Cells by ALT-803, AN IL-15 Superagonist

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Background/Objectives: Relapsed BL had more advanced progression (Miles/Cairo, 2012, BJH). Chimeric antigen receptors (CARs) T-cells have shown promising results in patients with ALL, CLL and DLBCL. However, some have developed a life threatening cytokine release syndrome (CRS) with CAR-T-cell therapy.

Our group has successfully modified expanded peripheral blood Natural Killer cells (exPBNK) with an anti-CD20 CAR to target rituximab-sensitive/resistant CD20⁺ BL cells in vitro and in NSG mice (Chu/Cairo, et al, *Can Imm Res* 2015). ALT-803 is a superagonist of an IL-15 variant bound to an IL-15 α Su-Fc fusion with enhanced IL-15 biological activity (Zhu et al. 2009 *J Immunol*). ALT-803 is currently in several clinical trials including refractory non-Hodgkin lymphoma (NCT02384954).

To determine the cytokines and chemokines released and anti-BL effect of anti-CD20 CAR NK cells stimulated by ALT-803.

Design/Methods: exPBNK cells were isolated after expansion with K562-mbIL21-41BBL. Anti-CD20-4-1BB-CD3 ζ mRNA was nucleofected into exPBNK. ExPBNK were cultured with 0.35 or 3.5ng/ml ALT-803. NK proliferation, cytotoxicity, and cytokine level were examined. NK-resistant BL cells Raji and Daudi were used as BL targets.

Results: ALT-803 induced granzyme B, IFN- γ , GM-CSF, MIP-1a, RANTES release from CAR exPBNK cells but did not induce IL-2, IL-6, IL-10, IL-12, IL-13, MCP-1, MIP-1b, MMP-9, and TNF-alpha release when CAR exPBNK cells were co-cultured with Raji or Daudi.

The in BL vitro cytotoxicity of anti-CD20 CAR exPBNK was significantly enhanced by ALT-803 compared to mock-electroporated exPBNK maintained in ALT-803 medium ($p<0.001$) and compared to anti-CD20 CAR modified exPBNK maintained in medium without ALT-803 ($p<0.01$). Additionally, we observed that the combination of anti-CD20 CAR NK and ALT-803 reduced the tumour burden in Raji xenografted mice.

Conclusion: CAR exPBNK cells cultured with ALT-803 do not release inflammatory cytokines associated with CRS. ALT-803 significantly enhanced BL in vitro cytotoxicity of CAR exPBNK and reduced tumour burden in BL xenografts.

O-056 | PD-1 Expression Is Associated with CD8+ T Cell Dysfunction and Clinical Outcomes in Paediatric Recipients of Hematopoietic Stem Cell Transplantation

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Background/Objectives: Hematopoietic stem cell transplantation (HSCT) is used to treat hematologic and neoplastic disorders in children. It was previously shown that high frequencies of CD8+ T cells expressed the PD-1 exhaustion marker during the early phases of immune

reconstitution in paediatric UCBT recipients and that higher frequencies of PD-1+ T cells were associated with leukemic relapse.

Design/Methods: Here, the expression of additional inhibitory receptors known to be associated with CD8+ T cell exhaustion, including CTLA-4, 2B4, TIM-3, BTLA and LAG-3, was examined over a 24-months follow-up period in paediatric patients who underwent HSCT as part of the treatment of neoplastic (n=21) or non-neoplastic (n=20) blood disorders.

Results: Flow cytometric analysis showed that all inhibitory receptors tested were expressed at very low levels in graft inoculums. A transient increase in the frequency of CD8+ T cells that expressed PD-1 was observed during the first 100 days post-HSCT, and similar kinetics of expression were also observed in the case of 2B4, BTLA, and LAG-3. Compatible with the role of PD-1 in T cell activation and the rapid loss of terminally-differentiated CD8+ T cells, frequencies of naïve (TN) and effector memory-RA (TEMRA) CD8+ T cells were lower in the PD-1+ subset as compared with PD-1- T cells. Proliferation of CD8+ T cells and expression of IL-2, TNF- α , IFN- γ and CD107a were negatively influenced by PD-1 expression. The polyfunctionality of PD-1+ cells was likewise reduced. Finally, high frequencies of CD8+ cells expressing PD-1 were associated with the occurrence of opportunistic viral infections and leukemic relapse in the post-HSCT period, but not with the incidence of acute GVHD.

Conclusion: Overall, these results indicate that expression of PD-1 and possibly other inhibitory receptors leads to functional impairment of CD8+ T cells in paediatric HSCT recipients. This functional impairment could compromise virus-specific and antitumoral cell-mediated immunity, leading to adverse clinical outcomes.

O-057 | Risk Factors for Paediatric Patients with Relapsed/Refractory NHL Who Underwent Hematopoietic Stem Cell Transplantation: Results of the Turkish Paediatric Bone Marrow Transplantation Study Group

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Background/Objectives: Hematopoietic stem cell transplantation (HSCT) is a treatment option for patients with relapsed or refractory non-Hodgkin lymphoma (rr-NHL), but there are limited data about this treatment in paediatric settings.

Design/Methods: We examined the role of HSCT for patients aged ≤ 18 years at the time of transplantation with rr-NHL who received autologous (n=38) or allogeneic (n=28) HSCT. The risk factors affecting survival were evaluated using a stratified Cox regression.

Results: The overall survival (OS) and event-free survival (EFS) rates were 67 and 57%, respectively, with a median follow-up of 39 months; the OS and EFS according to histopathological classification were 51 and 49% for lymphoblastic, 67 and 67% for Burkitt, 86 and 59% for anaplastic large cell, and 68 and 61% for diffuse large cell lymphoma cases, respectively. The outcomes of both OS and EFS were similar in patients who received autologous and allogeneic HSCT (68 vs 70% and 55 vs 62%, respectively). Both the OS and EFS among patients with chemo-sensitive disease at the time of HSCT were significantly higher than those in patients with chemo-resistant disease (72 vs 33%, p=0.001; 65% vs 11%, p<0.001; respectively). The multivariate analysis showed that chemo-resistant disease at the time of transplantation was the only factor predicting both limited OS (hazard ratio=5.46) and EFS (hazard ratio=4.73).

Conclusion: Intensive chemotherapy followed by either allogeneic or autologous HSCT is an effective strategy for children with rr-NHL and offers durable EFS for a significant group of paediatric patients, particularly for patients with chemo-sensitive disease at the time of transplantation.

O-058 | Second Stem Cell Transplantation for Relapsed High-Risk Neuroblastoma in Japan; is it an Effective Treatment Strategy?

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Background/Objectives: Patients with high-risk neuroblastoma who relapsed after high-dose chemotherapy and stem cell transplantation (SCT) have a poor outcome. Only little information

exists about the treatment strategies for such patients. We retrospectively analyzed the efficacy of second transplantation for relapsed advanced neuroblastoma in Japan.

Design/Methods: Eighty-five neuroblastoma patients who achieved second transplantation as a salvage therapy between 1983 and 2014 were analyzed retrospectively based on the transplantation registry of the Japan Society for Hematopoietic Cell Transplantation. We compared 85 second SCT patients with 280 patients who did not perform second SCT after relapse (CHEMO).

Results: Median time from first relapse to second SCT was 216 days (range: 11-1349). Five-year event-free survival (EFS) of second SCT was 6.7 \pm 3.0%, and 5-year over-all survival (OS) of second SCT was 12.4 \pm 4.1%, which was significantly better than OS of CHEMO (8.8 \pm 1.9%, p=0.0044). In a multivariate analysis, increased probability of OS was demonstrated for patients with second SCT, and with relapse >365 days after first SCT.

As with the type of second SCT, 5-year EFS of allogeneic SCT (ALLO; n=51, 7.6 \pm 3.9%) was similar to that of autologous SCT (AUTO; n=34, 6.7 \pm 4.6%) (p=0.95). There was no significant difference in causes of death between ALLO and AUTO (p=0.316); 42 out of 51 ALLO died of disease relapse (n=29) and of transplant-related mortality (n=13), and 30 out of 34 AUTO died of relapse (n=24) and of transplant-related mortality (n=6). Chronic GVHD occurred in 9 out of 39 evaluable patients, of whom 7 died of disease.

Conclusion: Although survival advantage for second SCT existed compared with chemotherapy alone, there could be a selection bias for second SCT. We could not show the superiority of ALLO compared to AUTO, which suggested that potential graft-versus-tumour effect might be compensated by transplant-related mortality. We need to explore a novel therapeutic approach for relapsed high-risk neuroblastoma.

FREE PAPERS SESSION 11: BONE TUMOURS - FASANELLI PRIZE SESSION

O-059 | Local Control and Survival in Pelvic Ewing Sarcoma (EwS) in the Euro-Ewing99 Trial

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Background/Objectives: Approximately 20% of EwS are localized in the pelvis and have a poorer prognosis, compared to tumors of the extremities. Aim of the study was to identify factors associated with local recurrence (LR) and overall survival (OS) in patients undergoing multimodal treatment.

Design/Methods: This is a retrospective analysis on 335 patients with newly diagnosed EwS registered in the Euro-EWING99 trial from centers in Germany, Austria, Belgium, Czech-Republic, Netherlands, Switzerland between 1998-2009. Primary outcome was local recurrence-free survival (LRFS), the interval between diagnostic biopsy and LR. Secondary outcome was OS.

Results: Localized tumors were diagnosed in 53%. Median follow-up was 3.1 years in all patients and 6.3 years in survivors, LRFS was 70.4% at 5 years, OS 46.7%. Primary tumour volume ≥ 200 ml (p=0.022/p=0.001) and metastases (p=0.003/p<0.0001) were associated with a poorer LRFS and OS. Tumour regression $\leq 90\%$ after chemotherapy (p=0.253/p=0.0001) and deviations from protocol (p=0.761/p=0.041) were associated with a poorer OS. Surgery and local radiotherapy improved LRFS and OS compared to surgery (p=0.009/p=0.005) or local radiotherapy only (p<0.0001/p=0.0002). Complete removal of the involved hemipelvis was associated with improved LRFS (p=0.007) and OS (p=0.001). Patients with >90% histological response to chemotherapy (n=118) had a higher LRFS (p=0.04) and OS (p=0.012) after combined local treatment with surgery and radiation. No differences in LRFS (p=0.564) were detected in patients with $\leq 90\%$ response (n=38). Intralesional resection was associated with a poorer LRFS and OS than marginal (p=0.028/p=0.012) and wide/ radical resection (p=0.001/p=0.001).

Conclusion: Patients with pelvic EwS seem to benefit in terms of local control and OS from a complete removal of the involved hemipelvis and a combined local treatment consisting of surgical resection and radiotherapy, even in cases with >90% response to neoadjuvant treatment. Persisting soft tissue infiltration prior to surgery appears to be a simple but important clinical prognostic factor in terms of survival.

O-060 | Combined Targeting of the EWS/ETS Transcriptional Program by BET Bromodomain and PI3K Pathway Inhibition Blocks Tumorigenicity and Increases Apoptosis in Ewing Sarcoma

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Background/Objectives: Ewing sarcomas (ES) are highly malignant bone or soft tissue tumors. Genetically, ES are defined by balanced chromosomal *EWS/ETS* translocations that give rise to chimeric proteins (EWS-ETS), which generate an oncogenic transcriptional program associated with altered epigenetic marks throughout the genome.

Design/Methods: By use of inhibitors blocking BET bromodomain binding proteins (BRDs) (JQ1) and PI3K/mTOR (BEZ235) the regulation of the predominant EWS-ETS protein EWS-FLI1 and its consequences were analyzed in ES.

Results: By use of JQ1 or BEZ235 we strikingly observed a strong down-regulation of EWS-FLI1 in a dose dependent manner in ES. Further microarray analysis revealed JQ1 treatment to block a typical ES associated expression program. The effect on this expression program was mimicked by RNA interference of BRD3 or BRD4 expression but not by BRD2 blockade. JQ1 treatment not only suppressed an ES specific expression profile but also blocked contact-dependent and independent proliferation of different ES lines. This inhibition was due to a partial G1 arrest and S phase elongation of the cell cycle. In addition, induction of apoptosis as demonstrated by PARP1-, CASP7-cleavage and increased CASP3 activity significantly contributed to the reduction of the proliferative ability of ES lines. Single or combination treatment with the PI3K/mTOR inhibitor BEZ235 further increased EWS-FLI1 down-regulation and apoptosis of ES cell lines although single treatment with BEZ235 was less effective than JQ1 application. Consequently, tumour development was dose dependently suppressed with increased formation of apoptotic bodies in a xeno-transplant model in immune deficient mice.

Conclusion: These results overall indicate that ES may be susceptible to treatment with epigenetic inhibitors blocking BET bromodomain activity and the associated pathogenomic EWS-ETS transcriptional program.

O-061 | Local Relapse in Patients Treated in the French OS2006 Study: Incidence, Risk Factors and Outcome

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Background/Objectives: To study the incidence, risk factors and outcome of local relapses in osteosarcoma patients treated according to the OS2006 protocol.

Design/Methods: All patients enrolled in the French multicentre OS2006 study for an osteosarcoma of the limb who underwent surgery of the primary tumour after pre-operative chemotherapy were included in the current analysis. Chemotherapy was based on high-dose methotrexate or API-AI according to the age. In addition to chemotherapy, 138 patients received 10 monthly injections of zoledronate allocated by randomization.

Results: From the 522 patients recruited in OS2006, 422 matched the eligibility criteria for the current analysis. With a median follow-up of 4.4 years, 27/422 patients experienced a local relapse, 22 as a first event (isolated in 9 cases and associated with metastasis in 13), 5 as a subsequent event. Taking into account the competing events (deaths without prior local relapse in 83 patients, mainly related to metastatic progression/relapse), the cumulative incidence of local relapse was 6.7% (95%CI, 4.5-9.5%) at 4 years. Overall survival was 27% (95%CI: 13-49%) 3 years after local relapse. In univariate analysis, the only factor significantly associated with the risk of local relapse was the presence of metastases at diagnosis (subHR=2.38, 95% CI, 1.05-5.39, p=0.038), whereas tumour size >10 cm, pathologic fracture at diagnosis, and a resection reported as marginal or intra-lesional were border-line significant (p=0.056, 0.078 and 0.058, respectively). No significant association was observed between these four possible prognostic factors and the risk of local relapse in multivariate analysis. We did not observe any significant impact of the number of patients operated by the surgeon during the whole study (p=0.93).

Conclusion: Incidence of local relapse is low in this population. The local relapses were mostly combined with concomitant metastases and associated with a poor outcome. The study failed to clearly identify risk factors of local relapse.

O-062 | Results of Methotrexate-Etoposide-Ifosfamide Based Regimen in Osteosarcoma Patients Included in the French OS2006/Sarcome-09 Study

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Background/Objectives: In most countries, the standard chemotherapy for osteosarcoma combines high-dose methotrexate (M) and doxorubicin-cisplatin (AP). Based on the randomized OS94-trial, the French reference pre-operative chemotherapy for children and adolescents with osteosarcoma combines M and etoposide-ifosfamide (EI). We describe here the outcome of the 411 patients included in the French OS2006-trial between 2007 and 2014 and treated with M-EI.

Design/Methods: Pre-operative chemotherapy combined 7 M-courses (12g/m²) and 2 EI-courses (E=75 mg/m²x4, I=3 g/m²x4). Post-operatively, patients with good histologic response (<10% viable cells) and no metastases received 12 M-courses, 3 EI-courses whereas patients with poor histologic response or initial metastases received 5 M-courses and 5 AP-courses (A=75 mg/m², P=120 mg/m²).

Results: Median age was 14.4 years (4.7-24.5). Tumour was axial in 27 (7%) cases, and associated with definite distant metastases in 69 (17%). Overall, 390 underwent surgery, conservative in 358 (88%); 258 (66%) patients had a good histologic response.

Among the 249 patients included in the randomized trial (with Zoledronate, n=125; without Zoledronate, n=124) and evaluable for toxicity, most patients experienced at least one episode of severe toxicities (grade-4 hematological or grade-3/4 extra-hematological): neutropenia (97%), transaminase elevation (92%), febrile neutropenia (83%), thrombocytopenia (45%), metabolic toxicity (39%), infection without neutropenia (39%), mucositis (34%), and other gastrointestinal toxicity (34%).

With a median follow-up of 4.8 years, an event was reported in 169 patients. Five-year event-free (EFS) and overall (OS) survivals were 56% (95%CI, 51-61%) and 71% (65-77%) respectively for the whole cohort, and 24% (15-36%) and 41% (29-54%) respectively for patients with definite metastases. Five-year EFS was 68% (61-74%) and 39% (30-49%) for good and poor responders respectively.

Conclusion: MTX-Etoposide-ifosfamide proved feasible and efficient leading to survival rates quite similar to MAP regimen, while sparing 40% of the patients from long-term toxicity of cisplatin and doxorubicin.

FREE PAPERS SESSION 12: RETINOBLASTOMA

O-063 | International Survey of Staging for Retinoblastoma Provides Evidence for the 2016 8th Edition AJCC TNM Retinoblastoma Cancer Staging

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Background/Objectives: Disparate staging schemes have undermined the quality of clinical retinoblastoma studies. We and the Ocular Oncology Task Force sought evidence to support prognostic staging of retinoblastoma for eye salvage, metastasis and survival for the 8th edition AJCC TNM cancer staging manual.

Design/Methods: An International Internet-based Survey was used to collect data and determine cancer stage by algorithms for 5 different eye and 3 systemic staging systems. The host institution (University Health Network) REB approved the retrospective study; each participating Centre obtained local approval.

Results: Seventeen Centres in 13 countries collected data on 2,293 children, 3,500 affected eyes, presenting between 2001 and 2011. "Success" to salvage eyes (avoidance of enucleation or external beam radiotherapy) was best predicted by the 2005 International Intraocular Retinoblastoma Classification. Both the 2006 variant Classification and 7th edition AJCC TNM failed to distinguish eyes at high risk for extraocular extension. Survey data, published literature and consensus discussions were used in development of the 8th edition AJCC TNM, which yielded improved prediction of ocular salvage compared to previous eye staging schemes when tested against the Survey data. A new category "H" for heritability is included, since germline *RBI* gene mutation imposes a lifelong risk of second cancers.

Conclusion: The Ocular Oncology Task Force and International Multicenter Survey produced globally applicable evidence for the 8th edition AJCC TNM cancer staging for retinoblastoma.

O-064 | Treatment of Unilateral Retinoblastoma. Preliminary Results of a Multicentric Prospective Study of Galop (Grupo De America Latina De Oncologia Paediatrica)

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Background/Objectives: To evaluate the efficacy of an intense adjuvant therapy of higher risk patients. To evaluate the use of pre-enucleation chemotherapy for children presenting with severe buphthalmia. To assess the safety of withdrawing adjuvant therapy for children with lower risk features.

Design/Methods: Single arm, multicentric, prospective study (2008-2014). Treatment: IRSG Stage 0: non-protocolized conservative therapy. Stage I, high risk (retrolaminar invasion and/or intra-scleral invasion), 4 cycles of adjuvant chemotherapy with carboplatin 500 mg/m²/days 1-2, etoposide 100 mg/m²/days 1-3; alternating with 4 cycles of cyclophosphamide 65 mg/kg/day, idarubicin 10 mg/m²/day and vincristine 0.05 mg/kg/day. Stage II-IV were reported to the COG-ARET 0321 protocol. Children with severe buphthalmia received pre-enucleation chemotherapy with the same agents and adjuvant therapy up to a total of 8 cycles.

Results: Stage 0=42; standard risk stage I = 84 and high risk stage I=41. There were 8 patients in the buphthalmia group. With a median follow-up of 40 months, the 3-year event free survival (pEFS) was 0.97 and overall survival 0.98. Events: Stage 0: no event, stage I (standard risk) 1 event (orbital relapse retrieved with second line therapy); stage I (high risk), 2 events (1 CNS relapse, 1 death of toxicity); buphthalmia group 1 event (orbital relapse followed by CNS relapse and death). For stage 0 patients receiving systemic chemotherapy (n=23), the possibility of radiotherapy-free eye preservation at 5 years was 0.35, compared to 0.6 for those treated with intra-arterial chemotherapy (n=19) (p=0.2).

Conclusion: The protocol was feasible at a multicentric level. Survival was excellent, avoiding adjuvant therapy in more than 40% of the children. The adjuvant therapy regimen was highly effective, however there was one toxic death. Pre-enucleation chemotherapy avoided the occurrence of tumour at the resection margin of the optic nerve. Children receiving intra-arterial chemotherapy had a higher eye preservation without risk of metastatic disease.

O-065 | Management of Uni- or Bilateral Retinoblastoma with Radiologic Optic Nerve Enlargement at Diagnosis

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Background/Objectives: To evaluate treatment and outcome of patients with uni- or bilateral retinoblastoma (RB) with radiologic optic nerve enlargement (RONE) at diagnosis.

Design/Methods: Retrospective clinical, radiological and histological review of patients with uni- or bilateral RB with RONE at diagnosis treated in the Institut Curie.

Results: Between 1997 and 2014, 936 patients with RB were treated in the Institut Curie. Eleven patients had detectable RONE confirmed by Computed Tomography and/or Magnetic Resonance Imaging. RB was unilateral in 10/11 patients, bilateral in 1. Median age at diagnosis was 29 months (range 12-96). The patient with the bilateral RB had a unilateral RONE. Three patients had an intraorbital RONE, 5 had a RONE in the optic canal, 2 had a prechiasmatic RONE and 1 had a chiasmatic RONE. Nine received neoadjuvant chemotherapy (CT) and 2 had a primary enucleation. Partial response to neoadjuvant CT was obtained for all the patients. Enucleation was performed in 10/11 patients, by anterior approach in 3 patients, by anterior and subfrontal approach in 7 patients. Three patients had positive ON margin and among them, 2 were primary enucleated. All enucleated patients received adjuvant treatment (conventional CT: 10, High Dose CT: 7 and radiotherapy: 5). Three patients died of meningeal progression (2 during treatment and 1 six months after the end of treatment). The patient with the bilateral RB was lost to follow up just after a meningeal progression during treatment. Seven are still alive (median follow up: 8 years, range: 1.5-17.5).

Conclusion: Neoadjuvant CT has an important place in the management of RB with RONE at diagnosis. Pretreatment accurate staging by orbital and brain MRI is mandatory, as well as preoperative reassessment. Surgery should be performed by experienced ophthalmologists and if necessary neurosurgical team in order to obtain the best conditions for a tumour-free resection margin in patients with RONE.

O-066 | Risk of Metastases and Orbital Recurrence in Advanced Retinoblastoma Eyes Treated with Systemic Chemoreduction Versus Enucleation

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Background/Objectives: To evaluate the risk of metastatic disease and orbital recurrence in advanced retinoblastoma treated by systemic chemoreduction (CRD) vs. primary enucleation (PE).

Design/Methods: Retrospective review of patients diagnosed with advanced retinoblastoma (Group D or E) in at least one eye from January 1, 1995 to August 1, 2015. Overall, 345 eyes of 294 patients were included; 180 were designated as Group E and 165 Group D. Eyes were treated with either CRD with vincristine, etoposide and carboplatin with local consolidation or PE. Outcome measures were orbital relapse and metastatic disease.

Results: Of 345 eyes, 139 were treated with CRD (102 Group D, 39 Group E eyes) and 206 with PE (63 Group D, 143 Group E). In the CRD group, 1 patient developed a metastasis and 1 developed an orbital recurrence. In the PE group, 2 patients developed metastases and 1 developed an orbital recurrence. After systemic chemotherapy, 30 Group D and 28 Group E eyes were enucleated due to treatment failure. The average time to enucleation from diagnosis was 14 months (range 1-118 months), and none of the eyes were found to have high-risk pathologic features. Average follow-up for the entire group of patients was 86 months.

Conclusion: Over a 20 year period, 345 eyes of 294 patients were treated for advanced (Group D/E) retinoblastoma at Children's Hospital Los Angeles. Rates of orbital recurrence and metastatic disease were exceedingly low and did not vary significantly by primary treatment modality or Group Classification. None of the eyes that were enucleated due to failure of CRD were found to have high-risk pathology, and these patients did not develop metastatic disease. This study suggests that attempted salvage of advanced eyes with systemic chemotherapy, with enucleation for poor therapeutic response, does not increase the risk of metastatic disease or orbital recurrence.

FREE PAPERS SESSION 13: CNS TUMOURS - EMBRYONAL

O-067 | Integrating Clinical and Molecular Genetic Data in AT/RT – Results from the European Rhabdoid Registry (EU-RHAB)

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Background/Objectives: EU-RHAB was initiated to prospectively collect clinical and genetic data of homogeneously treated patients, to define a standard of care and eventually lay the groundwork for phase I/II trials.

Design/Methods: One hundred and thirty patients with AT/RT were evaluable. Therapy followed the EU-RHAB guidelines. Analyses of *SMARCB1* (MLPA, FISH, sequencing) and the epigenome (450k Illumina analyses and tyrosinase staining) segregated molecular subgroups.

Results: 48% of tumors were located infratentorially and 3% were spinal; four demonstrated synchronous tumors. In 40 a complete resection was achieved. 87 completed EU-RHAB chemotherapy. HDCT was applied in 31 patients. 86 patients received radiotherapy, 18 of them protons. SAE were VOD (8%), radionecrosis (3%), leukoencephalopathy (1.5%) and secondary AML (0.7%). CR was achieved in 69 patients, in 13 by surgery alone and in 56 by additional chemotherapy.

In 20 of 96 evaluable patients germ line mutations were detected. Complete genetic analysis of *SMARCB1* was available in 57 patients and segregated three subgroups. 42% had homozygous deletions of *SMARCB1*, 31% had a mutation (frame shift, splice site mutation, intragenic deletion) in one and deletion of *SMARCB1* in the other allele and 19% demonstrated mutations on both alleles. Tyrosinase staining was performed in 58 patients, (34% TYR-subgroup). 450k methylation was investigated in 19 patients and resulted in 42% SHH-, 31% TYR- and 27% MYC-subgroup affiliation. TYR-subgroup affiliation suggested improved outcome.

Conclusion: EU-RHAB has defined a standard of care for AT/RT. It is the basis for improved insights into the clinical and molecular heterogeneity. Yet more data are needed to design clinical trials targeting defined subgroups. Supported by the „Deutsche Kinderkrebsstiftung“, KinderKrebsInitiative Buchholz Holm/ Seppensen, „Elterninitiative Horizonte“, „Elterninitiative Lichtblicke e.V.“ and the Fördergemeinschaft Kinderkrebszentrum Hamburg e.V.

O-068 | Assessment of Treatment Approach and Survival Outcomes in a Modern Cohort of Patients with Atypical Teratoid Rhabdoid Tumour (ATRT)

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Background/Objectives: Atypical teratoid rhabdoid tumour (ATRT) is a rare brain tumour occurring primarily in children under the age of 3 years. Here we evaluate treatment approach and outcome in a large cohort of patients treated in the United States.

Design/Methods: Using the National Cancer Data Base (NCDB), all ATRT patients aged 0-18 years with complete treatment data were included for analysis. Standard statistical analysis was utilized to evaluate prognosis and outcomes using Kaplan-Meier survival curves, Cox-regression, and Fisher's exact paired test.

Results: A total of 361 ATRT patients diagnosed between 2004-2012 were evaluated. The cohort consisted of 51.5% males and 48.5% females with 74% of patients diagnosed prior to the age of 3 years. Metastatic disease was present at diagnosis for 15% of patients. For the entire cohort, 3-year overall survival (OS) was 35.3% with significantly higher OS for children >2 years old (3-year OS 52.1% vs. 29.2%, $p < 0.001$). OS significantly improved over the study period (3-year OS 45.3% 2004-2008 vs. 26.6% 2009-2012, $P < 0.001$). The utilization of trimodality therapy (surgery, chemotherapy and radiation) significantly increased over the study period (27.7% in 2004-2008 compared to 45% in 2009-2012, $p = 0.001$). On multi-variable analysis the use of trimodality therapy significantly improved OS (hazard ratio 0.39 (95% confidence interval 0.29-0.53). The best outcome was seen in patients with localized disease receiving trimodality therapy (3-year OS 58.2%).

Conclusion: ATRT is a rare and aggressive brain tumour, however, these data demonstrate a significant increase in survival for patients treated between 2004-2012. The use of trimodality therapy significantly increased and was associated with improved outcome. For patients with localized disease receiving trimodality therapy, OS at 3 years approaches 60%. However, further research in to optimal management of children <3 years old is needed given their significant worse OS compared to older children.

O-069 | First-Line Treatment Failures in Young Children with Desmoplastic Medulloblastoma (DMB) and Medulloblastoma with Extensive Nodularity (MBEN) Treated According to the HIT Protocols

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Background/Objectives: Most early childhood DMB and MBEN, sonic hedgehog (SHH) pathway-activated medulloblastoma, can be cured with chemotherapy alone. However, little is known about prognostic factors for treatment failure and salvage strategies.

Design/Methods: (i) Analysis of treatment outcome in 115 patients with DMB (n=79) or MBEN (n=36) treated in Germany, Austria, and Switzerland according to the HIT protocols (SKK'87, SKK'92, HIT 2000, HIT Registry [i.e. HIT cohort]). (ii) Description of 29 patients (25 DMB, 4 MBEN) with failure of a primary HIT strategy (22 patients from the HIT cohort and 7 patients treated in France, Russia, and U.K.).

Results: (i) 8-year overall survival was 91%±3% (DMB, 88%±4%; MBEN 97%±3%), 8-year progression-free survival (PFS) 78%±4% (DMB, 73%±5%; MBEN 91%±5%). Independent risk factors for treatment failure (PFS) were initial metastases (HR 4.12, 95%-CI 1.85 to 9.20, $p = 0.001$) and DMB subtype (HR 3.76, 95%-CI 1.85 to 9.20, $p = 0.001$). (ii) Failures (12 local/7 distant/10 combined) occurred 0.2-4.7 (median 1.0) years after primary diagnosis. Gorlin syndrome was present and suspected in 1 patient with DMB each. Treatment after failure included surgery (5 patients), chemotherapy (19) incl. high-dose chemotherapy (11), SHH-inhibitor (1), none (2), unknown (1). Radiotherapy as part of salvage treatment was given in 19 patients (craniospinal, 13; local, 3; unknown field, 3) at the age of 3.7 (2.6-8.2) years. 5-year overall survival after failure was 64% (±10%). Status at last follow-up was NED, 14; SD, 5; DOD, 9; dead of secondary oligodendroglioma III⁺, 1; with a median follow-up time of 2.9 (0.3-14.1) years after failure. 4 patients survived without radiotherapy, 2 with only local radiotherapy.

Conclusion: HIT chemotherapy strategies are effective first-line therapies for infant DMB/MBEN. Most patients with failure could be salvaged, predominantly with multimodal treatment including radiotherapy. However, the role of radiotherapy at relapse is still unclear. Testing for Gorlin syndrome is warranted.

O-070 | CCL2 Mediated Hematogenous Dissemination of Medulloblastoma Contributes to Leptomeningeal Metastasis

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Background/Objectives: Medulloblastoma (MB) is a malignant childhood brain cancer. Poor outcome in patients with MB is due to the appearance of leptomeningeal metastasis, but the vast majority of MB research is focused on the primary tumour. There are no targeted therapies for MB metastases, as a result metastatic MB is almost universally fatal. Current paradigm states that MB metastasizes through cells navigating in the cerebrospinal fluid with subsequent distal re-implantation on the leptomeninges, as opposed to metastasis through the blood.

Design/Methods: We performed sequencing and transcriptome analysis of human matched primary tumors and metastasis to identify genetic drivers of metastasis. We used a combination of genetically engineered mouse models and patient derived xenografts. We performed tail vein injection, flank and brain implantations as well as surgical anastomosis (parabiosis) of mice.

Results: We present extensive data showing that MB metastasizes hematogenously, as tumour cells injected into the tail vein, or implanted in the flank of NSG mice cause leptomeningeal metastases. Mice that are parabiosed are xenografted with MB into the brain of one twin, resulting in leptomeningeal metastases in the other. We can observe circulating tumour cells in mice bearing fluorescently tagged tumors, and in human patients with MB undergoing sequencing of peripheral blood. Comparison of the transcriptome between human primary and metastatic MB reveals higher expression of *CCL2* in the metastases. *CCL2* is a chemokine known to play an important role in metastasis of other cancers, and in the recruitment of monocytes into the brain in the setting of inflammatory diseases. By the way of overexpression and silencing experiments we provide functional validation that *CCL2* expression drives MB metastasis *in vivo*.

Conclusion: These data upend our view of the mechanism of leptomeningeal metastasis, and provide exciting and novel avenues to both the diagnosis and treatment of metastatic MB.

O-071 | Recurrent Medulloblastoma: Improved Survival with a Metronomic and Targeted Antiangiogenesis Therapy – Experience in 28 Patients

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Background/Objectives: Patients with recurrent medulloblastoma have a poor prognosis with only around 8% of patients surviving more than 5 years irrespective of salvage therapy used. An evolving alternative approach to conventional chemotherapy is to target neovascularisation by interfering with tumour angiogenesis at various levels. We report on 28 patients from 5 institutions treated with an antiangiogenic combination therapy.

Design/Methods: From 11/2006 to 10/2015, 28 patients were diagnosed with a recurrent medulloblastoma (20 first, 8 multiple recurrences). Median age at start of antiangiogenic therapy was 10 years (range 1-27). Subgroup of medulloblastoma was available in 15 patients and was group 3 or 4 in all except two (one WNT, one SHH-infant with biallelic MSH2 loss). For their current relapse patients received an antiangiogenic combination therapy consisting of bevacizumab, thalidomide, celecoxib, fenofibrate, and etoposide alternating with cyclophosphamide, and augmented with intraventricular therapy (etoposide and liposomal cytarabine).

Results: As of 03/2016, 15/28 patients are alive at a median of 18 months (4 to 89) after their last recurrence. 9/15 surviving patients are currently in CR at 89, 86, 85, 59, 26, 20, 18, 18, and 15 months, and 8/9 off therapy for 69, 52, 50, 27, 6, 6, 5, and 2 months. Five patients are in partial remission 18, 12, 11, 10 and 4 months after their last recurrence and one patient is progressive after 15 months. One patient died of an accident without signs of tumour progression on MRI 23 months after initiation of antiangiogenic therapy. OS was 81±8% after 1 year, 67±10% at 2 years and 43±13% at 5 years. Therapy was generally well tolerated and toxicities were manageable.

Conclusion: Our results suggest that antiangiogenic metronomic chemotherapy has clinical activity in recurrent medulloblastoma. Further investigation with a formal international phase II study has started (MEMMAT; ClinicalTrials.gov Identifier: NCT01356290).

O-072 | Impact of Hydrocephalus on Neurocognitive Function One Year after Diagnosis with Medulloblastoma and Treatment on the ACNS0331: A Report from the Children's Oncology Group

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Background/Objectives: Children with medulloblastoma have well-documented neurocognitive deficits secondary to tumour and treatment. Although understudied in children with medulloblastoma, hydrocephalus has been implicated as a risk factor for cognitive decline. We report on hydrocephalus and neuropsychological functioning in patients enrolled on the Children's Oncology Group (COG) standard-risk medulloblastoma trial, ACNS0331.

Design/Methods: Enrolled children completed a neuropsychological evaluation 6-12 months after diagnosis. Assessments measured estimated IQ; working memory; processing speed; visual and verbal memory; and parent-reported emotional/behavioral functioning. Data were extracted from neurosurgical reports describing the presence of hydrocephalus at the time of surgery and if any hydrocephalus-directed procedure was performed (i.e., ventriculostomy, external ventricular drain, shunt), and whether hydrocephalus persisted post-surgically.

Results: Participants (N=278; 3 - 21 years; 62.2% male; mean age = 9.26, SD = 4.07) were assessed at an average of 7.12 (SD = 2.89) months post-diagnosis. The majority of the sample (n = 222, 80.2%) exhibited hydrocephalus at the time of resection, though only a third (n=93) received a hydrocephalus-directed procedure. Interventions included external ventricular drain (13.3%), shunt (13.3%), and third ventriculostomy (5.4%). Children receiving surgical intervention for hydrocephalus exhibited lower processing speed ($p = 0.036$) and inferior visual ($p < 0.001$) and verbal ($p = 0.017$) memory than those who required no directed intervention. Full-scale IQ was not affected by either the presence of hydrocephalus or any procedure required for its amelioration.

Conclusion: Identification of clinically meaningful hydrocephalus and its impact on neurocognitive outcomes may be critically important in children with medulloblastoma. While this analysis suggests that children with hydrocephalus requiring intervention show specific cognitive weaknesses, the somewhat subjective definitions of hydrocephalus and subsequent decisions about treatment make it difficult to discern the true risks. Our future plans include centralized

review of prospectively-obtained MRI scans to define and describe hydrocephalus with more specificity.

FREE PAPERS SESSION 14: LATE EFFECT - CARDIAC/CNS

O-073 | Cardiac Autonomic Dysfunction in Adult Survivors of Childhood ALL: A Report from the St. Jude Lifetime Cohort Study

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Background/Objectives: Although cardiac autonomic dysfunction (AD) has been suggested as a potential cause of diminished exercise capacity in survivors of childhood acute lymphoblastic leukaemia (ALL), the prevalence of and treatment-related risk factors for this impairment have not been reported in long-term survivors.

Design/Methods: Adult survivors of childhood ALL, treated between 1980 and 2003, and controls matched for age, sex and race were evaluated with cardiopulmonary exercise testing (CPET). Parameters of AD (abnormal resting heart rate [RHR] >80 beats/minute (bpm) or abnormal heart rate recovery [HRR] one minute post CPET \leq 12 bpm) at rest and in response to exercise were compared between survivors and controls and between survivors with and without AD. Treatment-related risk factors for AD among survivors were evaluated with multivariable generalized linear regression.

Results: ALL survivors (N=328, 49% female, mean age 28.5 \pm 6.0 years, mean age at diagnosis 6.8 \pm 4.5 year) had higher mean RHR (73.4 \pm 12.7 vs. 71.5 \pm 12.3 bpm, p=0.04), lower HRR (21.8 \pm 9.3 vs. 24.8 \pm 9.9 bpm, p<0.001), lower peak oxygen uptake (24.1 \pm 6.3 vs. 27.5 \pm 8.1 milliliters/kilogram/minute (ml/kg/min), p<0.001), and lower Duke Treadmill scores (9.9 \pm 3.3 vs. 11.1 \pm 3.1, p<0.001) than controls (N=325). The 33.7% of the survivors with evidence of AD had lower mean peak oxygen uptake (21.2 \pm 4.9 vs. 25.6 \pm 6.5 ml/kg/min, p<0.001) during CPET than the other 66.3% of the survivors without AD. In adjusted models, alkylating agent exposure was the only treatment factor associated with AD (Relative Risk (RR) 2.2, 95% Confidence Interval (CI) 1.3-3.4 for <7,500 mg/m² cyclophosphamide equivalent dose; RR 1.9, 95% CI 1.1-3.1 for \geq 7,500 mg/m² compared to no cyclophosphamide).

Conclusion: Cardiac AD is present in a third of ALL survivors and is associated with reduced exercise capacity. This impairment should be considered when caring for survivors, particularly those exposed to alkylating agents.

O-074 | Pharmacogenomic Strategies for the Prevention of Anthracycline-Induced Heart Failure: Validation of a Genetic Association with a Non-Synonymous Variant in RARG

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Background/Objectives: Anthracyclines are used in over 50% of childhood cancer treatment protocols, but their clinical usefulness is limited by anthracycline-induced cardiotoxicity (ACT) manifesting as asymptomatic cardiac dysfunction and congestive heart failure in up to 57% and 16% of patients, respectively. Candidate gene studies have reported genetic associations with ACT, but these studies have in general lacked robust patient numbers, independent replication or functional validation. Thus, the individual variability in ACT susceptibility remains largely unexplained. We performed a genome-wide association study in 280 patients of European ancestry treated for childhood cancer, with independent replication in similarly treated cohorts of 96 European and 80 non-European patients. We identified a non-synonymous variant (rs2229774, p.Ser427Leu) in RARG highly associated with ACT (P = 5.9 \times 10⁻⁸), odds ratio (95% CI) = 4.7 (2.7-8.3). Here we explore the impact of this variant on RARG function.

Design/Methods: RARG Ser427Leu was generated by site-directed mutagenesis and compared to wild type in a retinoic acid receptor (RAR) reporter assay. Gene expression in the H9c2 cardiomyoblast cell line was measured by quantitative RT-PCR. The MTT assay was used to measure H9c2 cell viability following doxorubicin treatment with and without co-treatment with an RAR ligand *all trans retinoic acid* (ATRA). Transient gene silencing was performed using siRNA constructs.

Results: RARG Ser427Leu was impaired in transcriptional regulation, particularly regulation of the ACT-related gene, *TOP2B*. We also showed that the RAR ligand, ATRA, induced the transcriptional repression of *Top2b*, putatively through RARG. Furthermore, we demonstrated that ATRA had cardioprotective properties in H9c2 cells that was RARG-dependent. These data suggest that RARG is a potential target for therapeutic intervention to prevent anthracycline-cardiotoxicity.

Conclusion: These findings provide new insight into the pathophysiology of this severe adverse drug reaction and support further investigation of RARG as a new target for strategies to prevent anthracycline cardiotoxicity.

O-075 | Neuropsychological Functioning One Year after Diagnosis of Paediatric Medulloblastoma: Results from Children's Oncology Group (COG) ACNS0331

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Background/Objectives: Cognitive late effects in survivors of medulloblastoma are well-documented; however, the onset and development of domain-specific difficulties have not been well-described in large, prospective cohorts. We aimed to examine neuropsychological functioning within the first year following diagnosis for children receiving treatment for medulloblastoma on a clinical trial.

Design/Methods: Children aged 8 and older diagnosed with medulloblastoma and treated on the Children's Oncology Group (COG) protocol ACNS0331 were invited to participate in neuropsychological testing as part of the original study design or, later, in conjunction with COG protocol ALTE07C1. All children received 23.4 Gy of craniospinal irradiation with a boost to 54 Gy to the entire posterior fossa (standard boost) or tumour bed (reduced volume boost), plus standard chemotherapy. Participants were evaluated at 9 (+3) months post-diagnosis with a battery measuring intellectual functioning, processing speed, and working memory.

Results: One hundred fifty-eight participants (mean age=12.3, range 8-20 years; 62.7% male; 78.5% white) were evaluated. Mean estimated IQ was in the average range, as measured by age-appropriate versions of the Wechsler scales (mean=96.1, SD=15.5), and did not differ significantly by radiation treatment group. Similarly, verbal and nonverbal working memory were not significantly impacted by boost volume. In contrast, overall processing speed scores were impaired (n=53; mean=81.0, SD=13.5), and children who received a standard radiation boost evidenced greater impairment (mean=76.6, SD=13.4) than those who received a reduced volume boost (mean=84.9, SD=12.6).

Conclusion: Children with medulloblastoma demonstrated impaired processing speed in the first year after diagnosis; scores were further diminished for children treated with a whole posterior fossa boost. Slower processing speed has been linked to reduced white matter volume in children treated with cranial radiation. Results suggest that processing speed deficits may be the first indicator of emerging, treatment-related cognitive late effects.

O-076 | Neuropsychological Outcomes on "Head Start" III: A Prospective, Non-Randomized Multi-Institutional Clinical Trial, 2003 - 2009

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Background/Objectives: Treatment on "Head Start" III protocol consisted of surgical resection, 5 cycles of induction chemotherapy, followed by consolidation with myeloablative chemotherapy and autologous hematopoietic progenitor cell rescue (AuHCR) with an aim of either avoiding or reducing the dose and volume of irradiation.

Design/Methods: Twenty-seven subjects underwent a mean of 3.6 comprehensive neuropsychological evaluations (range, 2-5), with average age at diagnosis of 34.3 months. Eleven were male (40.7%) and 16 were female (59.3%), 12 (44.4%) White, 10 (37.0%) Hispanic, 2 (7.4%) African-American, and 3 (11.1%) other. Thirteen (48.2%) were diagnosed with medulloblastoma. Tumour locations included: 17 (63.0%) infratentorial, 9 (33.3%) supratentorial, and 1 with leptomeningeal metastasis (3.7%). Eighteen subjects did not receive irradiation (66.7%), 4 (14.8%) received focal irradiation, and 5 (18.5%) received cranial-spinal irradiation with a boost to the primary tumour site. Neuropsychological assessment included standardized measures of verbal and nonverbal reasoning, working memory, processing speed, executive functioning, verbal and nonverbal learning and memory, adaptive functioning and social-emotional adjustment.

Results: Analysis of the most recent evaluation, obtained at an average of 6.08 years post-diagnosis (range, 1.56-9.79 years), indicated mean average abilities for verbal reasoning (VCI=90.75; sd=13.21) and nonverbal reasoning (PRI=93.10; sd=13.71), with low average processing speed (PSI=87.21; sd=15.72) and working memory (WMI=87.70; sd=17.42). Additionally, both mean verbal and nonverbal learning and memory were in the average range (Stories Delay=9.20; sd=3.27; CVLT-C=-0.25; sd=1.56; Faces Delay=9.94; sd=3.15; Dot Locations Delay=10.14; sd=3.20). Standardized parent-report indicated mean average executive functioning (BRIEF) and did not indicate significant concerns regarding mood, behavior or social functioning (BASC-2). Summary of change scores of those who had both pre- and post-evaluations indicated no significant change over time across all domains assessed.

Conclusion: Results suggest that mean neuropsychological functioning is preserved in survivorship, with average to low-average neurocognitive abilities, using this irradiation avoiding treatment strategy in the youngest of children.

O-077 | Epigenome-Wide Association Study Identifies Novel Susceptibility Loci for Treatment-Related Ototoxicity among Survivors of Paediatric Medulloblastoma

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Background/Objectives: Survivors of paediatric medulloblastoma exposed to cisplatin chemotherapy and craniospinal radiotherapy experience high rates of treatment-related ototoxicity, resulting in permanent hearing impairment. However, the mechanism responsible for ototoxicity is not fully understood and individual susceptibility is highly variable. Epigenetic mechanisms, including DNA methylation, are important regulators of gene activity. Our objective was to evaluate the role of DNA methylation on individual susceptibility to ototoxic therapy.

Design/Methods: Our study population included a discovery cohort (n=62) and a replication cohort (n=18) of survivors of medulloblastoma enrolled during the period 2005-2012 and treated with cisplatin-containing regimens. Audiograms were evaluated from the last available visit and graded according to the SIOP ototoxicity scale. Genome-wide DNA methylation was assessed with the Illumina HumanMethylation450 BeadChip array. Associations between cytosine-guanine (CpG) methylation and ototoxicity were examined using multiple linear regression, controlling for demographic and treatment factors. We accounted for multiple comparisons at a false discovery rate $q < 0.05$.

Results: In our population, the mean cumulative dose of cisplatin was 330 mg/m² (range: 100-720 mg/m²). The mean time from end-of-therapy to the last available audiogram was 6.9 years. Of the 435,233 CpG sites which passed quality control and filtering, six were associated with ototoxicity ($p < 5.0e-5$). Differential methylation at the top CpG site identified in the discovery cohort (cg14010619, *PAK4* gene) was replicated ($p = 0.029$) and reached genome-wide significance ($p = 2.73e-8$; $q = 0.011$) in a combined analysis (n=80). Based on data from the Gene Expression Omnibus (GEO), cg14010619 methylation correlated with *PAK4* mRNA expression ($p = 0.002$).

Conclusion: We identified and replicated a novel CpG methylation loci (cg14010619) associated with ototoxicity severity among similarly treated survivors of paediatric medulloblastoma. Methylation at cg14010619 corresponded to increased *PAK4* expression, a key regulator of caspase-dependent apoptosis. Notably *PAK4* expression has been implicated in cisplatin resistance in malignant cell lines. These findings warrant further exploration into the biological mechanism underlying ototoxicity susceptibility.

O-078 | Suicide and Violent Deaths in Survivors of Cancer in Young Age – A National Cohort Study

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Background/Objectives: The number of survivors after cancer in young age is increasing. Suicide is one of the most common causes of death in young people. We wanted to study suicide and violent deaths in a nationwide cohort including individuals diagnosed with cancer before 25 years of age.

Design/Methods: Through linkage of several national registries (Cancer Registry of Norway, Norwegian Causes of Death Registry, and the National Registry), a cohort of all live births in Norway during 1965-1985 was defined and followed through 2008. Those diagnosed with cancer before age 25 and the cancer-free references were compared using an extended Cox proportional hazard regression model, for the outcomes of suicide and non-suicidal violent deaths.

Results: The cohort consisted of 1,218,013 individuals, including 5,440 diagnosed with cancer before the age of 25. We found cancer survivors to have a heightened risk of suicide (Hazard ratio (HR)= 2.5; 95% CI 1.6-3.7), but not of violent deaths, suicide excluded (HR=1.0; 95% CI 0.6-1.7). There were 24 suicides in the cancer group, which were completed at a range of 6 to 497 months after diagnosis (median 146), and at a mean age of 28 years. The increased hazard of suicide was sustained regardless of being diagnosed in childhood (0-14 years); HR= 2.3 (95% CI 1.2-4.6), or during adolescence and young adulthood (15-24 years); HR=2.6 (95% CI 1.5-4.1). The suicide risk was in particular increased in survivors of bone/soft tissue sarcomas (HR=8.2; 95% CI 2.6-25.5), brain tumors (HR=3.9; 95% CI 1.9-8.3) and testicular cancer (HR=2.9; 95% CI 1.3-6.4).

Conclusion: In this prospective national cohort study, we found a 2.5-fold increased risk of suicide in survivors of cancer diagnosed before 25 years of age. These are novel findings, and important for building risk-stratified follow-up guidelines for survivors of cancer in young age.

FREE PAPERS SESSION 15: MOLECULAR PROFILING OF PAEDIATRIC TUMOURS

O-079 | Genome-Wide DNA Methylation Profiles Identify Two Distinct Wilms Tumour Subgroups

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Background/Objectives: Wilms tumours (WT) are clinically heterogeneous neoplasms. Their natural history can include both relapse and second primary malignancy - often in the contralateral kidney. These outcomes are difficult to predict and treatment decisions often must be made that increase the risk of late adverse events such as second malignancies. The clinical heterogeneity in WT is not accounted for by current knowledge of their biology. Alterations in DNA methylation are important in WT development as evidenced by the high prevalence of methylation changes at the 11p15 locus as well as at 3 recently identified regions.

Design/Methods: We examined genome-wide DNA methylation in 32 WT using the Infinium 450K methylation array platform in order to identify patterns that would account for their biological heterogeneity. Non-neoplastic kidney tissues obtained during nephrectomy for WT treatment were used as controls.

Results: An unsupervised analysis using genome-wide data identified 2 discrete subgroups of WT. Subgroup A clustered closely with control kidney samples and did not exhibit significant alterations in DNA methylation. Subgroup B, on the other hand, had distinctive methylation patterns with increased methylation particularly evident in genes associated with renal development and cancer-related processes. We also found that all four relapses occurred in subgroup B. Otherwise there was no clinical or demographic difference between the two groups. Loss of imprinting was evident in the majority of subgroup B tumors at multiple imprinting control centres such as those found at 11p15 and RB1. Conversely, most tumors in subgroup A maintained imprinting at these loci.

Conclusion: Analysis of genome-wide DNA methylation reveals two distinct subgroups of WT. While one seems to be widely affected by alterations in DNA methylation and imprinting, the other is more likely to be driven by other processes such as gene mutations. Genome sequencing will be undertaken on these tumors to test this hypothesis.

O-080 | Genome-Wide Analysis of DNA Methylation in Hepatoblastoma Tissues

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Background/Objectives: Objectives: DNA methylation has a crucial role in cancer biology. We performed a genome-wide analysis of DNA methylation in hepatoblastoma (HB) tissues to verify differential methylation levels between HB and normal tissues. As alpha-fetoprotein (AFP) has a critical role in HB, we also detected AFP methylation levels, using pyrosequencing.

Design/Methods: Methods: Normal and HB liver tissue samples were obtained from patients with HB. Genome-wide analysis of DNA methylation in these tissues was performed using an Infinium HumanMethylation 450 BeadChip, and results confirmed with quantitative RT-PCR (q-PCR).

Results: Results: The Infinium HumanMethylation 450 BeadChip showed distinctively less methylation in HB tissues than in non-tumour tissues. We also found methylation enrichment in positions near the transcription start site of AFP, which exhibited lower methylation levels in HB tissue than in non-tumour liver tissues. Lastly, we found a significant negative correlation between AFP mRNA expression and DNA methylation percentage, using linear Pearson's R correlation coefficients.

Conclusion: Conclusions: Our results demonstrate differential methylation levels between HB and normal tissues, and imply that aberrant methylation of AFP in HB could reflect HB development. Expansion of these findings could provide useful insight into HB biology.

O-081 | Genome-Wide Multi-Omic Analysis of Paediatric Pancreatoblastoma

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Background/Objectives: Pancreatoblastoma (PB) is a rare pancreatic malignancy that typically presents in young children. Although recurrent somatic alterations affecting Wnt/beta-catenin signaling pathway and allelic loss of chromosome 11p have been reported, genetic basis underlying the pathogenesis of PB remain to be elucidated. To describe genetic and transcriptomic landscapes of PB, we performed whole-exome sequencing (WES), whole-transcriptome sequencing (WTS) and SNP array analysis in 11 cases of PB.

Design/Methods: We performed WES of paired tumour-normal samples from 7 cases followed by target deep sequencing of *CTNNB1* in 11 cases. SNP array-based copy number analysis was conducted in 8 cases with fresh frozen samples. In 7 cases for which RNA was available, WTS was also performed.

Results: *CTNNB1* was only recurrently mutated in 6 cases, and following deep sequencing identified *CTNNB1* mutations in 7 of 11 cases. Uniparental disomy at 11p15.5, which causes loss of imprinting (LOI), was identified in 6 of 8 cases by SNP array analysis. One case had a

CTNNT1 mutation combined with 11p LOI as only genetic abnormality. Although no recurrent fusions were detected, expression clustering and pathway analysis in 7 cases and 10 normal pancreatic RNA samples revealed that PB, including 2 cases without *CTNNT1* mutations or 11p15.5 LOI, had a uniform expression profile clearly distinguished from normal pancreas. In accordance with the genetic changes, significant upregulation of Wnt signaling pathway including *CTNNT1* was observed in PB. In addition, 5 cases with 11p15.5 LOI overexpressed *IGF2*, which is imprinted at 11p15.5.

Conclusion: We have demonstrated that LOI at 11p15.5 and *CTNNT1* mutations are genetic hallmarks of PB and downstream expression profile is homogeneous, characterized by upregulation of Wnt signaling pathway. Although further genetic and epigenetic explorations for alterations affecting Wnt signaling pathway are required, our study revealed these shared abnormalities could be targets of small molecular therapy.

O-082 | Gene Expression-Based Classification of Paediatric Germ Cell Tumors

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Background/Objectives: Germ cell tumors (GCTs) are rare malignancies accounting for approximately 3% of cancers in children younger than 15 years. GCTs include several histological subgroups such as yolk sac tumour (YST) or teratoma. Since they derive from the same cell origin, the primordial germ cell, GCTs may have common genetic alteration. Although previous studies showed that adult GCTs are characterized by histology specific gene signatures and isochromosome of 12, genetic basis of paediatric GCTs is still to be elucidated due to its rarity.

Design/Methods: Our cohort includes 29 paediatric GCT samples (3 mature teratomas, 7 immature teratomas, 4 dysgerminomas, 12 yolk sac tumors, and 3 mixed germ cell tumors). We applied genome-wide analysis for genetic abnormalities using SNP array analysis in 29 cases, and whole-transcriptome sequencing (WTS) in 13 cases.

Results: SNP array analysis showed recurrent copy number gains at chromosomes 1q, 12p, and 21 (5 cases each). For gene expression profiling, we applied consensus clustering algorithms including expression data of normal ovaries or testes. WTS failed to find recurrent fusion genes, but consensus clustering of gene expression profiles identified that GCT samples stratify into 4 robust subgroups, which was clearly correlated with histological subtype. YST subtype showed distinguished expression profile compared with other subtypes or normal ovaries/testes. Intriguingly, *FGFR3* was significantly upregulated gene in YST, suggesting that activation of this gene have a potential role in the pathogenesis of YST.

Conclusion: Though no recurrent fusion genes were detected, we identified specific gene expression profiling of paediatric GCTs correlated with histological subtypes and significantly upregulated gene, *FGFR3*, in YST. To identify genomic basis of paediatric GCTs, further genome-wide analysis of each histology in large cohort is needed.

O-083 | Molecular Screening for Cancer Treatment Optimization (MOSCATO-01) in Paediatric Patients: A Prospective Molecular Stratification Trial

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Background/Objectives: This study (NCT01566019) explored the feasibility of on-purpose interventions at cancer recurrence or treatment failure and the characterization of genomic alterations in order to propose a targeted therapy. This report presents the paediatric part of the trial.

Design/Methods: Patients with recurrent or refractory solid tumour underwent after consent on-purpose tumour biopsy or surgical resection for molecular characterization by 180K CGHarray and 74 target genes sequencing. Since July 2014 Whole-Exome- and RNA sequencing was performed additionally. A molecular tumour board of scientists and clinicians reviewed results to determine biological significance of the alteration and match patients to the most relevant targeted therapy available.

Results: From December 2012 to January 2016, 78 paediatric patients were included into the study. 73 patients with a median age of 11 years (range, 0.8-24.3), 63% with solid and 37% with brain tumors, underwent on-purpose intervention without major complications. As 6 patients had a rebiopsy, in total 79 interventions were performed. The median tumour cell percentage was 70% (range, 0-100%). In 2 patients the presumed diagnosis was not confirmed but a secondary malignancy diagnosed. CGHarray and NGS determined gene alterations considered as 'actionable' with a treatment available addressing the gene/protein or the involved pathway in 43.8% and 24.7% of patients, respectively. Of 41 patients (56.2%) with targetable alterations 10 patients received an adapted targeted therapy, two of them twice. However, a considerable amount of patients was not treated due to non-availability of the drug and/or an open trial.

Conclusion: High throughput molecular analysis of recurrent/refractory malignancies in paediatric patients is safe and feasible. Presence of multiple genetic alterations and limited access

to targeted agents within paediatric clinical trials remain the main limiting factors. The subsequent international trial MAPPYACTS (Molecular Profiling for Pediatric and Young Adult Cancer Treatment Stratification; NCT02613962) is ongoing in several European countries.

O-084 | Cancer Fluid Biopsy Using Circulating Tumour Cells and Circulating Free DNA in Childhood Solid Tumors

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Background/Objectives: Circulating Tumour Cells (CTCs) and circulating free DNA (cfDNA) represent a "cancer fluid biopsy" of the tumour potentially allowing real-time monitoring of cancer biology and therapies in individual patients. Our aims are to determine the applicability of CTCs and cfDNA as a "cancer fluid biopsy" of the tumour potentially allowing real-time monitoring of cancer biology and therapies in childhood solid tumour patients.

Design/Methods: Fifty-two consenting children admitted with solid tumors between 2010-2015 were recruited. cfDNAs isolated from 0.5 mL plasma obtained at diagnosis and during the treatments were analyzed by next-generation sequencing. And CTCs were isolated from 5-8 whole blood by negative sorting of blood mononuclear cells followed by direct trapping of a single floating cell using specific antibodies, i.e. GD2, CD56, CD133 within a nanospray tip. Mass spectrometry of the isolated CTCs was carried out after sonication.

Results: Total amounts of cfDNA were 54-825 ng and were significantly associated with stage of disease. In cfDNA, 13 mutations (2 *ALK*, 3 *TP53*, 1 *SMARCB1*, 3 *CTNNT1*, 1 *APC*, 1 *KIT*, 1 *RET*, and 1 *CDNK2AT*) and 4 deletions (2 *SMARCB1* deletion and 2 *CTNNT1* deletion) were identified. Using a single cell isolation method, we could succeed in trapping CTCs from 15 childhood tumour patient's blood samples and obtain their lipido-metabolomic molecular profile at the single cell level. In addition to vital molecules such as amino acids, catechol amine metabolites, which are specific to neuroblastoma, and drugs included in the patient's course of therapy were detected.

Conclusion: These data demonstrate the feasibility and potential utility of mutation/deletion screening in cfDNA using NGS for the detection of tumour biomarkers in children with solid tumors. And this "direct single-cell lipido-metabolomic method" seems to be useful for direct and wide range molecular detection in CTCs, for future molecular diagnosis without surgical biopsy.

FREE PAPERS SESSION 16: ALL

O-085 | Epigenetic Landscape of Relapsed Childhood Acute Lymphoblastic Leukemia

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Background/Objectives: Relapsed paediatric ALL is characterized by significant drug resistance. Previously, we discovered that HDAC inhibitor vorinostat reverses relapse-specific gene expression signature and restores blast chemosensitivity. In addition up to 60% of relapse samples acquire mutations in genes that regulate epigenetic mechanisms. Thus we hypothesize that drug resistance is also driven by aberrant epigenetic mechanisms.

Design/Methods: To map relapse specific epigenetic alterations, chromatin immunoprecipitation sequencing (ChIP-seq) was performed on 16 diagnosis/relapse marrow samples from patients enrolled on COG protocols. We assessed histone marks associated with promoters (H3K4me3, H3K9ac), enhancers (H3K27Ac) and transcriptional repression (H3K9me3, H3K27me3).

Results: The majority (approximately 75% range 60%-85%) of peaks overlapped between relapse and diagnosis within each patient. Across all patients, a range of dynamic (significant) changes were observed in individual marks gained (20-30%) or lost (5-10%) at relapse within promoter regions. Gene-expression correlation from NCI's TARGET database, showed that 17-25% of dynamic histone marks were associated with a significant (>two fold) change in expression. Typical enhancers (TE) and super-enhancers (SE) were identified using the H3K27Ac mark (ROSE algorithm). Across pairs, 5-18% TEs and 3-12% SEs were gained while 20-25% TEs and 5-11% SEs were lost at relapse. SEs at *NCOR2*, *SMAD3*, *BTG1* and *LFNG* (proximity rule) showed significant changes. While a majority (60-75%) of changes overlay the protein coding regions, we have observed dynamic changes in lincRNA and miRNA regions, which may also impact in transcriptional regulation.

Conclusion: In a pilot ChIP-seq analysis, we show significant shifts in the epigenome many of which are shared across patients. We have also identified several candidate genes whose transcription appears to be epigenetically regulated. We are currently expanding the data set to include additional pairs, which will lead to a comprehensive description of epigenetic events in relapsed ALL that will guide future therapy.

O-086 | P190BCR-ABL1 Signaling Modulates the Function of Tumour Suppressor Protein IKZF1

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Background/Objectives: The chromosomal translocation *BCR-ABL1* represents a high-risk cytogenetic subgroup in childhood B-cell precursor acute lymphoblastic leukaemia (BCP-ALL). The disease is characterized by the almost obligatory presence of *IKZF1* gene aberrations, arguing that loss of *IKZF1* function is required for oncogenic transformation by p190^{BCR-ABL1}. *IKZF1* mainly acts as a transcriptional repressor protein, and we hypothesized that *BCR-ABL1* signaling may modulate *IKZF1*-dependent transcription regulation in a direct or indirect manner by altering its protein function.

Design/Methods: Luciferase reporter assays and microarray gene expression analyses were performed to study the effect of p190^{BCR-ABL1} expression on *IKZF1*-dependent transcription. Mass spectrometry on purified protein complexes revealed changes in post-translational modifications of *IKZF1* induced by p190^{BCR-ABL1} signaling.

Results: Luciferase reporter assays employing the human BAX promoter revealed that *IKZF1*-induced transcriptional repression was alleviated by p190^{BCR-ABL1} expression. This effect was reversed by Imatinib, suggesting that *BCR-ABL1* signaling interferes with *IKZF1* function. Next, we assessed effects of p190^{BCR-ABL1} expression on *IKZF1* using the murine lymphoid Tet-On Ba/F3 (TonB) cell line. Gene expression analysis showed that several target genes repressed by *IKZF1* in TonB cells were transcriptionally induced by co-expression of p190^{BCR-ABL1}. Mass spectrometry was performed on FLAG-affinity purified *IKZF1* from transiently transfected HEK293 cells with or without p190^{BCR-ABL1}. In these assays, p190^{BCR-ABL1} signaling induced *IKZF1* phosphorylation on specific serine, threonine and tyrosine residues as well lysine acetylation. Western blot analysis using phospho-specific antibodies showed that *IKZF1* is subject to tyrosine phosphorylation by p190^{BCR-ABL1}, both in HEK293 cells and TonB cells. *In vitro* kinase assays showed that *IKZF1* is directly phosphorylated by active recombinant ABL kinase.

Conclusion: Our studies show that p190^{BCR-ABL1} signaling induces various post-translational modifications on *IKZF1*, which modify its properties as transcriptional regulator. We propose that modulation of *IKZF1* tumour suppressor function by p190^{BCR-ABL1} signaling is the driving force for *IKZF1* gene deletions in *BCR-ABL1*-positive leukaemia.

O-087 | Baseline Clinical and Laboratory Features Predict Risk of Developing Symptomatic Thromboembolism (STE) During Antileukemic Therapy in Children with De Novo Acute Lymphoblastic Leukemia (ALL)

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Background/Objectives: Despite the high prevalence of thromboembolism (TE) in children with ALL, the predictors of ALL-associated TE remain uncertain. This study aims to define the effects of clinical [age, gender, ALL risk-group] and laboratory variables [hematological parameters, blood group, inherited and acquired prothrombotic defects (PDs)] at ALL diagnosis on the risk of developing symptomatic TE (objective confirmation of TE prompted by symptoms) in children receiving antileukemic therapy.

Design/Methods: This multicenter, prospective, analytical cohort study included consenting patients (1-18 yrs. of age) with *de novo* ALL enrolled on the Dana-Farber Cancer Institute 05-001 therapeutic trial. Samples collected prior to starting ALL-therapy were analyzed centrally for PDs [protein C, S, antithrombin, Factor VIII:C, von Willebrand factor (vWF), anticardiolipin antibodies and gene polymorphisms of methylene tetrahydrofolate reductase C677T, prothrombin G20210A, Factor V Leiden]. Age-adjusted standardized laboratory data defined PD. Details of patient demography, ALL diagnosis, therapy and sTE were collected. Regression analyses evaluated relationship between risk factors and sTE.

Results: Of 131 enrolled patients [mean age (range) 6.4 (1-17) yrs.; 70 boys], 21 (16%) developed sTE. Acquired or inherited PD, either alone or in combination, had no impact on the risk of sTE. Patients with sTE were significantly older ($p=0.048$), had significantly higher total count ($p=0.048$), hemoglobin ($p=0.041$) and presence of peripheral blasts ($p=0.02$) at ALL diagnosis than those without sTE. Multivariable analyses identified older age compared to age ≤ 5 yr. [Odds Ratio (OR) 1.9, $p=0.029$] and non-O blood-group (OR 4.27, $p=0.028$) compared to O group as independent predictors for development of sTE. Patients with peripheral blasts had higher odds of developing sTE (OR 7.79; $p=0.059$).

Conclusion: In addition to older age, non-O blood group and presence of peripheral blasts, but not PDs, predicted the risk of sTE during ALL therapy. We recommend evaluation of these novel risk factors in the development of ALL-associated TE.

O-088 | Immune Reconstitution in Children Following Chemotherapy for Acute Lymphoblastic Leukaemia

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Background/Objectives: Although survival rates for Acute Lymphoblastic Leukaemia (ALL) are now excellent, this is at the expense of prolonged (2-3 year) chemotherapy regimens. Here we report the long-term immune effects of such treatment.

Design/Methods: A prospective cohort of 104 children enrolled on the Pneumococcal-Conjugate vaccine clinical trial (ISRCTN: 12861513) and treated according to Medical Research Council UKALL 2003 protocol were studied. Peripheral blood lymphocyte subsets and immunoglobulins were studied during treatment and up to 18-months following treatment cessation.

Results: In our patient cohort (median age 6 years; range 2-17 years), total lymphocytes were reduced (21.62% of median for age) during maintenance chemotherapy and remained low (79.29% of median for age) at 18-months following treatment completion. CD4 cells and natural killer cells remained low at 18-months; CD8 cells recovered to near normal values. B-cell numbers fell much lower than T-cells during treatment, but recovered rapidly and rose above normal ranges following treatment completion (1.41% and 153.11% of normal median during treatment and one-year, respectively). Naïve B-cells followed a similar course. Memory B-cells, in particularly switched memory B-cells, remained low throughout. Of the immunoglobulins, IgM levels were most affected by chemotherapy; at 18-month follow-up low levels of IgM persisted in 25% of patients.

Conclusion: This study demonstrates that long-term immune reconstitution differs between lymphocyte compartments. Although total B-cell numbers rapidly recover following treatment cessation, derangement of memory/naïve compartment organisation persists at 18-months. Naïve cells contribute heavily to total B-cell numbers, suggesting that *de novo* B-cell generation is a major component to B-cell compartment reconstitution. In discordance with previous reports, the T-cell compartment demonstrated slow reconstitution with persistently low CD4 counts and only near normal CD8 T-cells counts by 18-months. This persistent disruption even 18-months following treatment completion further highlights the impact of modern chemotherapy regimens on immunity, and thus infectious susceptibility.

O-089 | No Benefit of High Dose Methotrexate (HD-MTX) in Intermediate Risk Childhood Acute Lymphoblastic Leukemia (ALL): Results of 2 Randomised Multicenter Trials in Russia

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Background/Objectives: HD-MTX is used in many protocols for therapy of childhood ALL. In the multicenter study ALL-MB (Moscow-Berlin) 2002 in 37 centers in Russia and Belarus 353 intermediate risk (ImRG) patients had been randomized to receive either low dose (LD) MTX 30 mg/m² IM weekly (n=182) or HD-MTX 3x2 g/m² biweekly (n=171). No benefit was seen for HD-MTX. To confirm the results, this randomization was continued in the subsequent trial ALL-MB 2008.

Design/Methods: Between Feb 21, 2008 and Jan 1, 2015, a total of 1314 patients from 46 centers were enrolled into MB 2008. In MB 2002, risk stratification was: standard risk (SRG): initial WBC < 50,000/mm³, non-T-cell, no CNS involvement, age > 1 year and CR on day 36; high risk (HRG): no remission on day 36; intermediate risk group (ImRG) all others. Since spleen enlargement ≥ 4 cm and WBC $\geq 30,000/mm^3$ were identified as adverse prognostic features, patients with these characteristics were no more allocated to SRG but to ImRG in MB 2008. Of 1314 patients, 669 were randomized to LD-MTX and 645 to HD-MTX.

Results: Results of MB 2002 are stable with event-free survival (EFS) rates of $78\% \pm 3\%$ and $73\% \pm 4\%$; $p=0.248$ for LD-MTX and HD-MTX, respectively, at 13-years. In ALL-MB 2008, 8-year EFS was $85\% \pm 2\%$ for LD-MTX and $82\% \pm 2\%$ for HD-MTX ($p=0.281$); overall survival was $88\% \pm 2\%$ and $88\% \pm 2\%$, respectively; $p=0.343$. Differences in favor of HD-MTX were also not seen in subgroups (T-ALL, WBC > 100x10⁹/l). Overall relapse rates for LD-MTX (7.9%) vs. HD-MTX (8.5%; $p=0.765$) and isolated CNS relapses (LD-MTX: 1.1% vs. HD-MTX: 1.1%; $p=0.842$), were not different between randomized groups.

Conclusion: In ImRG patients, HD-MTX during consolidation did not show any advantage compared with LD-MTX in 2 subsequent large scale MB protocols.

O-090 | Hydrocortisone as an Intervention for Dexamethasone-Induced Side Effects in Children with Acute Lymphoblastic Leukemia: Results of a Double-Blind Randomized Controlled Trial

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Background/Objectives: Dexamethasone is a key component in treating paediatric acute lymphoblastic leukaemia (ALL), but can induce serious side effects. Recent studies have led to the hypothesis that neuropsychological side effects may be due to cortisol depletion of the cerebral mineralocorticoid receptors. We examined whether including a physiological dose of hydrocortisone in dexamethasone treatment can reduce neuropsychological and metabolic side effects in children with ALL.

Design/Methods: We performed a multicenter double-blind, randomized controlled trial with a cross-over design. Fifty out of 116 potentially eligible patients (3-16 years) were enrolled and were treated with two consecutive courses of dexamethasone in accordance with Dutch Childhood Oncology Group ALL protocols. The patients were randomly assigned to receive either hydrocortisone or placebo in a circadian rhythm (10 mg/m²/day) during both dexamethasone courses. The primary outcome measure was the parent-reported Strength and Difficulties Questionnaire-Dut (SDQ), which assesses psychosocial problems. Other endpoint variables included questionnaires, neuropsychological tests, and metabolic parameters.

Results: Of the 48 patients who completed both courses, hydrocortisone had no significant effect on outcome. However, a more detailed analysis revealed that in 16 patients who developed clinically relevant psychosocial side effects, the addition of hydrocortisone substantially reduced their SDQ scores in the following domains: Total Difficulties, Emotional Symptoms, Conduct Problems, and Impact of Difficulties. Moreover, in nine patients who developed clinically relevant sleep-related difficulties, the addition of hydrocortisone reduced Total Sleeping Problems and Disorders of Initiating and Maintaining Sleep. In contrast, hydrocortisone had no effect on metabolic parameters.

Conclusion: Our results suggest that adding a physiological dose of hydrocortisone to dexamethasone treatment can reduce the occurrence of serious neuropsychological side effects and sleep-related difficulties in children with ALL.

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FREE PAPERS SESSION 17: NEUROBLASTOMA - BIOLOGY AND PRE-CLINICAL STUDIES

O-091 | Combination Therapy of Anti-PD-1 Antibody and CSF-1R Inhibitor Reverses Induction of Suppressive Myeloid Cells and Controls Spontaneous Neuroblastoma Progression

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Background/Objectives: We have previously demonstrated that neuroblastoma produces high levels of M-CSF and CSF-1R+ infiltrating myeloid cells are associated with poor clinical outcome in neuroblastoma patients. Combination of checkpoint blockade antibodies with CSF-1R inhibitors, targeting immune-suppression, might provide a novel treatment strategy for neuroblastoma.

Design/Methods: Distinct *in vitro* models were established to analyze the influence of neuroblastoma-derived factors and the role of M-CSF/CSF-1R signaling on 1) myelopoiesis of human CD34+ progenitor cells, 2) repolarization of primary human monocytes in tumour cocultures, and 3) the development of myeloid-suppressors from naive murine bone marrow cells. In preclinical studies the capacity of combination therapies (anti-PD-1 + CSF-1R inhibitor) was evaluated, and microarray analysis of tumour tissues revealed key factors crucial for the therapeutic benefits of this treatment.

Results: *In vitro*, neuroblastoma-derived factors hamper myelopoiesis of human progenitor cells, and induce suppressive myeloid cells from primary monocytes and murine bone marrow cells through M-CSF/CSF-1R interaction. Blockade of PD-1 signaling in combination with CSF-1R inhibitor, BLZ945 (Novartis), leads to superior tumour control in an aggressive transgenic mouse model of neuroblastoma (TH-MYCN). Microarray analysis of tumour tissues reveals significant increase of lymphocyte-recruiting chemokines CXCL9, 10 and 11 expressed by myeloid cells, and in line with these results tumors of combination treated animals show increased T-cell infiltration. *In vivo*, blockade of chemokine receptor CXCR3 hampers T-cell infiltration and abrogates combination treatment efficacy. Multivariate analysis of 59 immune cell subsets in spleens and tumors of treated mice demonstrates the correlation between PD-L1 expressing myeloid cells and treatment outcome.

Conclusion: Combination of anti-PD-1 antibody with CSF-1R inhibitor leads to efficient repolarization of suppressive myeloid cells, and in consequence to chemokine guided effector T-cell recruitment and anti-tumour activity. Combination of checkpoint blockade antibodies with inhibitors of M-CSF/CSF-1R signaling might increase patients' response rates, and should therefore be evaluated in clinical trials.

O-092 | Whole Exome Sequencing of Circulating Free Tumour DNA for Study of Spatial and Temporal Tumour Heterogeneity: Accumulation of New Mutations at Tumour Progression of Neuroblastoma

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Background/Objectives: Liquid biopsies are revolutionary tools to monitor tumour-specific genetic alterations. In neuroblastoma (NB), significant levels of circulating free tumour DNA (ctDNA) in the bloodstream enable the detection of tumour-specific markers including MYCN amplification or mutations. As clonal evolution plays a role in NB progression, monitoring of a single genetic marker will be insufficient for ctDNA-based disease follow-up.

Design/Methods: To study NB clonal evolution, we isolated ctDNA from plasma at diagnosis (n=19) and during follow-up (final time-point: partial or complete remission (PR/CR), n=7; progressive disease (PD), n=9) for 19 NB patients for whom primary NB and matched germline DNA whole exome/whole genome sequencing data (WES/WGS) was available. CtDNA (7-100ng) was subjected to Illumina 100PE WES following modified library construction and capture approaches to account for small ctDNA molecules (target depth 100x).

Results: CtDNA WES yielded satisfactory depth in all cases. At diagnosis, SNVs common to the NB and corresponding diagnostic ctDNA of a given patient were observed (mean number of SNVs: 19 [9-69]), with few SNVs specific to the NB (mean: 6; [0-18]), and others specific to ctDNA (mean:22; [9-69]), suggesting spatial heterogeneity with different ctDNA amounts released by different clones. In PR or CR ctDNA, lower numbers of SNVs were detected (mean: 11, [0-12]). Interestingly, PD ctDNA samples harboured higher numbers of SNVs, with additional relapse-specific SNVs (mean: 22; [0-55]) targeting, amongst others, the protein kinase A signaling pathway. Analysis of additional ctDNA samples obtained between diagnosis and relapse (2-6 samples/patient) using deep sequencing techniques will determine the time of appearance of new driver clones.

Conclusion: In conclusion, CtDNA WES proves to be an extremely powerful tool to study spatial and temporal heterogeneity in NB, providing further proof of the importance of clonal evolution in NB progression. Full characterization of ctDNA, which might represent more aggressive clones, might orient targeted treatment approaches.

O-093 | Genomic Copy Number Profiling Using Circulating Free Tumour DNA Highlights Heterogeneity in Neuroblastoma

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Background/Objectives: The tumour genomic copy number profile determines treatment of neuroblastoma (NB) patients. We have studied the genomic copy number profile of circulating cell free tumour DNA (ctDNA) and compared this to aCGH of the primary tumour.

Design/Methods: The analysis of 70 genomic copy number profiles of ctDNA was performed using the OncoScan[®] platform. The profiles were classified according to the overall genomic pattern, including numerical chromosome alterations (NCA), segmental chromosome alterations (SCA) and MYCN amplifications (MNA).

Results: Interpretable ctDNA profiles were obtained in 66/70 cases. An overall identical genomic profile between aCGH of the primary tumour and ctDNA was observed in 47 cases (3 NCA, 22 SCA, 22 MNA). In 1 case, additional SCA not detected by aCGH of the primary tumour was seen in ctDNA. In 14 cases ctDNA analysis did not reveal any copy number changes, 10/14 of them having localized disease. Finally, in 4/8 cases with a silent tumour aGCH profile, ctDNA analysis revealed a dynamic profile (3 SCA, 1 NCA). A total of 378 breakpoints common to both the primary tumour and ctDNA of any given patient were identified, 27 breakpoints were only seen by tumour aCGH, and 54 breakpoints were seen in ctDNA only, including two cases with interstitial gains encompassing IGFR1, and two alterations targeting TERT.

Conclusion: These results demonstrate the feasibility of copy number profiling using ctDNA in NB patients. This study highlights the heterogeneity of NB and suggests that ctDNA might reflect genetic alterations of more aggressive cell clones.

O-094 | Frequency of High and Low Level Clonal ALK Mutations in High Risk Neuroblastoma Patients. A Siopen Study

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Background/Objectives: In neuroblastoma (NB), activating *ALK* receptor tyrosine kinase point mutations are detected in 8–10% of patients at diagnosis using conventional sequencing. To determine the occurrence and the prognostic impact of *ALK* mutations in high-risk NB patients we studied *ALK* variation frequencies using targeted deep sequencing in samples of patients enrolled in the HR-NBL1/SIOPEN trial.

Design/Methods: Diagnostic NB samples from 524 high-risk NB patients were analyzed, focusing on the exons 23–24–25 containing the F1174, F1245 and R1275 hotspots respectively. DNA was amplified via a two-step-PCR approach, the second step consisting of addition of sample-specific barcodes for targeted resequencing in a single experiment. Amplicon sequencing (Illumina HiSeq2500) achieved an extremely high depth of coverage (80,000X). The background base variability in 32 control samples was 0.017%±0.010; thus a base frequency >0.06% was significantly different from background noise (Fisher's exact test). Mutated allele fractions (MAF) <20% were defined as low level clonal.

Results: At the F1174 hotspot, mutations were observed in 28/524 samples, 15 being high (MAF was >20%) and 13 low level clonal (MAF: 0.123%–11.688%). At the R1275 hotspot, mutations were observed in 31/524 samples, 18 high and 13 low level clonal. At the F1245 hotspot, mutations were observed in 3/524 samples, 2 high and 1 low level clonal. All clonal mutations were validated by Sanger sequencing. Validation of all other events and analysis of additional samples from collaborating groups is ongoing.

A correlation between *ALK* mutations and *MYCN* amplification was detected (chi-square, $p=0.0124$). No statistically significant difference in survival of patients with *ALK* wild-type versus *ALK*-mutated NB was observed.

Conclusion: Our study documents a high frequency of both high level (6.6%) and low level clonal *ALK* mutations (4.9%) in high-risk NB patients. These findings are of clinical importance given the potential role of *ALK* mutations in clonal evolution, and the possibility of *ALK*-targeted therapy.

O-095 | High Frequency of Mutations Detected in Chromatin Remodeling Genes in Neuroblastoma

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Background/Objectives: Chromatin remodeling complexes including SWI/SNF are implicated in a wide variety of cellular processes including nuclear organization, chromosomal stability and gene expression, and mutations in SWI/SNF components play an important role in many cancer types. In neuroblastoma (NB), recent whole-genome/whole-exome sequencing efforts results have detected genetic alterations in chromatin remodeling genes such as ARID1A and ARID1B.

Design/Methods: To explore the potential recurrence of genetic alterations in chromatin remodeling genes in a clinically representative cohort of NB patients (255 diagnostic samples), we designed a TruSeq Custom Amplicon panel (TSCA, Illumina) targeting 33 SWI/SNF genes (261,686bp). Libraries prepared from 50ng of genomic DNA were subjected to 150bp paired-end sequencing, with a high coverage (mean 2000X). After sequence alignment, two analyses were initiated. Clonal/sub-clonal mutations were detected by ACGT-base calling approach and statistical comparison between samples and controls. Structural variations will be searched by gene dosage normalization within and between samples/controls.

Furthermore, a series of 31 NB cell lines and 6 germline controls were included in this study.

Results: A total of 96 clonal mutations (allele fraction >20%) were detected. Overall, 35% of NB patients showed a mutation in at least one chromatin-remodeling gene; the most frequent mutated genes were ARID1A (10/255), ARID1B (3/255), BRD7 (3/255), MLL3 (10/255) and SMARCC2 (6/255) genes. Furthermore, 11 NB cell lines showed a clonal mutation in at least one of the studied genes. Mutations detected in NB cell lines were validated by RNA sequencing. Analyses to detect sub-clonal mutations and structural variations are ongoing.

No statistically significant differences in survival of patients with chromatin-remodeling genes wild-type versus chromatin-remodeling genes mutated at clonal level were observed.

Conclusion: The high frequency of clonal mutations highlights the dysregulation of chromatin remodeling in paediatric tumorigenesis and suggest potential new approaches for the management of patients with neuroblastoma.

O-096 | Revised Children's Oncology Group (COG) Risk Stratification Incorporating the International Neuroblastoma Risk Group Staging System

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Background/Objectives: The COG risk classification system previously used the International Neuroblastoma Staging System (INSS). Because the INRG staging system (INRGSS) has been adopted for clinical trials we integrated INRG stage with biological and clinical prognostic

factors to map patient categories, evaluate outcomes and develop a revised risk classification system.

Design/Methods: 4,255 newly diagnosed neuroblastoma patients were enrolled on COG Neuroblastoma Biology Study ANBL00B1 between 2006–2014. Staging per the INSS and INRG (using detection of Image Defined Risk Factor (IDRF)) was determined. Tumour biological and histologic features assessed in the centralized COG Neuroblastoma Reference lab included *MYCN* status, ploidy, INPC histology, and 1p and 11q LOH. Survival analyses were performed to identify independent prognostic factors and to calculate event-free and overall survival (EFS, OS) for combinations of variables used to determine risk group assignments according to both COG and INRG classification templates.

Results: With the current COG risk classification using INSS 1,309 low-, 1,007 intermediate- and 1,849 high-risk patients were identified. For metastatic (INSS 4/INRGSS M) categorization, the two staging systems differed only in terms of assignment for patients 12–18 months. For loco-regional tumors 1,122 (67%) had no IDRF (L1) and 545 (33%) had >1 IDRF (L2). Of the L1 patients 87% were INSS 1,2 while 61% of L2 patients were INSS 3. Subsets of L2 patients had sub-optimal outcomes (3-year EFS, OS): *MYCN* amplification (*MYCN*A) (73.5±7.9%, 79.0±7.1%), ≥18 mo and unfavorable INPC (75.3±7.2%, 83.2±5.9%), and ≥18 mo with 1p or 11q LOH (65.5±17.2%, 85.7±11.5%).

Conclusion: The COG revised risk classification proposes to designate L2 patients ≥18mo with *MYCN*A, unfavorable INPC histology, and/or segmental chromosome aberrations as high risk. Further analyses are underway to identify features of L2 patients who were differentially classified based on INSS or INRGSS. Additional prognostic biomarkers may enable further refinement of risk groups.

FREE PAPERS SESSION 18: SOFT TISSUE SARCOMAS

O-097 | Rhabdomyosarcomas in Children with Germline TP53 Mutations (Li Fraumeni Syndrome): Clinical Analysis, Therapeutic Issues, and Outcome

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Background/Objectives: Rhabdomyosarcoma (RMS) is one of the most frequent paediatric tumour in Li-Fraumeni syndrome (LFS). The aims of the study were to describe the characteristics and the evolution of RMS associated with LFS and to evaluate the risk of subsequent malignant neoplasms (SMN) according to treatments.

Design/Methods: Since 1993, the Department of Genetics in Rouen University Hospital screens for germline *TP53* mutations French patients with personal or familial history suggestive of LFS and updates the clinical data of the carriers and their family. Thirty-eight patients with a RMS and a *TP53* germline mutation were identified. Twenty-six patients with available clinical, radiological and histological data were included in the present analysis.

Results: RMS with LFS looked similar to sporadic RMS except for a younger age at diagnosis of RMS (median 22.5 months, range 5–612 months), a low proportion of alveolar RMS (1/26) and genito-urinary tumours : 10/12 (83%) patients had a partial response to pre-operative chemotherapy and 25/26 (96%) were in complete remission at the end of first line treatment.

With a median follow-up of 122 months (12–417 months), 4/26 patients were alive in first complete remission, 10/26 (38%) experienced a relapse, 18/26 (69%) patients had 35 SMN. Among the 15 patients treated with radiotherapy for the RMS or a relapse, 10 (66%) developed 17 SMN, including 7 in the RMS radiation field, while 8/11 (72%) patients treated without radiotherapy developed 18 SMN. The 10 year event free and overall survival were 27.9% (95CI 14–49) and 68.6% (95CI 48–84), respectively. The 10 year relapse free and second cancer free survival were 58.4% (95CI= 39–76) and 50.6% (95CI= 30–71).

Conclusion: Genotoxic treatment used to treat the RMS might contribute to the high incidence of SMN in patients with LFS. Early detection of tumours and adapted treatment might contribute to reduce multiple malignancies incidence.

O-098 | Title: Prognosis of Children with Localized Rhabdomyosarcoma (RMS) of Genitourinary Regions (GU) Treated in 5 Prospective Studies of the Cooperative Weichsteinsarkom Studiengruppe (CWS)

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Background/Objectives: Chemotherapy (CHT) for RMS has not changed substantially in the last 25 years in contrast to quality of diagnostic tools and local therapy modalities. The main purpose of the CWS studies was to reduce the therapy burden by adapting CHT and the type and extent of local treatment to the individual risk spectrum. We present the therapy results of patients with GU RMS treated in the five consecutive CWS-Studies CWS-81, -86, -91, -96 and -2002P.

Design/Methods: 472 patients aged 1-21 yrs were registered between 1981 and 2010. Distribution by site was: paratesticular 46%, bladder/prostate (BP) 40%, vagina/vulva 11%, uterus 3%. 94% were embryonal RMS. Two to four drugs (Vincristine, Actinomycin D, Cyclophosphamide or Ifosfamide, Doxorubicin) were used depending on study and risk group. Irradiation (32-54Gy) was recommended depending on RMS type, results of the primary or secondary resection, response to preoperative CTH and age.

Results: 5yr event-free-survival (EFS) and overall survival (OS) were 79% and 87% (embryonal RMS 80% and 88% and alveolar RMS 68% and 79%, respectively). EFS and OS by study were: CWS-81 79% and 85%, CWS-86 80% and 91%, CWS-91 76% and 83%, CWS-96 79% and 85%, CWS-2002P 81% and 90%, respectively. Local and combined relapse rate was 16%, metastatic 1%. The proportion of irradiated pts varied only slightly between studies (20-30%). 48% of pts with BP were irradiated but only 6% with paratesticular RMS. The 5yr EFS by irradiation dose (32Gy vs. >40Gy) was 80 and 75%. 5yr EFS and OS for irradiated vs. not irradiated pts with BP were almost equal (72% vs. 72%, and 82% vs. 78%, respectively).

Conclusion: About 80% of pts with GU RMS survived their disease. The prognosis remained very good over the studies despite the reduction of the therapy burden (CHT and irradiation dose) by better stratification.

O-099 | Influence of Time to Detection (TTD) on Clinical Outcomes in Paediatric Testicular Tumors

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Background/Objectives: Early stage testicular and paratesticular germ cell tumors (GCT) and rhabdomyosarcoma (RMS) are cured with minimal treatment. Advanced stage disease requires aggressive therapy, is associated with long-term toxicity, and has less favorable survival. It is not known whether prolonged time from initial symptoms to cancer diagnosis (time to detection, TTD) is associated with more advanced disease stage and inferior overall survival (OS).

Design/Methods: Single institution retrospective chart review (1969-2014) of paediatric patients with testicular tumors. The relationship between TTD, tumour size, disease stage, and age group (< 10 years or > 10 years) was studied by using a multivariable linear model. The association between OS, time to detection, and tumour volume was examined using multivariable Cox regression model.

Results: Fifty-nine RMS and 58 GCT patients were evaluable. Stage I disease was common in RMS (92%), whereas 57% of GCT were stage I and 43% were stage II-IV. The median age at diagnosis was 2.8 years (range: 0.3-19.9y) for GCT and 13.2 years (range: 0.2-20.7y) for RMS. TTD was 52 days (range 1-447 days) in GCT patients and 31 days (range 0-507 days) in RMS patients. Overall, longer TTD was associated with Stage II-IV disease (p=0.02) and age > 10 years (p=0.004) adjusting for disease type and tumour volume. Longer TTD did not predict maximal tumour diameter, but >5cm tumour diameter predicted inferior OS (p=0.009) adjusting for disease type and time to detection. Patients >10 years of age were more likely to have advanced disease (p=0.002) and larger tumour size (p<0.0001).

Conclusion: Longer TTD is associated with higher disease stage and older age in paediatric testicular GCT and RMS. Larger tumors, more likely in patients > 10 years old, are associated with inferior survival. Interventions to facilitate early diagnosis, particularly in adolescents, may improve the likelihood of survival and reduce long-term morbidity in survivors.

O-100 | Access to Clinical Trials for Adolescents with Soft Tissue Sarcomas: The Enrolment into the European Paediatric Soft Tissue Sarcoma Study Group (EPSSG) Protocols

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Background/Objectives: It is increasingly reported that adolescents with cancer are enrolled in clinical trials at far lower rates than children. This has been suggested as one of the reasons contributing to the lower survival of adolescents with certain tumour types compared to children with the same disease.

Design/Methods: The aim of the current study is to compare the number of adolescents (15-19 year-old) enrolled in the European paediatric Soft tissue sarcoma Study Group (EpSSG) protocols with the number of cases expected to occur according to the incidence rates drawn from population-based cancer registries contributing to the RareCareNet project, and draw a comparison with number of children enrolled. The analysis was restricted to the five countries contributing the majority of cases, France, Italy, UK (plus Ireland, considered together for the aim of the analysis), Spain and the Netherlands. The observed/expected (O/E) ratio was calculated from October 2008 to October 2015 (period when all four EpSSG protocols were open in the five major EpSSG countries).

Results: From March 2005 to October 2015, 3216 patients were registered in four different EpSSG trials from 15 countries. The O/E ratio for the five major countries as a whole was 0.64 for 0-14 year-old patients (0.77 for rhabdomyosarcoma RMS and 0.50 for non-RMS), and 0.27 for 15-19 year (0.59 for RMS and 0.16 for non-RMS). The O/E ratio was particularly low for non-RMS and differed across the five countries considered.

Conclusion: Though the EpSSG protocols were opened to patients up to 21 years, adolescents were under-represented in clinical trials. The problem of access to EpSSG protocols was more relevant for patients with non-RMS histotypes (that are adult-type tumors in most cases). Cooperation between paediatric and adult cooperative groups dealing with soft tissue sarcomas should be improved to increase the accrual of these patients to clinical trials.

O-101 | Localized Epithelioid Sarcoma in Children: An European Paediatric Soft Tissue Sarcoma (EPSSG) Study

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Background/Objectives: Epithelioid sarcoma (ES) is a rare malignant representing 4 to 8% of paediatric soft tissue sarcoma. ES includes the classic distal subtype and the proximal subtype; ES belongs to the SMARCB1 deficient tumors family. Surgery is the cornerstone of therapy. Role of chemotherapy, adjuvant radiotherapy and, more recently, targeted therapy, is still debated.

Objectives: To present the results of the EpSSG-NRSTS 2005 prospective study of patients (less than 21 years) with localized ES treated from 2005 to 2013.

Design/Methods: Protocol treatment guidelines were the following: surgery only for [IRS Group I/size < 5 cm; IRS-I> 5 cm/FNCLCC histologic grading Grade I; IRS-II/G 1] (15 patients); surgery and postoperative radiotherapy for [IRS-I>5 cm/G2; IRS-II/G2; IRS-II/G3/<5 cm] (3 patients); adjuvant chemotherapy (ifosfamide-doxorubicin) with radiotherapy for [IRS-II/G3/>5 cm] (1 patient); neoadjuvant chemotherapy (+/-) radiotherapy for [IRS-III/N+] (13 patients).

Results: The series includes 32 patients (3.4% of all NRSTS registered), median age 12.3 years (range: 4.2-20). Most tumors occurred in limbs (65.6%). IRS staging was, IRS-I: 15 cases, IRS-II: 4, IRS-III: 13. Only 2 cases had regional node involvement. FNCLCC histologic grading was G1 in 8 cases, G2 in 5 cases and G3 in 19 cases. With this strategy, for the whole series, 5 years EFS and OS were respectively 70.3% (CI 48.9 - 84.1) and 71.1% (CI: 48.0-85.3). 9 tumors relapsed and 7 patients died. Treatment failure occurred especially in IRS-III cases (7/13). Tumour response to neoadjuvant chemotherapy was important (82%) but was not correlate with outcome.

Conclusion: This EpSSG study confirms that ES in paediatric age is a rare tumour mainly occurring in adolescents. Our data suggest that outcome is favorable for patients with resectable disease at diagnosis, while it remains unsatisfactory in patients with initially unresected disease, despite of a high response rate to chemotherapy.

O-102 | Desmoid Tumors in Children and Adolescents: The Experience of the European Paediatric Soft Tissue Sarcoma Group (EPSSG)

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Background/Objectives: Desmoid-type fibromatoses are rare diseases, often locally invasive. In the past, tumour resection has been the main standard treatment, but iterative surgical resection is known to stimulate tumour growth, therefore, indicated only in case of rapidly growing tumours. Even though this lesion is not considered to be malignant, chemotherapy is used to significantly reduce the tumour, thus controlling the disease.

Design/Methods: The EpSSG NRSTS Committee encourages the registration of paediatric patients with desmoids for standardizing their treatment based on a minimally-aggressive strategy: considering "wait-and-see" strategy first, avoiding repeated resections or destructive surgery and adopting low-dose chemotherapy when systemic treatment is required.

Results: From 2005 to 2016, 163 patients were registered. Median age was 11.4 years (0.1-24); sex ratio=1. IRS-staging was: IRS-I (complete resection) 11.0%; IRS-II (microscopic residue) 11.7%; IRS-III (macroscopic residue) 77.3%. Tumour were frequently large (≥ 5 cm): 62%. Tumors mainly occurred in limbs (44.2%), trunk (27.6%) then head-and-neck (23.3%). Desmoid were multifocal in 4.9% with family history of desmoid in 2.2%. Desmoid occurred after trauma in 6.9%. At diagnosis, 47.9% had no immediate further therapy (60.0% of all IRS-I; 83.3% IRS-II; 40.4% IRS-III). After a median follow-up of 45 months (range: 0.8-102), among them, 59% had delayed therapy (85% medical drugs; 15% surgery) mainly after progression/relapse (87.5%), and 41% are still under observation. Immediate therapy after diagnosis was delivered in 52.1% (chemotherapy/medical drugs: 77%; surgery: 20%; both: 3%), mainly due to clinical/radiological progression or threatening site. Among IRS III patients, 31.8% had a successful wait and see strategy after 21.8 months (range 3.4-72.9). All patients were alive at the last follow-up.

Conclusion: Despite the rarity of the disease, EpSSG was able to collect important information about a large number of patients with desmoid tumour. Initial observation allows to select those that really need therapy.

Financial support: S Wisnia

FREE PAPERS SESSION 19: HIGH IMPACT CLINICAL TRIALS

O-103 | Very Favorable Complete Continuous Remission (CCR) and Overall Survival (OS) for Standard-Risk High (SRH) Acute Lymphoblastic Leukemia (ALL) Patients Treated on Cog AALL0331

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Background/Objectives: Outcomes for NCI SR B-ALL patients have improved over time although optimal therapy for those with higher risk features has not been defined. AALL0331 utilized a common 3-drug induction followed by risk-stratified therapy based on leukaemia genetics and early response. The SRH subset included patients with CNS3 disease, rapid response (RER) with MLL rearrangements, slow response (SER) by bone marrow morphology ($\geq 5\%$ blasts at induction day 15) or end-induction/extended induction MRD (0.1 to $<1\%$ by flow cytometry), and/or steroid pretreatment. These patients were non-randomly assigned to receive augmented therapy, an efficacious strategy in previous trials.

Design/Methods: AALL0331 enrolled 5311 SR B-ALL patients from 4/2005-5/2010. Following standard induction [dexamethasone (DEX), vincristine pegaspargase, intrathecal methotrexate], SRH patients received COG augmented BFM therapy as given to NCI high risk patients that included 2 interim maintenance (escalating Capizzi style methotrexate plus pegaspargase) and 2 augmented delayed intensification phases with standard DEX-based maintenance. After 6/2008, DEX was given alternate-week (days 1-7 and 15-22) during the delayed intensification phases to reduce osteonecrosis. Only CNS3 patients received cranial radiation (18Gy).

Results: At 5 years, continuous complete remission (CCR) and overall survival (OS) rates among 636 SRH patients were $85.7 \pm 0.02\%$ and $93 \pm 0.01\%$. The 5y cumulative incidences of isolated CNS relapse was $2.7 \pm 0.65\%$, isolated bone marrow relapse $7.2 \pm 0.01\%$, and combined relapse $0.65 \pm 0.003\%$.

Conclusion: Overall outcomes for SRH patients who received augmented therapy on AALL0331 were favorable, despite the identified adverse features. However, the outcomes for these patients was significantly inferior to that of other SR ALL patients treated on COG AALL0331 (5 year EFS and OS for SR-average of $88 \pm 0.01\%$ and $95 \pm 0.006\%$ with the 5 year

CCR and OS for SR-low of $95 \pm 0.006\%$ and $99 \pm 0.003\%$), indicating that new approaches to therapy are warranted.

O-104 | Results of the Randomized Intergroup Trial Inter-B-NHL RITUX 2010 for Children/Adolescents with High-Risk B-Cell Non Hodgkin Lymphoma (B-NHL) and Mature Acute Leukemia (B-AL)

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Background/Objectives: Rituximab (R) with chemotherapy (CT) improves survival of adult B-cell malignancies. No randomized trial evaluated efficacy and safety of R added to CT in childhood B-NHL/AL.

Design/Methods: The international randomized phase III trial sponsored by Gustave Roussy and COG compared standard LMB CT to identical CT+R in pts <18 years with high-risk B-NHL (stage III with LDH level $>2N$, stage IV) and B-AL. R was given (375 mg/m^2) on days -2 and 1 during the first 2 CT courses and on day 1 of the 2 following courses (total 6 infusions). The primary endpoint was event free survival (EFS). To detect a hazard ratio (HR) of 0.50 (increase in EFS from 84% to 92%), 72 events were required. 600 pts were planned to enroll. Interim analyses were planned after ~33% of events and yearly thereafter.

Results: The first interim analysis was conducted in Aug 2015 and based on 27 events (37.5% of information) occurring in 310 pts (155/arm) randomized since Dec 2011. 85% had Burkitt lymphoma. 51% were in group B (Stage III or IV, CNS neg), 39% in C1 (Stage IV/B-AL cerebrospinal fluid (CSF) neg) and 10% in C3 (CSF pos). With a median follow-up of 11.5 months, pts on the R arm achieved better EFS than those on the control arm: 1-year EFS (95%CI) was 94.2% (88.5-97.2) vs. 81.5% (73.0-87.8). The HR was 0.33 (90%CI: 0.16-0.69), one-sided p-value=0.006. This p-value was higher than the nominal alpha (0.0014) of this first interim analysis. However, the conditional power analysis demonstrated high likelihood of getting a positive study in later analyses (from 100% to 87% for HR=0.33 to 0.75). Thus, the randomization was stopped in Nov 2015 following the recommendations of the IDMC.

Conclusion: Rituximab in addition to standard LMB therapy improves EFS of children/adolescents with high-risk B-NHL and B-AL.

O-105 | Doxorubicin in Combination with Cisplatin/5-Fluorouracil/Vincristine is Feasible and Effective in Unresectable Hepatoblastoma: Preliminary Report from the Children's Oncology Group AHEP-0731 Study Committee

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Background/Objectives: Most children with newly diagnosed hepatoblastoma (HB) will have unresectable liver tumour at diagnosis. Additionally, small cell undifferentiated histology (SCU) has previously been hypothesized to confer a worse prognosis. Children's Oncology Group AHEP0731 Intermediate-Risk protocol investigated a novel therapeutic regimen designed to improve resectability and outcome.

Design/Methods: We enrolled non-metastatic patients whose primary tumour was either 1) unresectable at diagnosis; or 2) resected at diagnosis with small cell undifferentiated histology(SCU). Protocol chemotherapy included a planned total of 6 cycles of cisplatin/doxorubicin/5-fluorouracil/vincristine (C5VD), 4-preoperative and 2-postoperative. PRETEXT based surgical guidelines determined: 1) tumors to resect or biopsy at diagnosis; 2) need for early referral for possible liver transplantation (LT); and 3) timing and type of definitive surgical resection.

Results: 104 patients (median age 15 months, range 0-192) were enrolled between September 2009 and March 2012. Central review of radiographic imaging showed PRETEXT group I=3; II=32; III=55; IV=14. PRETEXT annotation factors: V=69; P=69; E=2; F=15. Median AFP decline with first 2-cycles of C5VD was 90%. Prior to protocol chemotherapy 94 had biopsy, 9 had primary resection (SCU histology), and one too unstable for biopsy. Definitive surgical resection followed chemotherapy in 84 patients: 55 partial hepatectomy (17 cycle2; 37 cycle4;

1 cycle6), 29 OLT (2 cycle2; 20 cycle4; 3 cycle6, and 4 incomplete data). Therefore a total of 93 patients (89%) achieved complete resection. Three-year event-free and overall survival was 87% (CI: 76-94%) and 94% (CI: 87-97%) respectively. Toxicity was within the realm of expectations.

Conclusion: Definitive surgical guidelines and early transplant referral, combined with the addition of doxorubicin to a standard regimen of cisplatin/5-fluorouracil/vincristine, was feasible and efficacious. This treatment approach yielded superior results to prior COG protocols and appears as a viable option for use in clinical trials going forward.

O-106 | Long-Term Results for Children with High-Risk Neuroblastoma Treated on the Randomized High-Dose Therapy Trial of Busulphan-Melphalan Versus Carboplatin-Etoposide-Melphalan: A Siopen Study

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Background/Objectives: High-dose chemotherapy and autologous stem cell rescue (HDT/SCR) was shown to improve outcome for patients with high-risk neuroblastoma (HR-NBL), however it is unknown which regimen has the greatest patient benefit. We tested the hypothesis that HDT/SCR with busulphan and melphalan (BuMel) results in a superior 5-year event-free and overall survival (EFS, OS) than HDT/SCR with carboplatin, etoposide, melphalan (CEM).

Design/Methods: Patients (<21years) with metastatic neuroblastoma over the age of one or INSS stage 2 - 4 with MYCN amplification (MNA) were randomly assigned just prior HDT/SCR to BuMel or CEM taking into account age, stage, MYCN and national group. Eligibility criteria were based on metastatic response requiring a complete bone marrow response and at least a partial response at skeletal sites, with three or less abnormal areas on 123iodine-metastiodobenzylguanidine scintigraphy. Induction treatments included Rapid Cojec chemotherapy, two additional courses of TVD in case of inadequate metastatic response and attempt of gross resection of the primary tumour. Further treatments after HDT/SCR were radiotherapy (21 Gray) to the primary site and 13-cis-retinoic acid.

Results: 676 patients were eligible, of whom 598 (88%) were randomized. EFS(+/-SE) and OS (+/-SE) was 45±3% and 54±3% in 296 patients in the BuMel group versus 33±3% and 41±3% in 302 patients in the CEM group (p=0.001). The cumulative incidence of relapse was significantly lower with BuMel (52%±3) compared to CEM (63%±3) (p=0.003). Severe toxicities (need for intensive care and toxic deaths) were lower with BuMel (4%) compared to CEM (10%) (p=0.012). BuMel had fewer grade 3&4 non-haematological toxicities, but had 22% veno-occlusive disease Bearman grades 1-3 (but only 4% grade 3) versus 9% with CEM (1% grade 3).

Conclusion: After Rapid Cojec induction, BuMel showed significantly improved EFS and OS in long-term outcome observation. An interaction of platinum based induction with CEM must be considered.

O-107 | Patients with Stage 4 High-Risk Wilms Tumours Enrolled in the SIOP WT 2001 Protocol: A Report of the SIOP Renal Tumour Study Group

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Background/Objectives: To determine the outcome of children with stage 4 and high-risk (HR) histology Wilms tumour (WT) enrolled in the prospective International Society of Paediatric Oncology (SIOP) WT 2001 study.

Design/Methods: Children and adolescent aged 6 months to 18 years with stage 4 HR-WT were selected from the total of patients registered in the SIOP WT 2001 study between January 2002 and August 2014.

Results: Of 525 patients with stage 4 WT, 74 patients (14%) met the inclusion criteria. Thirty-four (46%) and 40 (54%) patients had blastemal type (BT) and diffuse anaplasia (DA) histology, respectively. Patients with DA-WT had a higher incidence of liver disease (p=0.047) and a worse response of metastases to preoperative chemotherapy (p=0.014). Three patients died from a treatment-related toxicity. Recurrent disease was displayed in 16/34 patients with BT-WT, and in 27/40 patients with DA-WT, in all but one with metastatic disease. Median time to recurrence was 6 months (range 1-33). With a median follow-up of 4.9 years, 5-year progression-free survival (PFS) rates for BT-WT and DA-WT were 47±17% vs 31±15% (p=0.038), and 5-year overall survival (OS) rates were 56±17% vs 31±15% (p=0.013), respectively. In the whole cohort, patients in complete remission (CR) of metastases after chemotherapy only had a better outcome than patients in CR after chemotherapy and metastasectomy (5-year OS: 82% vs 32%, p=0.029). Metastatic status after preoperative chemotherapy (PCT) significantly correlated to outcome in DA-WT (p=0.000). Lung radiotherapy was correlated to a better survival in BT-WT by univariate (p=0.012) and multivariate analysis with time to relapse and response to PCT (p=0.025).

Conclusion: The prognosis of patients with stage 4 HR-WT remains poor, especially for DA-WT. The different behaviour of DA- and BT-WT within stage 4 HR-WT needs to be taken into account in the design of future treatment strategies.

O-108 | Phase II Trial of Molecularly Determined Treatment of Children and Young Adults with Newly Diagnosed Diffuse Intrinsic Pontine Gliomas (DIPG): Feasibility and Safety Update

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Background/Objectives: Imaging characteristics of DIPG have been considered sufficient for diagnosis such that surgical biopsy is rarely performed due to its perceived association with increased morbidity. We designed a multi-institutional clinical trial incorporating diagnostic biopsy and molecularly determined treatment stratification. We report the safety data of pre-treatment biopsy in DIPG combined with the feasibility of rapid upfront molecular stratification.

Design/Methods: Ages of eligible patients ranged from 3-18 years. All patients underwent biopsy prior to delivery of local irradiation with Bevacizumab. Tumour tissue was tested for presence(+) or absence(-) of MGMT promoter methylation and EGFR expression. Additional treatment was assigned based on this status as follows: erlotinib for cohort 2(MGMT-/EGFR+), temozolomide for cohort 3(MGMT+/EGFR-), and both temozolomide and erlotinib for cohort 4(MGMT+/EGFR+).

Results: Fifty of 53 enrolled patients were evaluable. Cohort 1 included 60% of patients; cohorts 2, 3 and 4 included 28%, 6% and 6%, respectively. There were no biopsy related deaths. Grade 3 biopsy-related morbidities included depressed consciousness and dysphagia in one patient and left hemiparesis in another. Grade 4 post-biopsy morbidities were limited to hematoma(n=1), hypertension(n=1) and apnea(n=1). These events were restricted to 3 patients and transient with the exception of the hemiparesis.

A mean of 5ug of RNA and 10ug of DNA were successfully extracted from single frozen cores for detailed molecular analysis. Following molecular stratification, remaining tissue was stored for future research. MGMT methylation was present in 12% of samples; EGFR overexpression or amplification was detected in 34% of samples. MGMT and/or EGFR status could not be determined in four samples. Mean time from sample submission to resulted MGMT status was 6 days (range 1-14). EGFR status was reported within 24-48 hours.

Conclusion: Pre-treatment biopsy is safe in patients with DIPG and incorporation of rapid molecular stratification for upfront enrollment feasible for future clinical trials in this disease.

FREE PAPERS SESSION 20: RARE TUMOURS

O-109 | Congenital Rhabdoid Tumors – A Retrospective International Series Demonstrates Dismal Outcome but no Futility of Therapy

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Background/Objectives: Congenital rhabdoid tumors (RT) (age <28 days) have repeatedly been described as almost unavoidably fatal. A systematic evaluation of patients treated on consensus therapy regimen has thus far not been presented.

Design/Methods: We prospectively registered 24 patients in the European Rhabdoid Registry (EU-RHAB), further 15 were from 10 different French centres and 3 from Moscow. All 42 presented with RT-related symptoms within the first 28 days of life and were treated according to either the EU-RHAB recommendation (n=21), Rhabdoid 2007 (n=4) (variation of EU-RHAB) and the remainder by individual combinations (n=17).

Results: Fourteen patients had AT/RT, 18 extracranial and 10 synchronous RT. Germ line mutations were discovered in 26 of 38 evaluable patients. 22 patients presented with metastatic disease. 38 patients received chemotherapy (range 1 – 16 courses), three patients received HD-MTX as induction, 11 patients HDCT as consolidation and 6 patients radiotherapy. No toxic deaths occurred and against expectations therapy was tolerated with acceptable toxicity. VOD was noted in 5 patients. Complete remission (CR) was achieved in nine patients and eight of these are still alive. Anatomical site or M+ disease had no significant impact on survival. There was a significant correlation with poor survival in patients with a germ line mutation (7.7% vs. 50%) potentially due to less intensive therapy. Additionally longer OS was demonstrated in patients with CR (0.9% vs. 19.5%). There was a trend for improved outcome in patients treated according to the EU-RHAB recommendations (11.7% vs. 30%).

Conclusion: Therapy of patients with congenital rhabdoid tumors remains a major challenge. Prognosis is in general bleak and in many cases therapy is initiated with a palliative intent. Nevertheless, attempting therapy is warranted, as therapeutic success is not limited to anecdotal cases.

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O-110 | Two Year Results of a Randomised Phase III Trial for Standard Risk Hepatoblastoma (SR-HB) SIOPEL 6; Cisplatin and Sodium Thiosulfate (STS) Vs Cisplatin Alone

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Background/Objectives: SIOPEL 6 is a phase III randomised trial in SR-HB defined as tumour limited to PRETEXT I, II or III, no portal or hepatic vein involvement, no intra-abdominal extrahepatic disease, AFP >100ng/ml and no metastases. A serious permanent side-effect of cisplatin (Cis) is bilateral high-frequency hearing loss; particularly debilitating when occurring in young children. STS has been shown to dramatically reduce hearing loss in children treated with cisplatin.

Design/Methods: Newly diagnosed SR-HB patients were randomised to Cis or Cis+STS for 4 preop and 2 postop courses. Cis 80mg/m² was administered i.v. over 6 hrs. STS was administered i.v. exactly 6 hrs after stop Cis over 15 minutes at 20g/m². Tumour response was assessed after 2 and 4 cycles preop with serum AFP and liver imaging. In case of progressive disease STS was to be stopped and chemotherapy changed to combination therapy with Cis and Doxorubicin 60mg/m². The primary endpoint of the trial is centrally reviewed absolute hearing threshold, at the age of ≥3.5 yrs, by pure tone audiometry.

Results: 109 patients (52 Cis and 57 Cis+STS) were recruited at trial closure in December 2014. The combination of Cis+STS was generally well tolerated. The median follow up is 32 months and provisional 2 yr EFS is Cis 86.3% and Cis+STS 89.0%; 2 yr OS is Cis 91.4% and Cis+STS 97.7%. Treatment failure defined as PD at 4 cycles was equivalent in both arms (3 Cis; 3 Cis+STS). As of February 2016, 5 patients had died (4 Cis; 1 Cis+STS), 1 had relapsed (Cis+STS) and 1 was still in PR (Cis+STS). Definitive results will become available end 2017.

Conclusion: This randomised phase III trial in standard risk hepatoblastoma of cisplatin alone vs cisplatin plus the otoprotectant Sodium Thiosulfate shows comparable 2 year EFS and OS with no evidence of tumour protection.

O-111 | Characterization of Pulmonary Metastases in Children with Hepatoblastoma

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Background/Objectives: Hepatoblastoma (HB) is the most common paediatric liver malignancy. For patients with metastatic disease, survival is poor ranging from 25-50%. While surgical resection of the primary tumour is paramount for cure, the management of metastatic pulmonary nodules remains incompletely evaluated. There are no prospective studies describing lung nodule characteristics and relation to chemotherapy response, metastatectomy, and event-free survival (EFS).

Design/Methods: Children's Oncology Group protocol AHEP0731 was designed for patients with newly diagnosed HB and included a stratum for patients with metastatic disease. Chest CT scans performed at diagnosis and at mandated timepoints during treatment were centrally reviewed. For each patient, lung nodules were recorded to a maximum of 10. Total nodule number, size, cumulative disease burden (CDB), laterality, and timing of resolution were also recorded.

Results: Of 30 eligible patients, only 10 (33%) had pulmonary nodules >10 mm at diagnosis, 7 (23%) had all nodules measuring <5 mm, and the remaining patients had nodules of intermediary size. Maximum individual nodule size did not correlate with EFS. Patients with bilateral disease, > 10 nodules, or a CDB greater than the cohort median sum of total diameters had a worse outcome. Eleven patients achieved complete clearance of all nodules (n = 8 with chemo, 3 with surgery + chemo). Four patients had residual lesions on CT < 3 mm at the end-of-therapy but remain alive without disease progression. Ten patients underwent metastatectomies; two as diagnostic biopsies and eight later in therapy. Metastatectomy was not correlated with EFS.

Conclusion: The presence of bilateral lung nodules and overall tumour burden are prognostic in HB. Lesions that measure <10 mm may contain viable tumour while residual visible lesions at end-of-therapy may constitute eradicated tumour/scar. For future trials, a consistent approach towards lung metastases should be developed with consideration of risk-stratification based upon these findings.

O-112 | Early Predicted Time to AFP-Normalization is not Prognostic in Paediatric Standard and High-Risk Non-Seminomatous Germ Cell Tumors Treated in the French TGM-95 Study

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Background/Objectives: Early predicted time to tumour marker normalization is an independent prognostic factor in poor-prognosis non-seminomatous germ cell tumors (NSGCT) in adults but has not been studied in children.

Design/Methods: Pediatric patients (≤18years) treated in the French TGM-95 protocol for AFP-secreting intermediate-risk (IR, non-metastatic, incompletely or unresectable tumour and AFP<15000ng/ml) with VBP-regimen (Vinblastine-Bleomycine-Cisplatin) or high-risk NSGCT (HR, metastasis and/or AFP>15000ng/ml) with VIP-regimen (Etoposide-Ifosfamide-Cisplatin) with 3 to 6 courses, including 2 after biological complete remission (CR). AFP was measured before chemotherapy and 3 weeks later. Predicted-time to AFP-normalization (pAFP-TTN) was calculated using a logarithmic formula (Fizazi, JCO, 2004). Tumors with pAFP-TTN≤9weeks were defined as good-response (GR).

Results: Between 01/1995 and 12/2005, 151 patients (median age 4years, sex ratio M/F: 41/110) were evaluable for AFP-decrease among 179 IR or HR patients included in TGM-95: 52/65 IR and 99/114 HR. Sites: 18 testes, 48 ovaries, 52 sacrococcyx and 33 others. Forty four patients had metastases.

83 tumors (55%) had GR. Risk-group distribution was: GR=34IR+59HR vs. PR=18IR+50HR (p=0.06).

After a median follow-up of 5.4years, 22 events (17 progressions/relapses/contralateral tumour, 1 accidental death in CR, 1 AML and 3 other secondary neoplasms) and 14 deaths occurred. pAFP-TTN was not associated in the whole population with progression-free survival (PFS, p=0.15) or overall survival (OS, p=0.88). In sub-group analysis, pAFP-TTN was not prognostic in SR patients (5y-PFS: 83.8% vs. 88.9%, respectively GR vs. PR, p=0.26) or in HR patients (5y-PFS: 87.5% vs. 91.3%, p=0.35). In very high risk patients (testis and extragonadal primary with age>10years, n=25), similar results were observed (5y-PFS: 66.7% vs. 77.8%, p=0.29).

Conclusion: Predicted-time to AFP-normalization was not prognostic in IR and HR NSGCT in TGM-95 study, but adaptation of the chemotherapy duration to AFP decrease (2 courses after biological CR) could have led to the disappearance of its prognostic value.

O-113 | Outcome and Long-Term Effects of Childhood Nasopharyngeal Carcinoma Treated with Modern Protocols

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Background/Objectives: To study survival and long-term morbidities of children with Nasopharyngeal Carcinoma (NPC) treated with modern protocols.

Design/Methods: Retrospective review of children with non-metastatic NPC treated in France between 1999 and 2015. Long term effects were analyzed. RT dosages depends onto initial chemotherapy response: "Standard doses" (59.4/54/45Gy) in case of VGPR/CR/PR>50-90% and "high doses" (66.6/66.6/45Gy) if response<50% or progressive disease (OR/PD), respectively on residual tumour/initial tumour volume /non invaded cervical area.

Results: We selected 95 patients (median age: 15 years). Most were male (64%) and had WHO III pathology (99%). TNM-staging was 55, 36 and 3 respectively for stages IV (IVA 33%, IVB 26%), III and II. All patients received radiotherapy (RT) to primary tumour and cervical RT. Intensity modulated radiotherapy (IMRT) was used in 57 patients. Other had conventional 3D-RT. After a median follow-up of 4.5 years [range: 3.6-5.5years], 14 patients experienced relapses. The 3-year overall (3Y-OS) and event-free survival (3Y-EFS) were 94% [85-97%] and 86% [77-92%]. Specific 3Y- EFS and 3Y-OS with IMRT were 89% [77-95%] and 93% [80-98%], but median follow-up of the IMRT group was shorter (2.9 years). EFS was better for patients with stage II-III-IVA vs. IVB (HR=3.1 [1.03-9.4], p=0.04).

The 5-year cumulative incidence of any morbidity, neck skin fibrosis, xerostomia, hypothyroidism, hearing loss, caries, trismus and odynophagia were 95%, 37%, 80%, 63%, 63%, 43%, 33% and 25% respectively. Two patients (3%) developed subsequent malignancies 6-8 years after NPC diagnosis. Significant reduction in odynophagia was observed in patients treated by IMRT: 55% vs. 7%, P = 0.015.

Conclusion: Survival rates are very favorable nowadays thanks to multimodal approach, but loco-regional long term tolerance remains poor despite improvement with the use of recent techniques. Those findings are in favor to use a RT protocol adapted to the initial tumour response to chemotherapy to improve durably patients' quality of life.

O-114 | Salivary Gland Carcinomas in Children and Adolescents – Analysis of 131 Patients Reported to the European Cooperative Study Group on Paediatric Rare Tumors (EXPERT)

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Background/Objectives: During childhood and adolescence, salivary gland carcinomas (SGC) are very rare tumors. There are no specific therapeutic guidelines for this age group, and most patients are treated in analogy to strategies established for adult SGCs. The aim of the study is to analyze a large cohort of SGCs for epidemiological and clinical patterns.

Design/Methods: Between 2000 and 2014, 131 SGC patients (median age 12.1 years, range 0-21) were reported to the partners within the European Cooperative Study Group on Pediatric Rare Cancers (EXPERT). Data were analyzed retrospectively.

Results: Site: 112 parotid, 12 submandibular and 17 minor glands. Median size: 2 cm (range 0,25-9cm). Histology: 73 mucoepidermoid carcinomas, 48 acinic cell carcinomas and 10 others. Fifteen patients with lymph node, and one acinic cell carcinoma with lung metastases. Advanced local stage and lymph node metastases correlated with poor grade of differentiation.

Therapy included tumour resection, in most patients as partial or total excision of the gland. In 9 patients, the facial nerve was sacrificed. Neck dissection was performed in 24 patients. Radiotherapy was administered to 27 patients (median dose 60Gy, range 40-70Gy), and 8 patients received chemotherapy. After a median follow-up of 23 months, 11 (10 locoregional, 1 metastatic) relapses have been reported. Two patients are alive with active disease but none have died.

Conclusion: Childhood SGCs are mostly low grade tumors and have a favorable prognosis. Poor histological differentiation is associated with locally more aggressive tumors and lymph node metastases. Complete resection is sufficient in well differentiated tumors. In poorly differentiated tumors, and following incomplete resection, intensified locoregional therapy should be installed, which may include second look resection, neck dissection and radiotherapy. Radiotherapy can be reserved to patients with nodal metastases or in relapse situations.

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FREE PAPERS SESSION 21: RENAL TUMOURS

O-115 | Treatment of Nephroblastomatos: The GPOH Experience 1993-2014

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Background/Objectives: To prevent development of nephroblastoma, treatment of nephroblastomatos consist of response adapted Vincristin and Dactinomycin on a 2-4 weekly base for one (earlier two) year(s). Here we report risk factors for events (EFS) to nephroblastoma and overall survival (OS).

Design/Methods: Retrospective Analysis of 78 out of 2347 patients who had been registered for a renal tumour having uni- or bilateral nephroblastomatos (intra- and perilobar) between 1993 and 2014 in the framework of SIOF93-01 and 2001/GPOH-Nephroblastoma studies.

Results: 3 patients were excluded for insufficient documentation. Median age at diagnosis was 13 months. 43 patients had bilateral nephroblastomatos, 28 showing diffuse kidney involvement. 32 patients presented with unilateral nephroblastomatos, 4 of whom had a diffuse involvement. 56% of the patients were treated based on radiologic diagnosis alone, 28% underwent biopsy and 16% initial tumour-resection. Radiologic diagnosis was conclusive in 62% when made by reference radiology and 30% without (p=0.012). Cutting needle biopsy was carried out in 13 patients and was conclusive in 3 cases as compared to 4 of 8 open biopsies. At the end of 1st-line-treatment, 8 patients had progressive, 6 minimal residual and 14 measurable residual disease. 42 patients achieved a CR. 28 patients suffered from relapse or progression of nephroblastomatos, 23 originating from residual lesions (8 nephroblastomas). One of 5 radiologic "de-novo" lesions was a nephroblastoma. Overall, 20 patients developed nephroblastoma, including 9 high-risk histologies (4 Diffuse Anaplasia, 5 Blastema). One patient died from 1st-line-treatment associated VOD, 4 from progressive nephroblastoma. 5y-EFS was 56%, 5y-progression-to-nephroblastoma-free-survival was 77%. 5y- and 15y-OS was 95% and 85% respectively. Risk factors for events were: diffuse involvement (74%/34%, p<0.001), non-CR at the end of 1st-line-treatment (18%/87%, p<0.001), bilateral lesions (41%/83%, p=0.003), female gender (43%/76%, p=0.03).

Conclusion: The overall risk of developing a nephroblastoma is 27% with an increased risk for fatal outcome. EFS is unsatisfactory, therefore new treatment approaches are needed.

O-116 | Microscopic Nephrogenic Rests in Unilateral Wilms Tumour: A Risk Factor for Recurrence?

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Background/Objectives: Nephrogenic rests (NR), considered as Wilms tumour (WT) precursors, are divided in two main subtypes (intra-lobar, ILNR, and perilobar, PLNR). When diffuse, they are known as nephroblastomatos, are mostly associated with bilateral disease and carry a higher risk of recurrence. The presence of microscopic NR in unilateral WT has been poorly studied. We aimed to review all French patients with unilateral WT enrolled in SIOF2001 trial, to describe NR distribution and analyze their influence on progression-free survival (PFS) and overall survival (OS).

Design/Methods: We retrospectively collected the clinical data from the SIOF database held in Lyon, France and the pathology data from the central pathology review forms. Patients with bilateral disease, no nephrectomy, progression before nephrectomy or follow-up less than 2 years were excluded. The prognostic value of NR was investigated by univariate Kaplan-Meier survival analysis.

Results: Among 568 patients included, NR were present in 256 (45.5%) patients, representing 149/312 (48%) females and 107/256 (42%) males and distributed as follow: 162 (29%) PLNR, 63 (11%) ILNR, 20 (4%) PLNR+ILNR, 7 (1%) diffuse NR (4 missing data). NR were more frequent in stage I (49.12%) and II (49.22%) than stage III (40.16%) and IV (32.05%) (p=0.0304). 76% of NR found in stromal WT were ILNR whereas PLNR was predominantly found in all the other histological subtypes. Among intermediate risk WT, all focal anaplasia and half of the other subtypes had NR whereas 40% of blastema and 28% of diffuse anaplasia WT had NR. The PFS and OS at 24 months for patients having NR versus those without was 92.5%[88.2-95.3] and 99.1%[96.5-99.8] versus 93.8%[90.3-96.0] and 97.8%[95.4-99.0] (p=0.81 and p=0.27) respectively.

Conclusion: The presence of NR on the nephrectomy specimen of patients with unilateral WT did not seem to influence PFS and OS. Further studies are needed to confirm these results.

O-117 | Prognostic Impact of TP53 Mutation Status in Wilms Tumors with Diffuse Anaplasia

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Background/Objectives: Wilms Tumour (WT) is the most common renal neoplasm in children. In the US WTs are divided in Favorable Histology WTs and Unfavorable Histology WTs (~5%), showing focal or diffuse anaplasia (DAWTs). Anaplasia is associated with *TP53* mutations in 50-86% of anaplastic WTs in small studies. The association between *TP53* mutation and outcome in DAWT is not clear.

Design/Methods: We analyzed all DAWTs (n=118) registered on the National Wilms Tumour Study 5 for *TP53* mutations and 17p13 copy loss. In-depth genomic analysis of 39 DAWTs was performed by Whole Genome/Exome Sequencing, gene expression analysis.

Results: Within 118 DAWT, *TP53* mutations were identified in 48%, 17p13 copy loss only in 11%, and 41% lacked both (defined as *TP53*-wildtype (wt)). *TP53*-wt tumors with stage III and IV (but not those with Stage I or II) disease showed significantly lower relapse and death rates than those with *TP53* abnormalities. By in-depth genomic analysis of 39 DAWTs, we identified 18% (7/39) to be *TP53*-wt. These 7 DAWTs lacked mutations of other genes in the *TP53* pathway, and showed significant up-regulation of genes involved in the *TP53* pathway, supporting an active *TP53* pathway. However, abnormal p53 protein accumulation was identified by immunohistochemistry in all *TP53*-wt tumors with available blocks containing anaplasia. Retrospective histology review of these cases demonstrated a very low volume of anaplasia in 6/7 *TP53*-wt DAWT.

Conclusion: These results support the key role of *TP53* in the development of anaplasia in DAWT, and suggest that most tumors determined to be *TP53* wild-type on the basis of analysis of a single randomly selected tumour sample will show evidence of *TP53* mutation in carefully selected samples. It emphasizes the clinical impact of residual anaplastic tumour following surgery. Lastly, it supports the potential role for assessment of volume of anaplasia in predicting relapse.

O-118 | Treatment of Stage I Focal or Diffuse Anaplastic Wilms Tumour: A Report from the Children's Oncology Group

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Background/Objectives: In the fifth National Wilms Tumour Study (NWT5-5), the 4-year event-free survival (EFS) and overall survival (OS) estimates for 27 patients with stage I focal (n=8) or diffuse (n= 19) anaplastic Wilms tumour (AWT) treated with vincristine and dactinomycin without flank radiation were 70% and 81.5%, respectively. Median time to relapse was 6.4 months after diagnosis; sites of relapse included the lung, abdomen, operative bed, liver, and bone. The Children's Oncology Group (COG) AREN0321 study evaluated whether adding doxorubicin and flank radiation improved survival for these patients.

Design/Methods: Patients were eligible to enroll on the AREN0321 stage I AWT treatment stratum if they underwent upfront nephrectomy, and had their tumour histology and stage confirmed by real-time central pathology, surgery and radiology review via the AREN0321 Renal Tumour Biology and Classification Study. Patients received a 25-week regimen of vincristine, dactinomycin and doxorubicin (cumulative dose 150 mg/m²) with 1080 cGy radiation to the affected flank (Regimen DD-4A). The study was approved by the Pediatric Central Institutional Review Board (IRB) and local IRBs according to institutional policy. The log-rank test was used to compare EFS and OS on AREN0321 and NWT5-5.

Results: Eighteen patients with stage I AWT (8 focal and 10 diffuse) were enrolled on AREN0321. The median follow-up time was 4.6 years. The 4-year EFS and OS were 100%. One patient with diffuse AWT had a pulmonary relapse 4.12 years after diagnosis. The EFS and OS for stage I AWT appeared better for patients treated on AREN0321 compared to NWT5-5 (p=0.057).

Conclusion: The addition of doxorubicin and flank radiation to vincristine and dactinomycin appears to have improved the EFS and OS for patients with stage I AWT. The risks of this additional therapy should be balanced against the apparent reduction in relapses and deaths.

O-119 | Feasibility of Complete Resection of Residual Lung Nodules after Chemotherapy in Patients with Stage IV Favorable Histology Wilms Tumour

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Background/Objectives: In Children's Oncology Group (COG) study AREN0533, patients with Favorable Histology Wilms Tumour (FHWT) with complete response (CR) of pulmonary lesions by 6 weeks of standard chemotherapy avoided pulmonary XRT with excellent overall survival. Partial response/stable disease (PR/SD) patients all received pulmonary XRT. It is possible that some of these patients had benign lesions, necrotic or well-differentiated WT, and/or could have obtained a surgical CR. On SIOP protocols, XRT is omitted for Stage IV FHWT patients that achieve a surgical CR. The purpose of this study was to examine the extent and feasibility of surgical resection that would have rendered a surgical CR for PR/SD patients enrolled on AREN0533, allowing the potential to omit XRT.

Design/Methods: Patients enrolled on COG AREN0533 with stage IV FHWT due to pulmonary metastasis only, and had either PR/SD with < 10 lesions after 6 weeks of chemotherapy were eligible. Surgical and Radiologic reviewers evaluated number, location and resectability of residual lesions. Resection was considered "feasible" if lesions were peripheral, required only wedge resection, and could be performed thoroscopically without lobectomy.

Results: AREN0533 enrolled 302 patients from 2007-20013. At 6-weeks, 189 had PR/SD. Of these, 93(49%) had less than 10 lesions (14 SD, 79 PR) and were further evaluated. 83 of this 93 (89%) had < 3 lesions, 38 had only one lesion. Thoroscopic surgery to reach CR was found feasible in 67/93 (72%) patients: requiring single wedge resection in 20, 2-3 wedge resections in a single lobe in 5, 2-3 wedge resections in different lobes of a single lung in 24, and 18 which would require resections in both lungs.

Conclusion: In this exploratory study, thoroscopic resection to achieve CR was considered feasible in 35% (67/189) of PR/SD patients on AREN0533, supporting that selected PR/SD patients may be candidates for surgery to potentially allow omission of XRT.

O-120 | Genetic and Epigenetic Evaluation of Potentially Important Subtypes of Clear Cell Sarcoma of Kidney (CCSK)

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Background/Objectives: Clear Cell Sarcoma of Kidney (CCSK), the second most common paediatric renal malignancy, is an aggressive tumour of unknown cellular origin. Recently, an Internal Tandem Duplication (ITD) within the c-terminus of *BCOR*, encoding the PUF domain, important in interaction with PCGF1 and thereby in the formation of the variant-Polycomb Repressor Complex 1, was identified in 20/20 CCSKs. Interestingly, none of these cases expressed the *YWHAE-NUTM2* transcript, previously described in a minority of CCSK by the O'Sullivan group, and which constitutes the only previously known recurrent genetic event observed in this cancer. This observation raises consideration for distinct mutational subsets of CCSK.

Design/Methods: We studied 159 CCSK tumors for *BCOR*-ITD and *YWHAE-NUTM2* fusion by RT-PCR and Sanger sequencing. Clinical-data were available for 130/159 cases. In addition, we screened for alternative or additional oncogenic drivers by Whole Genome Sequencing (WGS). Furthermore, we performed Chromatin Immunoprecipitation-Sequencing (ChIP-Seq) to identify regulatory regions of interest genome-wide and thereby elucidate cellular origin.

Results: Our findings show distinct subsets of CCSK with these *BCOR* and *YWHAE* alterations. Furthermore, a substantial proportion (11.8%) of CCSKs bear neither mutation, raising the possibility of distinct aetiologies for subsets of CCSK. Clinical and gene expression differences observed between these subsets support this notion. *BCOR*-ITDs consisted of 5 main forms of duplication with additional minor variations, resulting in a total of 15 mutation types, all sharing a common 13-amino-acid motif. Moreover, cross-correlation between WGS and ChIP-Seq data provides new insights into the genomic and epigenomic landscape of this potentially lethal tumour.

Conclusion: Our studies have revealed distinct subsets of CCSK with initial indications of divergent molecular biology and clinical behavior. These observations prompt further exploration of CCSK biology with a view to development of individualized treatment strategies, in an effort to replace more toxic regimens currently in use.

FREE PAPERS SESSION 22: LYMPHOMAS - NHL

O-121 | Value of FDG PET/CT in the Initial Staging of Paediatric Non Hodgkin Lymphoma. A Report from the French PET Lymphoma Study

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Background/Objectives: 18F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) is performed for staging of adult Non Hodgkin Lymphoma (NHL) as a standard of care whereas there is still limited information on the feasibility and the diagnostic performance of PET/CT in the initial staging of paediatric NHL.

Design/Methods: All patients aged 3-21y treated for main NHL paediatric subtypes: Burkitt lymphoma (BL), diffuse large B cell lymphoma (DLBCL), primary mediastinal B cell lymphoma (PMBCL), lymphoblastic lymphoma (LL) and ALK+ anaplastic large cell lymphoma (ALCL) with the current SFCE protocols and for whom a PET/CT could be organized for the evaluation of remission have been prospectively included in this French multicentric study. PET/CT at initial staging was recommended but not mandatory for inclusion. No therapeutic decision was based on PET/CT only. We report here the results of initial PET/CT.

Results: Out of 230 patients (median age 10.7) included from 2011 to 2015, 153(70%) had a PET/CT for staging: 55/83(66%) BL, 25/28(80%) DLBCL, 16/20(80%) PMBCL, 34/57(60%) LL, and 23/29(79%) ALCL. In all patients, except those with completely resected lymphoma, at least a lesion exhibited significant FDG uptake at PET/CT. Overall, 14.5% of the lesions detected on PET/CT were not detected on conventional imaging. Only 11/32 patients with cytologically/histologically proven bone marrow involvement has a bone or bone marrow FDG uptake on PET/CT. Finally, PET/CT findings resulted in a change in staging in only 3/230(1.3%) patients (not considering patient with bone lesions (n=10) as stage IV).

Conclusion: PET/CT is feasible at diagnosis in a large proportion of paediatric NHL. However, its impact on initial staging is limited and the results only rarely lead to a modification of treatment plan as compared to staging with conventional imaging only. Bone marrow involvement is underestimated by PET/CT and BM evaluation is still mandatory for initial staging.

O-122 | Burkitt Lymphoma in Children: Is a Second Cycle Pre-Induction Chemotherapy Effective in Critically ILL Children?

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Background/Objectives: Patients with advanced-stage Burkitt lymphoma are at risk of death (3%) from treatment related complications, especially at early phase of therapy. Protecting them from toxicity of antineoplastic therapy is important. Our aim is to analyze the outcome of sick patients who could not receive their induction phase on time and were given a second CVP, and to measure the impact of delay to start induction course on disease outcome.

Design/Methods: The data of children with Burkitt lymphoma, having a second CVP, was retrospectively gathered. An initial workup laboratory, body CT, PET, bone marrow aspirate and biopsies, and CSF analysis. Biopsy, from all patients with pathological, and cytogenetic confirmation of Burkitt lymphoma.

Results: 45 patients received 2nd CVP, 29 males and 16 females. Primary disease was abdominal (34), pelvic (5), iliac bone (1), ovarian (1), lumbar mass (1), bilateral renal mass (1), paraspinal (1), and maxillary sinus (1). Nineteen patients were stage IV, 26 patients were stage III. Twenty five patients were group C (55.5%), 20 were group B (44.5%). After the 1st cycle of CVP, 8 had stationary disease, 34 had Regressive disease while 3 showed disease progression. A second CVP was given due to renal impairment in 4 patients, 3rd space fluid in 13 patients, convulsions in 6, encephalitis in one, 4 patients had poor general condition, and 17 were neutropenic. Follow up revealed 29 alive (64.5%), and 16 dead (35.5%) (7 immediately post 2nd CVP). Five patients died from disease progression, 10 patients died from septicemia, one from multisystem organ failure. The period until patients had their Induction ranged from 6-45 days.

Conclusion: Although a second CVP is tolerated well, a high death rate (35.5%) was found, either from disease progression or sepsis. An alternative approach for those patients should be sought.

O-123 | Reduced Burden of Therapy in Intermediate Risk Mature B-Cell Non-Hodgkin Lymphoma (B-NHL): Preliminary Results of the Reduced Burden of Oncologic Therapy (REBOOT) Trial

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Background/Objectives: Childhood B-NHL has a ≥90% EFS with intensive multi-agent chemotherapy, though associated with high rates of mucositis and infection (Cairo et al. JCO, 2012). The safety of reducing therapy in Group B patients and of adding rituximab to chemotherapy in children were previously reported (Patte/Cairo et al. Blood 2007; Goldman/Cairo et al. Leukaemia 2013). The REBOOT trial seeks to further reduce therapeutic burden and toxicity by reducing total intrathecal chemotherapy doses with intrathecal liposomal cytarabine (IT L-Ara-C) and reducing anthracycline exposure with addition of rituximab in Group B B-NHL patients.

Design/Methods: FAB Group B mature B-NHL patients, ages 3-30 excluding PMBL, were enrolled on the multicenter study. All patients receive six rituximab doses during two induction (two doses/course) and two consolidation (one dose/course) courses with 60% doxorubicin dose reduction. IT L-ARA-C (35mg 3-16 year and 50mg >16 years) was given with concurrent dexamethasone following HD-MTX clearance in each induction cycle.

Results: Through January 2016, 18 Group B patients (2 stage II, 16 stage III, 5 LDH >2xULN), median age 12 years (range 3-25), 7 Burkitt/11 DLBCL have enrolled. No rituximab or L-Ara-C related serious adverse events have been reported. Grade ≥3 mucositis and febrile neutropenia has occurred during 5.5% of induction cycles. Sixteen patients achieved CR with Group B therapy and cumulative doxorubicin 50mg/m². Two patients with residual renal lesions after first consolidation were escalated to Group C therapy achieving a CR. With median time from study entry of 65 weeks (range 17-163), the EFS and OS are currently 100%.

Conclusion: Preliminary results suggest it is safe to reduce total anthracycline exposure in intermediate risk B-NHL with a significant reduction in acute toxicity and still maintain a high 1 year EFS. Additionally, IT L-Ara-C is well tolerated when administered after HDMTX clearance. Funded in part by Sigma Tau Pharmaceuticals.

O-124 | Outcome of Relapse in Children/Adolescents with B-Cell Non-Hodgkin Lymphoma (B-NHL) and Mature Acute Leukemia (B-AL) Treated in the Rituximab (R) Era

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Background/Objectives: To describe relapsed B-NHL/AL in children/adolescents initially treated with LMB regimen and their outcome in the R era and to analyze response to second line chemo-immunotherapies, relapses in the French LMB2001 study were reviewed.

Design/Methods: Between February 2001 and December 2011, 37 patients of 803 (4.6%) relapsed: 29 had Burkitt (BL) and 8 large-cell histology. There were 25 males and median age at diagnosis was 10.3 years (R, 1.9-17.9). One patient was initially treated in risk Group A, 24 in Group B and 12 in Group C. Twenty-seven patients had LDH level > 2N.

Results: Mean time to relapse after diagnosis was 4.7 months [2.4; 10.8] in BL and 10.9 months [3.9; 31] in large-cell histology. Twenty-one patients had a relapse in one site (5 in the central nervous system (CNS)) and 16 at multiple sites. Relapses occurred in the primary site in 16 pts (43%) in the bone marrow in 14 pts (38%), and in the CNS in 11 pts (30%). Data on second line treatment are currently available for 29 patients. Among them, 24 received R as salvage therapy mainly in addition to ICE (n=15 pts) and/or CYVE (n=13 pts) and/or high-dose MTX (n=4 pts) regimen. Salvage response (complete + partial remission) rates were 46% (6/13 patients) with R+CYVE after group B therapy and 50% (7/14 evaluable patients) with R+ICE after group B or C therapy. Eighteen patients also received high-dose chemotherapy followed by autologous (n=12) or allogeneic (n=6) transplant. With a median follow-up of 5.3 years, the 3-year survival rate of the 37 patients was 37.6%.

Conclusion: In the rituximab era, survival remains poor after relapse in children and adolescents with mature B-cell lymphoma/leukaemia. Response rates to second line chemo-immunotherapies including rituximab are insufficient and new drugs are urgently need to improve disease control before consolidation.

O-125 | Clinical Outcome of 688 Children with Non-Hodgkin Lymphoma Treated in a Single Center from China

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Background/Objectives: The outcome of childhood NHL chemotherapy had been improved recently. This study aimed to investigate the clinical characteristics of NHL in Chinese children and evaluate the efficacy of BCH-2003/2009-NHL protocol.

Design/Methods: 688 NHL were treated between February 2003 and June 2015. 2 treatment groups enrolled 194 & 494 cases respectively. In group 2, we identified the MDD & MRD in BM and PB by PCR or flow cytometry. ALL the pathology results were center reviewed by more than 3 pathologists.

Results: There were 246 B-cell NHL including 195 BL, 7 BLL, 40 DLBCL, 3 FL and 1 PMDLB, 359 LBL and 83 ALCL, 500 boys and 188 girls with a median age of 7y old. B cell NHL typically presented with abdomen mass or acute abdomen. T-LBL generally

presented with mediastinal mass and leukaemia stage, head & facial mass were commonly seen in B-LBL. 642 cases had stage III-IV disease. 98 had CNS involvement (B-cell 51, LBL39, ALCL8) and 401 cases had BM involvement: B-cell 106; LBL 294; ALCL 9. The median follow-up time was 87.3m. The 5y-OS & EFS were 90.3% & 84%. B-cell NHL, 5-year OS & EFS were both 83.1±4.4% group 1, 88.6±2.4% & 83.8±4.5% respectively in group 2. For LBL, group 1 : 5-year OS & EFS were 85.2±2.1% & 82.7±2.3%; group 2 : 86.7±3.7% & 84.3±4.0% respectively. ALCL group 1 : 5-year OS & EFS were 91.9% & 79.6%, group 2 were 89.5±3.4.0% & 83.1±3.9.0%. 74 patients had event, treatment related died (n=22) or relapse & refractory (n=52). 15 patients got CR2, 37 patients died. Univariate analysis showed stage IV disease, failure to achieve CR after 3 months treatment, bulky mass were associated with poor prognosis.

Conclusion: LBL is the most common subtype of NHL in China, the percentage of T-LBL is lower than western. We have achieved excellent treatment outcome using revised international protocols. Treatment-related complications and relapse remained the main reasons of treatment failure.

O-126 | Utility of Quantitative Plasma Epstein-Barr Virus DNA for Paediatric Lymphoma Diagnosis and Treatment in Malawi

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Background/Objectives: Epstein-Barr virus (EBV) is causally associated with the two most common paediatric lymphoma subtypes in sub-Saharan Africa, Burkitt lymphoma (BL) and Hodgkin lymphoma (HL). Plasma EBV DNA may be useful for diagnosis, risk stratification, and response assessment, but data are scant from the region.

Design/Methods: Children with suspected lymphoma were enrolled in Malawi between June 2013 and October 2014, and those with confirmed lymphoma were followed until death or censoring in December 2015. All diagnoses were confirmed by United States and Malawian pathologist review. Plasma for EBV DNA quantification was collected at enrollment for all children, and mid-treatment and treatment completion for those with lymphoma.

Results: Of 84 enrolled children, 82 (98%) had baseline plasma EBV DNA measurement, including 61 with BL, 7 with HL, and 14 with non-lymphoma. Plasma EBV DNA was detected in 51 (84%) children with BL (median 6.1 log₁₀copies/mL, range 2.4-8.8), 6 (86%) with HL (median 4.3 log₁₀copies/mL, range 3.5-5.9), and 1 (7%) with non-lymphoma (3.7 log₁₀copies/mL). Plasma EBV DNA detection was more common in lymphoma versus non-lymphoma (p<0.001), with a trend toward higher viral loads in BL versus HL (p=0.065). For BL, EBV DNA detection declined at mid-treatment (23/34, 68%) and treatment completion (16/25, 64%), as did median viral load at mid-treatment (median 3.7 log₁₀copies/mL, range 2.2-6.6) and treatment completion (median 3.4 log₁₀copies/mL, range 2.5-6.4; p<0.001 for mid-treatment vs baseline and completion vs baseline comparisons). For BL, baseline plasma EBV DNA was associated with mortality, with a hazard ratio of 1.15 per log₁₀copies/mL (p=0.043) for all children, and 1.38 per log₁₀copies/mL (p=0.005) among children with detectable baseline viral loads.

Conclusion: Plasma EBV DNA was detected in most paediatric BL and HL in Malawi, and may be useful to distinguish lymphoma from non-lymphoma, distinguish BL from HL, and improve BL risk stratification and response assessment.

FREE PAPERS SESSION 23: CHIMERIC ANTIGEN RECEPTOR T CELL THERAPY

O-127 | Efficacy of Retreatment with Humanized CD19-Targeted Chimeric Antigen Receptor (CAR)-Modified T Cells in Children with Relapsed ALL

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Background/Objectives: Targeted immunotherapy with CTL019, CD19-specific chimeric antigen receptor (CAR)-modified T cells, can produce potent and sustained responses in children with relapsed/refractory acute lymphoblastic leukaemia (ALL). However, a subset has limited persistence. We now report on retreatment with murine (CTL019) or humanized (CTL119) CD19-directed CAR T cells.

Design/Methods: Patient-derived T cells were transduced ex vivo with a lentiviral vector encoding a CAR with CD3z, 4-1BB, and murine or humanized anti-CD19 scFv domains and activated/expanded with anti-CD3/CD28 beads.

Results: Of 55 patients in CR at 1 month after murine CTL019 infusion (55/59 CR), 3 patients were re-infused with CTL019 for CD19+ relapse, with 1/3 achieving remission. Of 3 children reinfused for CD19+ MRD, MRD decreased in 2, while 1 progressed to CD19+ relapse. Repeat infusion re-induced B cell aplasia in only 1/8 treated for B cell recovery. Conversely, 6/7 children reinfused for CD19+ hematogones demonstrated continued B cell aplasia 7-23 months after repeat infusion, 5 remain in remission 12-30 months after initial infusion, and 2 experienced a CD19- relapse.

Ten children previously treated with murine CAR-modified T cells (CTL019, n=6; other, n=4) were treated on a phase 1 study of humanized CTL119 for B cell recovery (n=4), CD19+ relapse (n=5), or no response to prior murine CAR T cells (n=1). Cytokine release syndrome (CRS), seen in 6 patients, did not require vasopressor or respiratory support. Responses were seen in 6/10 with ongoing CR of 1-9 months in 4 patients. Two responding patients were previously resistant to repeat infusion of murine CTL019.

Conclusion: Reinfusion of murine CTL019 may be effective in specific subgroups. In the first demonstration of humanized anti-CD19 CAR efficacy, CTL119 induced remission in patients previously treated with murine CD19-directed CAR T cells. Further investigation into anti-CAR responses will be vital to improve durable remission rates in this highly refractory population.

O-128 | Immunotherapy of Acute Leukemia by Chimeric Antigen Receptor-Modified Lymphocytes Using an Improved Sleeping Beauty Transposon Platform

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Background/Objectives: Chimeric antigen receptor (CAR)-modified T-cell adoptive immunotherapy is an emerging therapeutic option proven effective in the treatment of hematological malignancies. However, the success of CAR-engineered T cells strictly depends on the optimization of several critical parameters related to cell manufacturing and gene therapy.

Design/Methods: In this regard, we sought to develop a novel clinical-grade culture and gene-modification protocol of cytokine-induced killer cells (CIKs) using the Sleeping Beauty (SB) transposon system. Administration of irradiated PBMCs overcame cell death of stimulating cells induced by non-viral transfection, enabling robust and stable gene transfer together with an efficient T-cell expansion suitable for clinical application.

Results: Upon single stimulation, we reached an average of 60% expression of two distinct 3rd generation CARs (CD28/OX40/TCRzeta), specific for CD123+ acute myelogenous leukaemia (AML) and CD19+ acute lymphoblastic leukaemia (ALL). Furthermore, modified cells displayed persistence of cell subsets with memory phenotype, specific and effective lytic activity against leukemic cell lines and primary blasts, cytokine secretion, and proliferation. Overall our method achieved consistent results in terms of expansion, CAR expression and functionality, even upon comparison with conventional T-SB platforms. Adoptive transfer of CD123.CAR or CD19.CAR lymphocytes led to a significant antitumor response against AML and ALL disseminated diseases in NSG mice. Notably, we found no evidence of integration enrichment near cancer-related genes and transposase expression at the end of the differentiation.

Conclusion: Taken all together, our findings describe a novel donor-derived non-viral CAR approach characterized by efficient cell transfection and expansion that may widen the repertoire of available methods for T cell-based immunotherapy.

O-129 | Tuning of Anti-Cd123 Chimeric Antigen Receptor (CAR) Binding Affinity and Balance with Car Density in An in Vitro Model of Acute Myeloid Leukemia

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Background/Objectives: Chimeric Antigen Receptors (CARs)-redirected T lymphocytes are a promising novel immunotherapeutic approach, nowadays object of accurate preclinical evaluation also for the targeting of Acute Myeloid Leukaemia (AML).

Design/Methods: In this context, we recently developed a CAR against CD123, over-expressed on AML blasts and leukaemia stem cells. However, the potential recognition of low CD123-positive healthy tissues, through the "on-target-off-organ" effect, limits the safe clinical employment of CAR-redirected T cells. Therefore, in search for a CAR design optimization, it has been found that several variables can modulate CAR-T cell functional profiles in a context-dependent manner, such as CAR binding affinity for the target antigen, CAR expression and target antigen density.

Results: Given the difficulties of studying these features in the absence of other interfering elements, we exploited computational structural biology tools to design point mutations in the anti-CD123 CAR antigen binding domain, in order to investigate their impact, in terms of different CAR affinity and expression, on *in vitro* CAR T-cell early and later effector functions. We were able to define both "lytic" and "activation" antigen thresholds showing that, while the early T-cell cytotoxic activity is not affected neither by CAR expression nor by CAR affinity tuning, later effector functions are principally impaired by CAR expression. Moreover, a promising balance in the efficacy and safety profiles of CAR T cells was observed by the lowest affinity mutant, in response to targets with different antigen densities.

Conclusion: Overall, the full dissection of all these variables offers additional knowledge for the proper design of a suitable anti-CD123 CAR for the treatment of AML.

O-130 | Chimeric Antigen Receptor-Engineered Gamma-Delta T-Cells for Neuroblastoma Immunotherapy

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Background/Objectives: Novel therapies for high-risk neuroblastoma that target cancer cells whilst sparing healthy tissue are a research priority. Chimeric antigen receptor (CAR)-engineered T-cells targeting GD2 on the surface of neuroblastoma cells, is a highly promising strategy with success dependent on the ability of effectors to home to the tumour site, specifically kill cancer cells, and generate immunological memory. Conventional approaches utilise alpha-beta ($\alpha\beta$) T-cells as the effector of choice, however gamma-delta ($\gamma\delta$) T-cells possess additional functional properties potentially advantageous for cancer immunotherapy. $\gamma\delta$ T-cells adopt an antigen presenting cell (APC) phenotype upon activation, and here we demonstrate the combined ability of GD2-CAR-transduced $\gamma\delta$ T-cells to kill GD2-expressing cancer cells and demonstrate functional and phenotypic features of professional APCs.

Design/Methods: $\gamma\delta$ T-cells were pre-stimulated with zoledronate and transduced with a second-generation GD2-CD28-CD3 ζ CAR. Memory phenotype, presence of exhaustion markers, and expression of APC-associated surface proteins was determined by flow cytometry. $\gamma\delta$ CAR T-cell cytotoxicity was assessed by chromium-release assay. Professional antigen presenting capacity was examined by co-culture of MART-1 tumour antigen pulsed HLA-A201⁺ CAR $\gamma\delta$ T-cells with CellTraceTM labelled HLA-A201-restricted MART-1 TCR-specific $\alpha\beta$ responder cells.

Results: Following zoledronate activation and retroviral transduction $\gamma\delta$ T-cells were enriched within the PBMC population to over 85% following 13-day culture, with an average transduction efficiency of 30%. $\gamma\delta$ CAR T-cells were of 'effector memory' phenotype, and simultaneously adopted an APC phenotype with high expression of CD86 and HLA-DR. $\gamma\delta$ and $\alpha\beta$ CAR T-cells showed equivalent specific killing of GD2-positive targets. Activated and expanded $\gamma\delta$ T-cells following incubation with MART-1 peptide antigen were capable of inducing specific HLA-A201-restricted MART-1 TCR-specific $\alpha\beta$ T-cell proliferation.

Conclusion: We conclude that $\gamma\delta$ CAR T-cells with an inducible APC phenotype can be generated in sufficient number for immunotherapy of neuroblastoma and other GD2-expressing cancers. This approach may represent a novel paradigm for CAR T-cell therapy.

O-131 | Adoptive Therapy of Ewing Sarcoma with GD2 Antigen-Specific Car-Engineered NK Cells Induces Upregulation of Immune-Inhibitory HLA-G

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Background/Objectives: Activated allogeneic NK cells are cytotoxic against single Ewing sarcoma (EwS) cells *in vitro*, but multicellular tumour cell clusters were found to be resistant, which limits the therapeutic potential of this strategy. We aimed to enhance the potency of NK cells to eliminate EwSs by genetic engineering with chimeric antigen receptors (CARs).

Design/Methods: To this purpose, we expressed CARs directed against surface ganglioside GD₂ in *in vitro* activated allogeneic NK cells. We used both second generation CARs containing either 4-1BB or 2B4 costimulatory signaling, or third generation CARs with both types of costimulation.

Results: Expression of GD₂ antigen-specific CARs increased the cytolytic activation responses of activated NK cells to GD₂ + EwS and also neuroblastoma cells in an antigen-specific manner. Resistance of individual cell lines to NK cell lysis was efficiently overcome. Second and third generation CARs were equally effective. However, activated and CAR gene-modified NK cells could not prevent or delay tumour growth in xenograft models, both by intraperitoneal and intratumoural delivery. A candidate search for potential immune-inhibitory ligands in the tumour microenvironment by histopathology review of tumour autopsies revealed that the immunosuppressive ligand HLA-G was upregulated in tumour xenografts in mice treated with NK cells. HLA-G1 expressed by Ewing sarcoma cells using retroviral gene transfer, suppressed the cytotoxic activity of NK cells against the tumour cells *in vitro*, confirming the potential relevance of our finding.

Conclusion: This work identifies HLA-G as a candidate immune checkpoint in EwS. Inhibiting HLA-G along with adoptive transfer of CAR gene-modified NK cells may enhance the therapeutic efficacy of tumour targeting.

O-132 | Chimeric Antigen Receptor 4SCAR-GD2/CD56-Modified T Cells in the Refractory and Recurrent Paediatric Solid Tumors

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Background/Objectives: To preliminarily explore the safety and efficacy of chimeric antigen receptor (CARs)-transduced T cell (CAR-T) in the treatment of refractory and relapsed paediatric solid tumors; to observe the side and toxic effects of GD2 and CD56-CAR-T; to determine the therapeutic efficacy based on the international therapeutic effect criterion of paediatric solid tumors, and to provide the basis for further clinical researches.

Design/Methods: 16 patients with refractory and relapsed paediatric solid tumors during May 2015 to March 2016 were included. Features of the subjects: 13 were male and 3 were female. The preliminary diagnosis ages were between 13 and 107 months. 13 patients were diagnosed with stage IV NB. The targets were all GD2. 2 patients were diagnosed with RMS and the targets were all CD56. 1 patient was diagnosed with glioblastoma multiforme and the target was GD2. Patient's peripheral T cells were transduced with a 4th generation, safety-engineered. Patients received Fludarabine+ Cyclophosphamide as pre-CAR-T lymphodepleting chemotherapy.

Results: Among the 13 NB patients, 9 were noted with increased cytokine level represented by IL-6 and IL-10, 2 RMS patients didn't show obvious cytokine storm. All patients suffered from moderate (Grade 1-2) CRS reactions. Changes of cellular immune functions: 11 of the 13 NB patients were noted with decreased CD4/CD8, reduced THL and increased TSL. 11 of the 13 NB patients achieved a total effective rate CAR-T of 81.8%. 2 RMS patients showed progression disease before CAR-T therapy. 1 patient with glioblastoma has showed SD.

Conclusion: The preliminary results of the treatment of 16 child patients with solid tumors using GD2 and CD56-CAR-T showed superior safety. Despite the high effective rate of GD2-CAR-T in treating NB, the therapeutic efficacy is related to the tumour burden before transfusion. Our results suggest that CAR-T technology is a relatively safe and effective consolidation therapy for the child patients with high risk glioblastoma. Also.

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O-133 | Final Results of 406 Patients with Short-Term Infusion CH14.18/CHO Randomised for Subcutaneous Aldesleukin and Results in 161 Confirmatory Patients: The Current SIOPEN HR-NBL1 Front-Line Experience

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Background/Objectives: This SIOPEN Phase-III trial (APN311-302)(EudraCT:2006-001489-17) investigated effects of ch14.18/CHO monoclonal antibody ± subcutaneous interleukin-2 (scIL2) in high-risk neuroblastoma (HRNBL1) front-line patients (pts).

Design/Methods: Between 2009-2011, 406pts were randomized for immunotherapy (IT:"R2") (MycN amplified (MNA) stages 2-4 all ages <21yrs and stage 4 >1yr without MNA) when starting maintenance. Eligibility included COJEC induction ± 2TVD; enrolment on the HDT randomisation ("R1", BUMEL vs CEM) with R1-response criteria. Local treatments aimed at gross surgical resection and radiotherapy (21Gy). Pts received either 100mg/m² ch14.18/CHO (d8-12) as 5 daily 8-hour short-term infusion (STI) alone (STI-A) or combined with 6x10⁶IU/m² scIL2 (d1-5;8-12) (STI-B) for a total of 5 IT cycles; both had 6 cycles of oral 13-cis-RA (160mg/m², d19-32). The median age at diagnosis was 3yrs (1month-19yrs) and the median observation time 3.1yrs. The trial allowed a confirmatory cohort (CC) receiving STI-A regimen (161 HRNBL1pts) after closing "R2". Outcomes are reported as 3-yrs event free/overall survival rates (EFS/OS).

Results: The EFS/OS for pts treated with ch14.18/CHO without and with scIL2 was 0.57±0.04/0.66±0.04(200pts)(NS) and 0.60±0.04/0.67±0.04(206pts). The EFS for CR-pts (or VGPR/PRpts) on STI-A was 0.68±0.05 (0.46±0.06) and with STI-B 0.65±0.05 (0.53±0.06) indicating no benefit for scIL2. Early termination of IT occurred in 18% in STI-A, but in 44% in STI-B (36% toxicity-related, 8% progressions). A Lansky performance status of ≤30% was found 17% STI-Apts but in of 39% STI-Bpts (p<0.001). CTC-grade 3&4 allergic reactions were observed in 9% and 20% of STI-Apts and STI-Bpts (<0.001). Incidence of capillary leak and CTC-grade 3&4 fever was significantly lower in STI-A (1% and 14%) vs. STI-B (9% and 40%). The CC-STI-A confirmed the results of randomised STI-Apts.

Conclusion: The EFS/OS rates at 3yrs show a clear improvement to previous SIOPEN experience. A markedly reduced toxicity without IL2 and equivalent outcome suggest a ch14.18/CHO only approach.

O-134 | Long-Term Infusion of Anti-GD2 Antibody CH14.18/CHO in Combination with Interleukin-2 (IL2) in a Multicenter Phase II Clinical Trial in Patients with High Risk Neuroblastoma

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Background/Objectives: Delivery of anti-GD₂ antibody ch14.18/CHO by long term infusion (LTI) may improve the toxicity profile but maintain effective immune modulation and clinical activity in patients (pts) with high risk relapsed/refractory neuroblastoma (NB).

Design/Methods: 124 pts were enrolled into an open label SIOPEX Phase II clinical trial (EudraCT 2009-018077-31) to receive up to 5 cycles of 6x10⁶ IU/m² sc IL2 (d1-5; 8-12), LTI of 100 mg/m² ch14.18/CHO (d8-17) and 160 mg/m² oral 13-cis-RA (d19-32)(APN311-202). Primary efficacy endpoints were antibody (>1μg/ml) and NK-cell levels. Toxicity endpoint was i.v. morphine free antibody delivery after 5 days of cycle 1 in >80% patients. Secondary endpoints were increased ADCC levels over baseline, Fc gamma receptor (FCGR) polymorphisms, objective clinical responses and progression as well as overall survival.

Results: Per protocol treated patients met primary efficacy endpoints with an increase in ADCC in all evaluable patients. Toxicity observed in this trial was improved compared to standard delivery methods. Objective clinical response rate observed in this trial was 40%. The survival update of the cohort revealed a 2-y OS of 64±6% (mean OS 2.7±0.2 y, median EFS 3.7 y (95% CI: 2.0-3.7 y)) and a 2-y EFS of 53±6% (mean EFS 2.0±0.2 y, median EFS 2.3 y (95% CI: 1.2-3.3 y)). This result is clearly superior to historical controls not treated with ch14.18/CHO (p<0.05), indicating clinical efficacy of the treatment.

In this cohort, we found 63/124 pts with low affinity FCGR alleles (FCGR2A-H131R/R and/or FCGR3A-V158 F/F). These patients showed lower EFS and OS rates compared to 59/124 patients with high affinity FCGR polymorphisms (p<0.05). These findings underline FCGR mediated ADCC as mechanism of action of this treatment modality.

Conclusion: Efficacy, clinical activity and improved toxicity profile of a new delivery method of ch14.18/CHO was demonstrated.

O-135 | Survival of Neuroblastoma Patients Treated by Long-Term Infusion of Anti-GD2 Antibody CH14.18/CHO Correlate with Killer-Cell Ig-Like Receptor (KIR) Genotypes and Fcγ-Receptor Polymorphisms

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Background/Objectives: Receptors expressed on natural killer (NK) cells and their ligands on target cells involved in antibody-dependent cell-mediated cytotoxicity (ADCC) may predict outcome in neuroblastoma (NB) patients (pts) treated by long-term infusion (LTI) of anti-GD₂ antibody ch14.18/CHO.

Design/Methods: 53 pts received 6x10⁶ IU/m² sc IL-2 (d1-5; 8-12), LTI of 100 mg/m² ch14.18/CHO (d8-17) and 160 mg/m² oral 13-cis-RA (d19-32) in a closed single center program (53 pts) (APN311-303). Polymorphisms in Fcγ-receptor genes 2A (H131R), -3A (V158F) and -3B (NA1/NA2), and KIR- as well as KIR ligand expression (HLA-C1; HLA-C2; HLA-Bw4+) were determined by real-time PCR.

Results: The survival update of the cohort revealed a 5-y OS of 56.4±7.1% (mean OS 4.35y [0.3-6.2y]) and a 5-y PFS of 29.1±6.3% (mean PFS 2.4y [0.1 - 5.9y]). Median TTP/PFS was 1.35 y (95% CI: 0.21-2.48 y). This result is clearly superior to historical controls not treated with ch14.18/CHO with a 5-y OS of 14.8±6.8% (p<0.005), indicating clinical efficacy of the treatment.

In this cohort, we identified 26/53 pts with the NK- stimulatory KIR haplotype (2DS2+) who had superior OS- and PFS-rates compared to 18/53 pts with an inhibitory haplotype and KIR/KIR-ligand match (2DS2-, 3DL1+, Bw4+) (p<0.02). Similarly, we found 33/53 pts with low affinity FCGR alleles (FCGR2A-H131R/R and/or FCGR3A-V158 F/F). These patients showed lower PFS rates compared to 20/53 patients with high affinity FCGR polymorphisms (p<0.01).

Importantly, ADCC analysis on day 15 of cycle 1 showed higher levels in the pt group with NK-stimulatory versus NK- inhibitory KIR/KIR ligand haplotypes (23±6% vs. 6±2%, p<0.01). A similar effect was observed in pts with high affinity FCGR polymorphisms with an ADCC increase of 20±6% compared to 11±2% in the low affinity FCGR control.

Conclusion: KIR-haplotypes and FCGR- polymorphisms correlated with the functional immune parameter ADCC and clinical outcome, and may therefore be useful biomarkers for LTI with ch14.18/CHO.

O-136 | Myeloablative Busulfan/Melphalan (BUMEL) Consolidation Following Induction Chemotherapy for Patients with High-Risk Neuroblastoma. A Children's Oncology Group (COG) Study

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Background/Objectives: The COG conducted a groupwise study of a Busulfan/Melphalan (BuMel) myeloablative regimen in patients with newly diagnosed, high-risk neuroblastoma (ANBL12P1). Previously used in SIOPEX studies, this is the first trial using BuMel following a COG induction platform. The primary objective was regimen-related toxicity, with a specific focus on pulmonary and hepatic events.

Design/Methods: Five cycles of induction were administered, followed by intravenous busulfan (daily, days -6 to -3), melphalan (140mg/m², day -1) and stem cell rescue. Age and weight based dosing were used for busulfan administration. First dose busulfan pharmacokinetics were mandated and adjustments made to target an AUC <5500 (micromole/liter)*minute. Following hematologic recovery, patients were eligible to receive external beam radiotherapy to primary and residual metastatic sites and then proceed to maintenance immunotherapy. Unacceptable pulmonary toxicity was defined as Grade 4 pulmonary events (CTCAEv.4.0). Sinusoidal Obstructive Syndrome (SOS) was a composite definition using Baltimore criteria.

Results: Between 4/2013 and 4/2015, 150 patients were enrolled. One hundred thirteen patients were evaluable for end-induction response assessment, with 27 (25%) CR, 27 (24%) VGPR and 39 (35%) PR, for an overall response rate of 82%. At the time of consolidation, 101 patients are evaluable for toxicity. The incidence of unacceptable pulmonary toxicity was 3.0% (n = 3), SOS 5.9% (n = 6), and combined hepato-pulmonary toxicity 8.9% (N = 9) during consolidation (days 0–28). There were 0 toxic deaths during consolidation. For all subjects (n=98), the median busulfan AUC was 3554 (range: 2360-4555) micromole/liter*minute, with a median AUC of 4558 (range: 3462-5189) micromole/liter*minute for those developing SOS (n =6) and 3232 (range: 3010-5037) micromole/liter*minute for those developing severe pulmonary toxicity (n = 3).

Conclusion: BuMel following COG induction regimen is well tolerated with acceptable pulmonary and hepatic toxicity in high-risk neuroblastoma.

O-137 | Improved Long-Term Survival after Myeloablative Chemotherapy with Autologous Stem Cell Transplantation in High-Risk Neuroblastoma Patients. Results of the NB97 Trial

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Background/Objectives: Myeloablative chemotherapy (MAT) with autologous stem cell transplantation (ASCT) improved the survival of high-risk neuroblastoma compared to oral continuation chemotherapy (CC). This effect, however, could either be result of better long term cure rates or to delay of relapses leading to similar long-term survival rates. Therefore, we have re-analyzed the patients of the randomized trial NB97 in order to detect if the survival benefit of MAT/ASCT is stable during long-term follow-up.

Design/Methods: Patients with stage 4 neuroblastoma older than 12 months and all patients with MYCN amplification were eligible. Treatment consisted of six-cycle induction chemotherapy, primary site tumour resection, consolidation either with MAT/ASCT or CC, MIBG therapy for MIBG avid residual disease, radiation therapy for active local disease present after operation, and post-consolidation therapy either with single drug anti-GD₂ antibody ch14.18 or with 13-cis-retinoic acid. Outcome was analyzed by logrank test and Cox regression analysis.

Results: A total of 295 patients were randomized. The median observation time was 11.6 years. The 10 year event-free survival (10yEFS) was 40.0+/-4.0% in 149 patients randomized for MAT and 29.4+/-3.8% in 146 patients randomized for CC (p=0.027). The 10 year overall survival was 55.2+/-4.1% and 44.6+/-4.2% in patients randomized for MAT and CC, respectively (p=0.077). The last relapse occurred 12.7 years after diagnosis, so far. In the subgroup of stage 4 patients >18 months at diagnosis randomization for MAT was associated with better EFS (p=0.023) and a trend for better OS (p=0.098). Multivariable analysis identified stage, MYCN status, age, MAT, and treatment with ch14.18 as independent prognostic factors for EFS and also for OS.

Conclusion: Intensive multimodality treatments can achieve survival rates of 50% in high-risk neuroblastoma patients. The benefit of MAT with ASCT is stable during long term follow-up ant, therefore, not simply due to delay of relapses.

O-138 | The Way Towards an International MIBG Skeletal Score for High Risk Neuroblastoma: The Statistical Perspective

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Background/Objectives: A collaborative effort was undertaken to derive an internationally agreed semi-quantitative meta-iodobenzylguanidine (mIBG) scoring method in neuroblastoma by harmonising previously established scoring systems, which were each found to have prognostic value at the end of induction (Evanik JNM 2013). The aim of this analysis was to investigate the individual effect on event-free-survival (EFS) of the two components of the scoring system: 1) the number of involved anatomic regions and 2) the scoring value within each segment and to evaluate the prognostic value of the new proposed scoring system.

Design/Methods: COG and SIOPEN merged data of children with stage 4, mIBG avid, neuroblastoma entered on the COG-A3973 (216pts) and the SIOPEN/HR-NBL1 trial (341 pts) for first line therapy. Two independent nuclear medicine review teams scored mIBG scans pre and post induction according to Curie- and SIOPEN-methodologies. Here, the SIOPEN score evaluating the skeletal (mIBG) uptake on a 0-6 scale in 12 anatomical regions was chosen for the statistical analysis due to the greater range of values. The two study cohorts were investigated separately and a bootstrap-based internal validation was performed.

Results: In 557 pts the cumulative SIOPEN-score post induction had a significant prognostic impact with 5-years EFS of 41%, 33% and 15% for total scores of 0, 1-3 and >3, respectively. However, no increasing hazards with increasing scores per segment were observed. In contrast, the number of positive segments alone had a highly significant impact with 5-year EFS of 41%, 32% and 14% for patients with 0, 1-2 and >2 positive segments post induction.

Conclusion: The number of positive segments was the most important prognostic factor. Weighting the involvement within segments did not improve the prognostic value of the scoring system. These results suggest a possible simplification of MIBG scoring, facilitating future international collaborations.

CCI: RESEARCH FINDINGS

O-139 | Parents' and Childrens' Experiences with Early Clinical Trials

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Background/Objectives: Early clinical trials are in our country offered by three designated paediatric oncology centers under the auspices of DCOG. Both DCOG and VOKK wanted to know why and how parents choose to participate in early clinical trials and if the quality of care in this specific situation was adequate or should be improved.

Design/Methods: In 2014 VOKK reviewed the experiences of parents and children who had participated in an early clinical trial in one center through an online questionnaire. The purpose was to know why and how parents and children decide, to evaluate quality of current care and, if needed, to improve information and care and aftercare.

We invited 31 families to participate in our study; 15 families gave consent. Of these 7 children had died. 6 parents also gave consent for their child. Parents and children filled out separate questionnaires. Topics in the questionnaire were transition, information, decision making, reasons for participation, treatment, burden, support, evaluation, information of study results. Based on the results of our study we drafted recommendations for improvement.

Results: Most parents were content with their participation in the early clinical trial. Hope played a relatively important role in decision making. All parents would decide the same again. The majority of parents would recommend participation to other parents. Some parents and children were willing to act as a sounding board for others in a similar situation. Travel time was a burden for many. Issues for improvement were information about the goal of the study, evaluation after finishing treatment and feed-back of the results of the study.

Conclusion: Although parents' and children's experiences with early clinical are overall positive there are points for improvement. These are taken on by DCOG and VOKK. Our recommendations are shared with the other two centers in order to improve care on a national level.

O-140 | Lower Treatment Abandonment among Paediatric Oncology Patients Enrolled in Research Studies in Lilongwe, Malawi Compared with Standard of Care

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Background/Objectives: Treatment abandonment is a significant barrier to curative outcomes in paediatric oncology worldwide, with rates as high as 50% reported in cohorts in sub-Saharan Africa.

Design/Methods: Using the SIOP Paediatric Oncology in Developing Countries working group definitions of treatment abandonment, we compared abandonment rates in 3 cohorts of paediatric oncology patients at Kamuzu Central Hospital in Lilongwe, Malawi. We evaluated a retrospective cohort of all children diagnosed with cancer from 2011-2013 and two prospective cohorts of paediatric oncology patients enrolled in clinical research studies performed between 2013-2015: one for children with Kaposi sarcoma (KS) and another for children with Burkitt lymphoma (BL). All patients received financial support for transportation to and from the hospital.

Results: Total numbers of patients in the 3 cohorts were as follows: general paediatric oncology cohort (n = 240), paediatric KS research cohort (n = 25), and BL research cohort (n = 73).

Demographic data was available for the research cohorts only. The majority of patients enrolled in the research studies lived outside Lilongwe district (56% of patients with KS, 72% of patients with BL), with estimated travel times >2 hours to the hospital. The same team of clinical officers and nurses provided care to all patients, but additional support staff was available for research cohorts to assist in data-keeping and patient-tracing. The abandonment rate for the general paediatric oncology cohort was 15% (36/240), compared to 4% for both the KS (1/25) and BL (3/73) research cohorts.

Conclusion: Treatment abandonment rates are lower for paediatric oncology patients enrolled in research studies at our center in Malawi despite equal provision of financial support for transportation. While factors that influence treatment abandonment are multiple and complex, we demonstrate that very low abandonment rates (<5%) can be achieved in sub-Saharan Africa when organizational infrastructure and support staff are provided to support retention.

CCI: MOBILISING SUPPORT

O-141 | Grassroots Parent/NGO Led Group to Mobilise Public Support to Improve Development Of, and Access To, Kinder Drugs for Children with Cancer

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Background/Objectives: Unite2Cure was set up last year (2015) as a pan-European parent/NGO led movement for change. Our will mobilise public support and initiate links and conversations with all parents/NGOs working to speed up development of, and access to, better kinder drugs for children and teens with cancer. The group is highly professional and includes: journalists; media specialists, lawyers, scientists, doctors and project managers. All founding members have lost a child of, or had a child treated for, cancer. We work across boundaries/countries in close collaboration with other stakeholders, whilst retaining our independence. Our main areas of interest are:

- to campaign for change to current European law to ensure better incentives and obligations for industry
- to share information on new models of care that are being designed to assist drug development

Design/Methods: We have:

- A website www.unite2cure.org
- A mission statement
- Set of agreed principles
- Clearly defined communications strategy/plan

Results:

- an online petition to change European legislation
- already been signed by some 1,500 people. Signatures and comments are from a wide range of stakeholders including: doctors; academics; pharmaceutical representatives; lawyers and politicians.
- A collective submission to the SIOPE response to how European regulations need to be changed.
- Programme of speaking events.
- A toolkit of communication/lobbying materials that will be available for use by other parent groups/NGOs across Europe.

Our website is reaching an average of 6,000 people each week.

Conclusion: Unite2Cure has been formed to exploit the huge talent potential already working in this field. There are many parents/NGOs who have put enormous amounts of time and effort into individual projects for change. Unite2Cure wants to mobilise all this talent and passion and created a highly professional, targeted approach to change. This approach is underpinned by high level industry experts and a highly experienced communications team.

O-142 | Leading Ireland's Fight Against Childhood Cancer - Setting Up Ireland's Parent Led National Paediatric Cancer Charity

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Background/Objectives: Childhood Cancer Foundation (CCF) was established in 2013 by a group of parents and family members of children with cancer. This article looks at the practical experience of setting up a national paediatric cancer charity, the challenges faced and resulting benefits for children and families affected by paediatric cancer.

Design/Methods: CCF has clear goals based on acknowledged needs of the childhood cancer population in Ireland. The mission is to be Ireland's National Paediatric Cancer Charity to improve the situation and outcomes for children facing cancer. The objectives are to raise public awareness of childhood cancer issues, to advocate for improved services and to help fund vital supports for children and families who are affected by a childhood cancer diagnosis.

This presentation details the growth of the charity starting with Ireland's first national childhood cancer awareness campaign in 2013 called Light It Up Gold. We developed a website designed as an information hub for families faced with childhood cancer.

CCF advocates to ensure improved services and facilities. We represented the childhood cancer patient cohort at the New National Cancer Strategy 2016-2025 working group and during the New National Children's Hospital planning stages.

Results: CCF supports all children affected by cancer by working with Ireland's National Paediatric Oncology Centre to introduce and fund psycho-social support programmes including play services, Beads of Courage™ and a complementary therapy services research project. We collaborate with the Irish Cancer Society on provision of information and developing a Parent Peer To Peer Support Programme.

Conclusion: By telling our story, this presentation shows how a dedicated parent group has collaborated with medical professionals, policy makers, national and international stakeholders to establish a national paediatric oncology organisation to help ease the trauma and isolation of a childhood cancer diagnosis on children, their families and the wider community.

CCI: FREE PAPERS SESSION 1

O-143 | Cancer in Refugee Children in Turkey

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Background/Objectives: Treatment of cancer in refugees is of increasing importance, it causes a substantial burden on the health systems of the host countries. We aimed to evaluate the demographic features and outcome of refugee children with cancer, mostly Syrian, treated in Turkey and to evaluate the problems encountered.

Design/Methods: A survey on the demographic data, treatment and outcome of cancer in refugee children in Turkey was conducted. The records of refugee children with cancer treated in various regions in Turkey between June 2011 and October 2015 were evaluated retrospectively.

Results: Twohundredandtwelve (212) children with cancer treated in 17 centers in 10 cities were evaluated retrospectively, 197 patients were from Syria. Male: female ratio was 1.5. Median age was 5 years (1-17 years). The diagnosis were acute leukaemia in 52 (24.5%), lymphomas in 35 (16.5%), brain tumors in 31 (14.6%), neuroblastoma in 29 (13.6%), bone and soft tissue sarcomas in 34 (16%), Wilms tumour in 13 (6.1%) and other. The frequency of neuroblastomas ($p < 0.0005$) and bone tumors ($p = 0.0058$) in refugee children were higher than in Turkish children. Fifteen patients underwent hematopoietic stem cell transplantation. Most patients (67.6%) were treated in the south and southeast of Turkey close to the border. All treatment for registered refugees has been provided free of charge. 159 (75%) patients are alive, 31 (14.6%) have died, 22 (10.3%) were lost to follow up. The most frequent problems encountered were accommodation, social and psychological problems, language barriers, compliance with therapy and financial problems.

Conclusion: The distribution of most types of cancer and preliminary outcome in refugees was similar to children in Turkey. Shelter, hygiene, language barriers, compliance were major problems. Preliminary results of this survey may help to inform future responses in children with cancer who are forced to migration.

O-144 | Web Based Application for Online Registration and Follow Up of Children with Malignancies and Non-Malignant Hematological Diseases in Vietnam

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Background/Objectives: Lund Vietnam Childhood Cancer Program has been active in Vietnam since 2008. We have identified 9 hospitals in 4 cities treating children with malignant diseases. The epidemiology of paediatric malignancies, follow up, and survival data are fragmented. Bringing together institutions and staff dealing with paediatric cancer in one network creates conditions for further development of paediatric oncology in Vietnam.

Design/Methods: A web based online registration program was designed. The patients' records contain demographic data and medical information (diagnosis according to ICCC, type and start of treatment). The program permits registration of follow up visits with specification of contact reason and certain events: relapse, abandonment, lost-to-follow-up or death. Electronic transfer of patients between hospitals is possible. Visualization with figures showing real-time registration status and disease distribution, both at the national and local, level is available. Kaplan-Meier survival curves for diagnoses or groups of patient are drawn automatically. A flexible filter and export function is featured. Notifications are generated if the records are not updated for a certain time period.

The database was created to register malignant diseases and was subsequently extended to register children with non-malignant hematological diseases.

The next step is to initiate an inbuilt calendar function that will allow for scheduling of coming visits.

Results: The registration was launched on the 1st of August 2015 in 9 hospitals. 2,250 children have been registered until March 2016 (66% malignancies, 34% non-malignant hematological diseases, monthly registration ranges from 167 to 482 patients).

Conclusion: This is the first nation-wide registry for paediatric haematology and oncology in Vietnam. It can be used by health care providers and policy makers for more efficient allocation of resources.

This registry allows for better control of follow up and may identify main problems influencing the outcome. It is also a ready-to-use platform for future clinical and epidemiological trials.

CCI: FREE PAPERS SESSION 2

O-145 | PASTEC: A Prospective, Single-Center, Randomized Cross-Over Trial of Pure Physical Versus Physical/Attentional Activity in Children with Cancer

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Background/Objectives: Among disease- or treatment-related long-term effects of childhood cancer, peripheral neuropathies, deficits in global coordination, balance, attention capacity and quality of life have been demonstrated. Several publications mention a potential benefit of physical activity in improving long term outcome of such complications. Our study aimed primarily at evaluating the feasibility of a weekly physical activity program for children with cancer and secondly at assessing if the type of physical activity proposed could impact the pattern of improvement.

Design/Methods: We set up a weekly, 1-hour program of physical activity during the school year from August 2015 to June 2016. 24 patients aged 6 to 18 years with various types of tumors were approached and asked to participate. Included patients were separated in two age-groups (6-11 and 12-18 years) and randomized to have either pure physical or physical/attentional activities. After 5 months, patients were crossed-over in the other group. Neurological, coordination, neuropsychological and fitness testing were administered at 4 time-points during the study. Individual distance and speed was recorded at each session by a dedicated camera.

Results: As the study is ongoing, most of the evaluation results will only be available after the planned termination in June 2016 and will be analyzed and reported on the final poster. Twenty-three patient on the 24 approached accepted to participate, one dropped off after 2 months. Attendance after 8 months is 81% (SD 15%), which is slightly above the 80% limit that we had set to consider a weekly schedule as feasible.

Conclusion: Final results are not yet available as the study termination is planned for June 2016. Attendance after the first part is good at 81% of the sessions. Offering such a program once every two weeks could potentially decrease the burden put on families of a weekly schedule and improve attendance.

O-146 | Taking One for the Team: Examining the Effects of Childhood Cancer on the Parental Relationship

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Background/Objectives: The tone and quality of the parental relationship has profound effects on the physical, emotional, mental, and spiritual health of the child. A child's relationship with parents is often the most significant relationship influencing the child's well being; in fact, this relationship has formative and lasting imprints on a child. The state of the marital relationship itself has impact on the child so attending to the parents' relationship is primary prevention in caring for the child. This study offers a deep understanding of the effects of childhood cancer on the parental relationship.

Design/Methods: Data consisted of the content of 24 interviews with a total of 30 participants. Data analysis of the transcribed interviews was conducted using the research method of hermeneutics. Of the interviews, 10 were individuals/couples whose child had died; 7 where the child had lived but was experiencing long term side effects; 7 had a child treated, cured, and living with little to no side effects.

Results: The state of the relationship prior to the diagnosis seemed to have some impact on how the couples were affected in terms of their relationship. This, however, did not account for all of the effects which included: changes in degrees and kinds of intimacy; putting the relationship "on hold" while trusting that reclamation would be possible; discovering style differences in each other that worked and differences that divided; and humor and friendship as a way to connect.

Conclusion: In this study, we learned of courage, sacrifice, commitment, trust, friendship, loneliness, disenchantment, differences, and repair (that was sometimes successful and sometimes not). The team of the family seemed to be what was at the heart of this endeavor, and the parents deeply committed that, at whatever the cost personally or to their couple relationship, they were prepared to "take one for the team."

CCI: SUPPORT SERVICES AND MECHANISMS

O-147 | Support Parents on the Ward as Part of the Team

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Background/Objectives: In 2006 parents united in VOKK and professionals united in DCOG took the initiative to concentrate care and research for children with cancer in a national center in order to further improve survival and quality of life. VOKK-membership was very much in favor although travel distances would become longer and family life would be more disrupted. One condition: parent support should be more visible in the hospital.

Design/Methods: A first department of the national center would open in October 2014. Therefore VOKK started the project "oudersteuners" mid 2014. We mapped the kind of support parents need through focus groups and questionnaires and drafted a job description. We started recruitment, training and selection of support parents – parents of survivors and bereaved parents. Extensive conversations with the professional team led to the conclusion that the VOKK support parents would become part of the team on the ward, thus embedding the support service in the system. In January 2015 the support parents started on the ward, first two shifts a week but soon three and then five. Currently there is a team of 15 support parents filling five shifts a week, during the day, evening and in the weekend.

Results: In May 2016 we evaluated the project among parents, professionals and support parents. It is evident that support parents are indeed part of the team and can't be missed anymore. They are there to listen, to provide information, but also to pick up feedback from parents of patients about quality of care. This feedback is collected by the project leader (a VOKK professional) who discusses it with the care manager and immediately takes actions for improvement.

Conclusion: The program is a success. Parents feel empowered, staff recognizes the benefits. The plan is to expand the program to 10, ultimately 14 shifts.

O-148 | We Need to be Needed. A Prospective Survey of a Formal 20 year Volunteer Programme Run by the CHOC Childhood Cancer Foundation

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Background/Objectives: CHOC Childhood Cancer Foundation is the largest children's cancer charity in Africa, and has had a formal volunteer programme for 20 years. This study represents an audit of the volunteer programme to determine motivations and expectations to assess if changes were necessary.

Design/Methods: A prospective survey, consisting of 47 structured and five unstructured questions, was conducted of current and past volunteers in the programme. Data captured include basic demographics, reasons for volunteering, expectations of the programme and reasons for discontinuing this service.

Results: The response rate was 29/35 (83%). The median age was 51 years (range 25 to 75 years) and all respondents were women. Volunteers stayed in the programme for a mean duration of 8.9 years (range 1 to 20 years). The most common reasons for volunteering were giving back to the community (23/29, 79%), contributing to a cause they believed in (22/29, 76%) and the love of children (21/29, 72%). Very few people named reasons such as empty nest syndrome and boredom. Every respondent reported that they feel they add value to the programme and in the main, their expectations were met. Reasons for discontinuation included excessive travel distance, competing commitments and a sense of completion.

Conclusion: Most volunteers felt appreciated and that they made a difference to the patients and their caregivers. From a volunteers' perspective, this programme is successful. In resource-limited settings, volunteer programmes such as ours offer invaluable psychosocial support which contributes to the holistic management of the patient. The fact that most volunteers engage in this work for self-reported altruistic rather than selfish reasons is encouraging, and should be taken into account when recruiting new participants.

O-149 | Including Siblings in the Provision of Support Services Important for a Family's Adjustment to Childhood Cancer

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Background/Objectives: A diagnosis of childhood cancer impacts all members of a family. The childhood cancer journey is a rollercoaster for everyone, with young cancer patients fighting for their lives and parents living with the multiple challenges that result in tremendous financial and emotional stress.

Siblings of childhood cancer patients can get lost as family life takes on a new normal. Parents learn to juggle the ever-changing challenges that focus on the critically ill child, managing their work obligations with often lengthy absences from the job, a loss of income, and the uncertain future that is a part of childhood cancer.

Parents have told us they "feel badly" for not spending more time with siblings and that they are often "too tired" to do something special with non-patient children. This can result in an increase in emotional distress.

Design/Methods: Candlelighters Sibling Support initiatives are a direct response to an expressed desire from parents when Candlelighters asked in a program evaluation survey how we could improve or expand our services. Hospital staff have also indicated sibling support would be very beneficial for families.

Candlelighters Smiling Siblings started as a monthly watercolour workshop and has grown to also provide personalized mail delivered to the home for siblings. There are special outings and activities for school aged children and the plan for older siblings is to provide movie theatre passes and restaurant vouchers to enjoy with friends.

Results: Acknowledging siblings and the changes in daily life that they must also endure helps to balance the loss of attention from parents.

While the brothers and sisters are not the actual cancer patient and don't experience the physical aspects of having been diagnosed with cancer, they too experience changes in their lives.

Conclusion: Sibling Support helps demonstrate recognition that siblings are also impacted by the childhood cancer diagnosis.

O-150 | Mapping the Journey – A Family Support Work Flow Tool to Assist Coordinators Determine the Right Support at the Right Time for the Right Reasons

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Background/Objectives: Child Cancer Foundation (NZ) employs 19 Family Support Coordinators, both full and part time, to support children and their families on a one-to-one basis throughout New Zealand. We work in the treatment centres and in communities throughout the country and we aim to build resilience, provide practical support and empower our families throughout their experience.

Our Family Support Coordinators have, on average, 180 families each month that are at various stages in their cancer journey – from newly diagnosed through to successful end of treatment, palliative and relapsed. The Family Support team is supported by volunteer parent support groups who provide social contact for families during and after treatment.

Design/Methods: While every family's experience is unique, there is a consistent core of support services that we provide. Mapping The Journey is an iterative process that describes how we support the families at various stages. It serves four purposes – building a comprehensive picture of the family's history and current status, ensuring that all families have access to the same level of care and support, identifying any gaps or additional support opportunities and, going forward, to form discreet 'service' packages that may attract financial support from outside parties. The resulting document is a pictorial tool that was compiled by team discussion and consensus.

Results: Without limiting the type of support it now provides our Coordinators with a comprehensive guide of what our children and families may experience and how we can support at a particular time or for a particular reason.

Conclusion: Mapping The Journey is a dynamic desktop tool that, for the first time in our organisation's history, simply and visually explains how we support families in a psycho-social sense that helps overcome the stress and isolation that children and their families feel at various times.

O-151 | Barretstown's Hospital Outreach Programme (HOP)

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Background/Objectives: Barretstown in Co Kildare, Ireland has been developing and delivering a suite of therapeutic recreation programmes to children and families from Europe affected by serious illness since 1994. The aim of this presentation is to describe how the Barretstown's Hospital Outreach Programme brings the positive, playful spirit of Barretstown to children and families in the hospital setting.

Design/Methods: A key element of Barretstown's development has been ongoing reviews of the programmes and opportunities to offer for children and their families.

Results: These reviews allowed the organisation to identify a gap within the hospital setting. Through one-on-one interactions and group activities, and by offering unique, creative and developmentally appropriate activities and interactions, we help to restore joy and laughter in a time often laden with fear, stress and uncertainty.

Conclusion: We work within the hospital environment to create activity-based programmes focused on improving the quality of life during treatment. The Hospital Outreach Programme continues to bring the happiness and fun of the Camp's summer programming to children living with a serious illness all year round.

IPSO: SESSION 1: NEUROBLASTOMA

O-152 | Resectability and Local Relapse Pattern of Abdominal High-Risk Neuroblastoma

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Background/Objectives: The impact of surgical technique on relapsed/progressing high-risk neuroblastoma (R-HR-NB) is not clearly defined, and there is almost no data on the influence of abdominal topography on resectability and local relapse pattern.

Design/Methods: Forty-seven patients with R-HR-NB enrolled in the German neuroblastoma trials between 2000-2010 were evaluated by 2 board-certified paediatric surgeons. We analyzed the resectability and local relapse pattern of tumour burden within 6 standardized abdominal regions by means of reports on pre- and postoperative imaging and surgery. Abdominal tumour burden (ATB) location lateral to aorta or inferior vena cava, interaortocaval, and above or below the left renal vein led to assignment to 6 standardized topographical regions, as follows: left upper (LU), right upper (RU), left lower (LL), right lower (RL) lateral region, upper interaortocaval (UAC), and lower interaortocaval (LAC) region.

Results: Distribution of tumour burden in the left upper lateral region (LU) was as follows: Initially detectable tumour persisted from initial diagnosis throughout progress in 19 patients (A), surgically resected tumour disappeared forever in 6 patients (B), surgically resected tumour re-occurred in 3 patients (C), the region was always tumour-free in 3 patients (D). Resectability and relapse pattern were influenced by the anatomic region: RU (A=10/B=5/C=10/D=5), LL (A=11/B=12/C=2/D=4), RL (A=4/B=12/C=4/D=7), UAC (A=6/B=9/C=7/D=4), LAC (A=6/B=11/C=6/D=5).

Conclusion: The surgical analysis of R-HR-NB revealed a high rate of limited resections, with a high subsequent progress rate. It reveals the need for standardized surgical approaches, based on the specific anatomical regions affected by the tumour. Consequently, we present a tactical surgical approach based on the assignment of tumour burden to 6 standardized anatomical regions.

O-153 | Outcomes after Surgery for Intermediate-Risk Neuroblastoma: Experience from An Indian Tertiary Cancer Centre

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Background/Objectives: Surgery forms an important modality in the multidisciplinary treatment of neuroblastoma. The extent of surgery and the complications associated with it for intermediate-risk neuroblastoma are not well defined. This study reports the surgical outcomes from an Indian tertiary cancer centre.

Design/Methods: All patients who underwent surgery for intermediate-risk neuroblastoma between January 2005 and January 2015 were included in the analysis. Imaging Defined Risk Factors (IDRF) were assigned to all patients in retrospect and surgical details including the extent of resections, complications, chemotherapy and radiotherapy particulars were evaluated. The Kaplan-Meier method was used to compute the survival curves, while the log-rank test was used to analyze it.

Results: Of the 229 patients who underwent treatment, including surgery in the study period, 75 patients had intermediate-risk tumors. All patients received preoperative chemotherapy; gross total resection was achieved in 64%, more than 95% resection in 25%, and the remaining had incomplete resections. The most common postoperative complication was chyle leak (14.6%) followed by intestinal obstruction (5%) and transient nerve paresis (5%). After a median follow up of 46 months, the five years overall survival was 88.6%, with an event-free survival of 77.6%. There was no difference in survival between patients who underwent complete resection as compared to those who underwent lesser degrees of resection (p=0.789). There was no significant difference in the incidence of intraoperative complications between patients who underwent complete resection as compared to near complete resection (p=0.638).

Conclusion: Survival after surgical excision of intermediate-risk neuroblastoma is favorable and is not influenced by the extent of resection.

O-154 | International Survey on Minimally Invasive Surgery of Neuroblastoma: A Siopen Study

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Background/Objectives: Despite several reports, the indications to use minimally invasive surgery (MIS) remain controversial for neuroblastoma (NBL) and international guidelines are lacking. The aim of the study was to evaluate the practice of MIS for NBL around the world.

Design/Methods: A survey by the SIOPEN surgical committee in 2015 including a questionnaire was sent to various paediatric surgeons in different countries.

Results: A total of 44 surgeons (85% of responses) from 14 countries completed the survey. Thirty one surgeons (70%) performed MIS for neuroblastoma and reported 212 MIS procedures. The most important criteria (88%) to indicate laparoscopy/thoracoscopy was preoperative imaging criteria (Image defined-risk factors, IDRFs). The rate of conversion to open surgery was 5%. Macroscopic resection was achieved in 189 cases (90%). Ninety percent of the surgeons participated in the survey anticipate more laparoscopic/thoracoscopic procedures in the future.

Conclusion: Minimally invasive surgery represents an evolving approach for surgical treatment of neuroblastoma. Further detailed study will be set up by SIOPEN to evaluate this approach in terms of morbidity and oncological outcome in order to delineate consensual guidelines.

O-155 | Analysis of Surgery for Neuroblastoma in the Netherlands

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Background/Objectives: To evaluate the morbidity and mortality caused by surgical excision in Dutch patients diagnosed with neuroblastoma.

Design/Methods: A retrospective review was performed of patients diagnosed and treated for neuroblastoma in the Netherlands between 1998 and 2014. Morbidity and mortality caused by surgical intervention was documented.

Results: Surgical excision was performed in 206 patients: Stage I (15%), Stage II (10.7%), Stage III (14.6%), Stage IV (58.3%), Stage IVs (1.5%).

Peroperative complications occurred in 101 patients (49%), varying from minor vessel injury to removal of organs or structures, the majority involving stage IV patients (62.4%).

Unplanned removal of organs or structures occurred in 45 patients (21.8%), e.g. total nephrectomy (6.8%), partial nephrectomy (2.4%), partial hepatectomy (1.9%), partial gastrectomy (n=1), total pneumonectomy (n=1).

Postoperatively, 79 children (38.3%) experienced Clavien-Dindo grade 1 or grade 2 complications, including renal ischemia in 6 children, leading to complete renal atrophy in 3 patients.

Clavien-Dindo grade 3, 4 or 5 complications occurred in 16 children (7.8%).

Secondary surgery due to short-term complications was necessary in 6 patients: subtotal colectomy for intestinal ischemia, secondary nephrectomy for complete renal atrophy, surgical reduction of intestinal intussusception, surgical drainage of chyloabdomen and surgical drainage of chylothorax (n=2).

Long-term postoperative ICU admission was necessary for two children who both endured severe sepsis, caused by an aspiration pneumonia after tube-dislocation and a peripheral intravenous line infection.

Long-term complications involved, among others, scoliosis, Horner syndrome and intestinal adhesions, leading to surgical adhesiolysis in 2 children.

Peroperative mortality occurred in one patient; a 2-year old child with stage IV disease. Laceration of a liver vein caused an air embolus due to low intrathoracic pressure, leading to irreversible cardiac arrest.

No postoperative mortality was reported.

Conclusion: Surgical excision for Neuroblastoma is associated with significant complications and peroperative mortality, especially in patients with Stage IV disease.

O-156 | Surgery of Neuroblastoma: Results of a Single Centre Experience of 340 Children over 15 Years

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Background/Objectives: Resection of neurogenic tumors remains a challenging regarding the weak efficiency of neoadjuvant chemotherapy to decrease the IDRFs. Beside overall and event free survival, functional outcome has been poorly reported. The aim of this study was to report a large single centre experience of neuroblastoma (NB) surgery with long-term follow-up.

Design/Methods: All NB treated by the same team over the last 15 years were analysed regarding anatomical, clinical, surgical features and complications, with a particular attention to functional outcomes (osteomuscular, neurological, bladder, intestinal, or pulmonary function).

Results: 334 children were operated during the period for a neurogenic tumour (143 metastatic and 191 localized). 91 patients still presented IDRFs when operated. Resection was at least 90% for the whole cohort. Location were mainly abdominal (244) followed by thoracic (69), pelvic (15) and cervical (6). Complications were observed in 4 patients (1.2%), 2 thoracic and 2 abdominal tumours. Sequelae were observed in 30 patients (9%) mainly linked to thoracic dumbbell NB (14 patients, p=0.0002 Chi square test). Metastatic relapse was observed in 37 patients and local relapse in one with abdominal NB (0.2%). OS were respectively 50% and 85% for metastatic and localized NB, with a median follow-up of 5 years (1 month-17 years).

Conclusion: Despite presence of IDRFs in 50% of patients, low local relapse and complication rate were observed in this single centre series of neurogenic tumours. Long-term sequels were observed mainly in paravertebral dumbbell NB where surgery was mandatory because of neurological threatening symptoms in spite of chemotherapy.

IPSO: SESSION 2: RENAL TUMOURS

O-157 | Renal Tumours in Children Older than 10 years – Should we be doing Upfront Nephrectomy?

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Background/Objectives: The incidence of Non-Wilms Renal Tumours (NVRT) is highest in early infancy and adolescence. Current SIOP guidelines only advocate upfront nephrectomy (UN) for children aged <7 months. We explored the potential role for UN in patients ≥10 years old.

Design/Methods: Data on patients with renal tumours at Birmingham Children's Hospital from Dec 2005–Aug 2015 were retrospectively analysed for demographics, biopsy and operative histology, timing of nephrectomy and intraoperative complications.

Results: One hundred and nine patients were identified with renal tumours (Median age 3.45 years, Range 15 days–16.57 years, M:F 51:58) including 10 aged ≥10 years and 7 aged <7 months. Twenty-five were identified as NVRT, including 5 patients ≥10 years old. Of the patients ≥10 years; 7 had biopsy at presentation; 1 underwent UN without biopsy and 1 had chemotherapy for presumed Wilms without biopsy. Diagnoses on biopsy were 5 Wilms tumours, 1 renal cell carcinoma (RCC), 1 desmoplastic small round cell tumour (DSRCT). Following nephrectomy, the diagnosis changed for 2 patients; 1 Wilms to RCC and 1 DSRCT to Wilms. The diagnoses for the 3 patients that underwent UN were angioleiomyoma, unclassified epithelial tumour and anaplastic sarcoma. Nine patients ultimately had nephrectomy while 1 patient with metastatic RCC died prior to surgery. No tumour rupture occurred. One early complication occurred in the UN group and 4 in the delayed nephrectomy group. Two local recurrences occurred in the biopsy group.

Conclusion: Our data support the known diagnostic challenges associated with renal tumours in >10 year olds. In our cohort, UN was not associated with increased complications and may have avoided the diagnostic inaccuracy we observed with biopsy. This study suggests further investigation of biopsy vs UN in national/international cohorts is indicated to confirm if UN should be recommended for renal tumours in children >10 years old, as for <7 month olds.

O-158 | Long Term Outcome of Children with Wilms Tumour (WT) Having Inferior Venacaval Thrombus (IVC-TH)

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Background/Objectives: To evaluate the prevalence and management of patients of Wilms tumour (WT) with inferior venacaval thrombus (IVC-TH) and determine their long-term outcomes.

Design/Methods: Prospective case control study of all children of WT with IVC-TH from June 1999–December 2015 at a single center. All patients with IVC-TH received 4–6 weeks of neo-adjuvant chemotherapy, surgery and adjuvant chemotherapy according to AIIMS WT-99 protocol. The patients were categorized as metastatic and non-metastatic and their 5-year overall survival(OS) and event-free survival(EFS) were analyzed using Kaplan-Meier survival analysis.

Results: In the study period, of 319 patients of WT, 29(9.1%) had IVC thrombus(IVC-TH). Their age ranged from 8m–84m(mean 46.1). There were 19(65.5%) non-metastatic (Stage 2,3 and 5: 2,16 and 1 respectively) and 10 (34.5%) stage 4 patients. Two of 29 (6.9%) could not be operated because of progressive disease. In 6(20.7%), the thrombus had resolved completely on neoadjuvant chemotherapy. In 21 (72.4%) thrombectomy was required (cavotomy 17 and cavectomy 4) at the time of nephrectomy. In addition, 3 of these 21 required atriotomy under cardio-pulmonary bypass(CPB). Overall 18/29 survived(5-year OS 51.2%; 95 CI 29.9–69.3). Survival was 15 of 19 (78.9%) among non-metastatic patients while it was only 2 of 10(20%) among metastatic patients. Seven of 27(25.9%) resected patients developed recurrence and 5 (71.4%) of these died while 16 of 20(80%) without recurrence survived (5-year OS 68.4%). Among the operated patients, recurrence was observed in 3/18 (16.7%) non-metastatic patients and 4/9(44.4%) metastatic patients. The 5-year EFS was 50.1%(95CI 29.7–67.5).

Conclusion: The prevalence of inferior-venacaval thrombus was 9.1% among WT patients and 35% of these were stage 4 disease. Following neoadjuvant chemotherapy, in 21% the thrombus resolved completely, while 72% required thrombectomy (with CPB in 10%). The 5-year OS and EFS was poor(51.2% and 50.1%). Stage-4 patients had a higher recurrence rate (17% vs 44%) and poorer survival (79% vs 20%).

O-159 | Long-Term Renal Function Time Trends after Uninephrectomy in Children

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Background/Objectives: Whether renal function after ablation of 50% of renal mass deteriorates, or recovers, or stabilizes remain unclear. We investigated time trends of glomerular function in children who underwent nephrectomy for unilateral oncological and non-oncological causes.

Design/Methods: We evaluated cross-sectional observations of estimated glomerular filtration rate (eGFR) among a cohort of 79 children who underwent nephrectomy between 1960 and 2014 at our institution. Renal dysfunction was defined as eGFR<90ml/min/1.73m².

Results: After nephrectomy the pre-operative glomerular dysfunction probability on average decreased during adolescence (9 children with pre-operative dysfunction recovered to two-kidney eGFR values). After adolescence the glomerular dysfunction probability on average significantly increased (Figure). At follow-up, children who underwent nephrectomy associated with chemotherapy and/or radiotherapy presented on average no significant differences in eGFR in comparison with children who underwent nephrectomy alone.

Conclusion: In children the response to 50% loss of renal mass is characterized by an increase in eGFR to restore two-kidney values up to adolescence. However, renal function present a progressive deterioration with aging.

O-160 | Surgical Management of 12 Cases of Wilms Tumour with Intra-Cardiac Extension - A Single Centre Experience

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Background/Objectives: The aim was to review the surgical management of children with Wilms tumour who have intra-cardiac extension.

Design/Methods: Data were collected from patient notes regarding presentation, operative details and outcome.

Results: From 1984 through 2016, 329 children with Wilms tumour (out of 3706 cancers) were treated at our hospital. Twelve (3.6%) had cavo-atrial extension of tumour thrombus. The thrombus extended into the right ventricle in three children. In these 3 and a further 3, it involved the hepatic veins. Pre-operative chemotherapy was administered in 11 children with complete regression of the intra-cardiac tumour thrombus in two. One child died preoperatively of septicemia after two doses of chemotherapy. Nine children with intra-cardiac tumour underwent surgery. Operation consisted of excision of the renal tumour, control of all branches of the inferior vena cava (IVC), full mobilization of the liver off the IVC up to the hepatic vein confluence, removal of the renal tumour, venotomy and extraction of all tumour thrombus in the IVC and iliac veins and under cardiopulmonary bypass (CPB) with deep hypothermia and circulatory arrest (DHCA) removal of tumour thrombus from the heart chambers and hepatic veins as required with repair using a pericardial patch onto the hepatic vein confluence when needed. The mean ischemic time was 30 min. There was one peri-operative death in a child with hepatic vein involvement and Budd–Chiari syndrome. All others made a good postoperative recovery. To date 7 children are still alive and disease free. Three children have died as a result of pulmonary metastases.

Conclusion: Intra-cardiac extension of Wilms tumour is rare, and management is technically challenging. Pre-operative chemotherapy is effective. CPB and DHCA for excision of the cavo-atrial tumour thrombus may be necessary. Distant metastatic disease is common and determines long-term prognosis. Hepatic vein extension complicates surgery and remains challenging.

O-161 | Outcomes of Surgery for Renal Tumours with Intravascular Extension

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Background/Objectives: The aim of this study was to review the management of children with Wilms tumour who had intravascular thrombus.

Design/Methods: Data regarding the presentation, response to chemotherapy, surgical management, complications and outcomes were evaluated.

Results: The study cohort included 31 patients with intravascular thrombus treated from 2006 to 2015. The thrombus extent at presentation was: Intrahepatic inferior vena cava (IVC) -19, retrohepatic IVC -6, suprahepatic IVC -1 and Atrium -5. All patients received preoperative chemotherapy (with 3 drugs), except in two. There was complete clearance of the tumour thrombus in 11/31 patients following chemotherapy. Regression of the thrombus occurred in the remaining patients and the extent was: Intrahepatic IVC -6, retrohepatic IVC -4, suprahepatic IVC -2 and Atrium -3, renal vein -2. Due to regression of the tumour thrombus from the atrium into the IVC cardiopulmonary bypass could be avoided in 2 patients. In all patients the thrombus had to be dissected off from the tunica intima due to dense fibrosis around the thrombus. The only major complication was massive bleeding in one patient with atrial thrombus. There was no perioperative or 30-day postoperative mortality. Histopathological examination of the tumour thrombus resected showed viable tumour in 13 patients. The 3-year OS and EFS was 89.3% and 77.8% respectively.

Conclusion: Intravascular tumour thrombus extension although a surgical challenge are associated with favourable outcomes after contemporary multidisciplinary treatment. Chemotherapy aids in surgery due to the tumour regression and adhesion to the wall which prevents tumour

fracture and embolisation and also may obviate the need of cardiopulmonary bypass in atrial thrombus. Extensive caval repair or grafting is usually not required.

O-162 | Liquid Tumour Biopsy in Nephroblastoma Patients: Detection of Tumour Protein Epitopes Within Peripheral Blood Macrophages

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Background/Objectives: So far, a tumour-specific serum marker for nephroblastoma has not been described. A sensitive and specific method of diagnosing tumour occurrence in the peripheral blood could possibly contribute to an improved prognosis of affected patients. Different reactions of the immune system to tumors have been observed so far; these reactions include phagocytosis of tumour cells by monocytes/macrophages. The Epitope-Detection Test in Monocytes (EDIM) allows detection of intracellular tumour-protein epitopes in peripheral blood monocytes/macrophages after phagocytosis of tumour compounds. Our aim was to assess the possible role of this method in nephroblastoma patients.

Design/Methods: We analyzed blood samples from 8 consecutive nephroblastoma patients. The time point of analysis was before tumour operation. Macrophages were isolated using flow cytometric cell sorting. Isolated immune cells were assessed for the presence of intracellular epitopes of tumour proteins Apo10 and TKTL1 using the EDIM test. We also analyzed 20 healthy blood donors as control group.

Results: Incorporated tumour proteins Apo10 and TKTL1 were detected in the macrophages of all analyzed patients. In all cases the cut-off value for significant correlation with tumour disease was surpassed. A relation to Apo10 and TKTL1 expression in tumour samples from the patients was observed. Control samples were all negative.

Conclusion: We describe a new and innovative method for detection of tumour proteins in macrophages within the peripheral blood of nephroblastoma patients. This method might serve as additional tool for stratification at initial diagnosis, for monitoring of the treatment course, and for an early detection of tumour relapses. Further studies including longitudinal analyses are necessary to correlate EDIM results with tumour-specific characteristics and imaging data, and thus determine the possible role of this method for the treatment of nephroblastoma patients.

O-163 | Technical Considerations for Nephron Sparing Surgery in Children Pretreated with Chemotherapy. What is Really Needed to Preserve Renal Units?

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Background/Objectives: Chemotherapy is used preoperatively for children with bilateral Wilms tumour (BWT) or unilateral high risk Wilms tumour (UHRWT) to promote tumour regression in order to facilitate renal preservation with nephron sparing surgery (NSS). However, renal failure can occur following NSS from lack of viable renal units and/or vascular thrombosis. Vascular clamping, cooling, and auto-transplantation are some of the techniques recommended to prevent renal loss. Few studies have examined the need for surgical adjuncts in NSS in children exposed to pretreatment chemotherapy.

Design/Methods: We performed a multi-institutional retrospective review of patients with BWT or UHRWT. Patient demographics, tumour size at diagnosis, tumour size following neoadjuvant chemotherapy, utilization of surgical adjuncts including intraoperative ultrasound (IOUS), cooling and vascular isolation, margin status, complications, renal function, and follow up were recorded.

Results: Twenty-two patients comprised the cohort: 17 BWT, 2 UHRWT, and 3 solitary kidney patients. Median tumour size at diagnosis was 5.6cm on the right (range 1.8-14.2cm) and 5.5cm on the left (range 1.0-18.2cm). Following neoadjuvant chemotherapy, median tumour size prior to surgical resection was 4.5cm on the right (range 0.2-17cm) and 2.5cm on the left (range 0.2-14cm). Twenty-one of the 22 patients had successful NSS. One patient was rendered anephric. IOUS was utilized 17 times, although 4 still had positive margins. Cooling/vascular clamping was employed only 8 times, in an older subgroup (median age 107 months vs 42 months of the entire cohort). With a median follow up of 25.5 months (range 4-132), median eGFR Schwartz is 125ml/min/1.73m² (range 69-280ml/min/1.73m²) and median Cre 0.38mg/dL (range 0.21-0.96mg/dL) in the 21 patients who had successful NSS. There have been no tumour recurrences.

Conclusion: In patients with BWT and UHRWT, vascular clamping and cooling are uncommonly required, and when utilized are typically employed in older patients with larger vasculature. IOUS does not guarantee negative microscopic margins.

IPSO: SESSION 4: (PBC-SESSION): THE ROBERT J. ARCECI BEST OF IPSO

O-164 | Surgical Resectability and Tumour Response to Preoperative Chemotherapy in Hepatoblastoma Patients Treated by the Japanese Study Group for Paediatric Liver Tumour (JPLT)-2 Protocol

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Background/Objectives: Survival of patients with hepatoblastoma has improved over the past decades due to results of clinical trials that evaluated a combination of chemotherapy and surgical resection. A good response to chemotherapy and completeness of tumour removal are considered important prognostic factors. In this study, we aimed to clarify whether surgical resectability and tumour response after preoperative chemotherapy (preCTx) represent prognostic factors for patients with hepatoblastoma (HBL) in the JPLT-2 study (1999-2012).

Design/Methods: Patients (N=342) with HBL who underwent preCTx were eligible. PRE-TEXT, CHIC risk stratification (standard [SR], intermediate [IR] and high risk [HR]) at diagnosis, POST-TEXT, and tumour resectability were evaluated by imaging. Patients were classified by tumour response as responders (CR or PR) or non-responders (NC or PD) according to RECIST criteria.

Results: There were 7 PRETEXT I, 106 II, 143 III, and 86 IV, including 71 metastatic HBLs. In POST-TEXT staging, 12 PRETEXT II, 42 III, and 58 IV were down-staged. The 5-year EFS/OS of 198 SR, 73 IR, and 71 HR-HBLs were 82/94%, 49/64%, and 28/34%, respectively. In 198 SR, 154 of 160 responders and 24 of 38 non-responders survived event-free ($P < 0.01$). In 73 IR, 12 of 24 whose tumors remained unresectable recurred, and 9 of them were non-responders ($P < 0.01$). In 71 HR, chemoreponders with resectable tumors after preCTx correlated with favorable outcomes ($P < 0.05$).

Conclusion: Evaluation of response and tumour resectability after preCTx is useful for predicting prognosis in HBLs. To improve outcomes, we should reconsider and select surgical procedures according to resectability and chemoresponsiveness.

O-165 | Conservative Surgery and Brachytherapy for Bladder-Prostate Rhabdomyosarcoma : Outcome and Functional Results for 100 Children Treated in a Single Institution

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Background/Objectives: To report on results of a conservative strategy (surgery+brachytherapy), for children with bladder-prostate rhabdomyosarcoma (BPRMS).

Design/Methods: From 1991 to 2015, 100 patients (pts) (88 males, median age: 28 months, range: 5,6 months-14 years) were referred for the local treatment of BPRMS, 96 pts for a residual mass after initial chemotherapy, 4 pts after local relapse (LR). All pts underwent conservative surgery with preservation of bladder-neck and urethra, systematically followed by brachytherapy (BT) encompassing the prostate and bladder-neck/trigona area. BT (median dose: 60 Gy) was delivered according to Paris system rules, using low or pulse dose-rate modalities. Urodynamic studies were performed in case of urinary symptoms after 6 years of age.

Results: Surgical procedure was mucosectomy/tumorectomy (19 pts), partial cystectomy (38 pts), partial prostatectomy (37 pts) or both (6 pts) with urethral reimplantation in 63 pts. After surgery, 63 pts had a macroscopic tumour residuum. At a median follow-up of 4 years (5 months-25 years), 94 pts are alive. Twelve pts relapsed: 7 LR (3 deaths), 1 nodal relapse (alive), 4 metastatic relapse (3 deaths). Five survivors underwent a total cystectomy, 3 for LR and 2 for bladder dysfunction. One female had a bladder enlargement. Information about urinary continence was available in 51 pts older than 6 with intact bladder, among 56 survivors. Forty pts (78%) have normal urinary continence (3 with enuresis), 11 have diurnal dribbling (3 with night-time incontinence). Urodynamic studies showed a small bladder capacity with hyperactive or uncompliant bladder in 6 pts. Two pts had urethral stenosis. Two pts were submitted to intermittent catheterism. All males have erections except one.

Conclusion: This series confirms the previously reported experience with high local control rate in BPRMS treated with conservative surgery and BT. Longer follow-up is needed to ensure that the functional results are maintained over time.

O-166 | Microwave Resection of Liver Malignancy, Bloodless Procedure of 320 Cases

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Background/Objectives: Hepatectomy is the critical treatment of liver malignancy. Many device and methods had been used in the hepatectomy. Hereby we report experience of 320 cases of microwave resection as the bloodless procedure.

Design/Methods: From Jun.2007 to Jan. 2015, 320 cases of liver malignancy accepted hepatectomy with microwave resection. The malignancy included 302 cases of hepatoblastoma, 2 of hepatocellular carcinoma, 16 of undifferentiated embryonal sarcoma, of which 10 cases were relapsed disease for the second resection, 3 for the third resection. The microwave dissector was used in all the procedure.

Results: For 302 cases of hepatoblastoma, 33 were PRETEXT 1, 190 in PRETEXT 2, 75 in PRETEXT 3 and 4 in PRETEXT 4 stage. Except of 33 cases in PRETEXT 1, 256 (95%) patients accepted chemotherapy before operation. The duration of operation was 75 minutes in the minimum and 490 in the maximum. Although occlusive belt was prepared in every operation, only 20 cases used inflow occlusion and 5 used inflow and outflow occlusion. For the 320 cases, the blood lose were 5 to 20 milliliter in 285 cases, 20 to 50 milliliter 30 cases. No hemorrhage occurred after operation. Different size of encapsulated hydro were founded near the resection area in 32 case and severe bile leakage and bile duct infection occurred in 3 cases, of which 2 accepted re-surgery and 1 adopted liver transplant.

Conclusion: Microwave resection is safe and good at haemostasis, usually without inflow and outflow control and even blood transfusion. The damage of bile ducts need to be protected.

O-167 | Pheochromocytomas and Paragangliomas in Children: Data from the Italian Multiinstitutional Study (TREP project) on Rare Tumors in Childhood (2000-2014)

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Background/Objectives: Pheochromocytomas are neuroendocrine tumors arising from the chromaffin cells of the adrenal gland, and paragangliomas are their extra-adrenal counterparts arising from ganglia along the sympathetic/parasympathetic chain. Surgery is the cornerstone of treatment. An inherited mutation is commonly associated either sporadically or hereditarily. The National cooperative project on rare paediatric tumors (TREP), launched in 2000, also includes these forms.

Design/Methods: Among the 945 patients registered into the TREP project from 2000 to 2014, 45 were affected by pheochromocytoma and paraganglioma. All clinical and therapeutic data were evaluated.

Results: Twenty-four had pheochromocytoma and 21 paraganglioma. Age at diagnosis was 5-20 years, mean 12 for both groups. Thirty-two had symptoms related to catecholamine hypersecretion; in 7/45 diagnosis was done during assessment for a familial syndrome, in 4/45 due to tumour mass effect. In all cases CT/MRI were effective to confirm the diagnosis. In addition, 28 functional imaging (¹⁸F-FDG, ¹⁸F-DOPA) were positive in 17 (61%). Forty-three patients were eligible for surgery: a complete surgery was more easily achieved in pheochromocytomas than in paragangliomas (21/24 vs. 5/21). All relapses were treated with surgery (5 pheochromocytomas and 2 paragangliomas) and surgery plus chemotherapy (2 paragangliomas): one pheochromocytoma with metastasis at diagnosis received radiotherapy. All but one (who is alive with disease) are in 1st, 2nd or 3rd complete remission (9/43 recurred; 7/9 with a mutation). One patient treated with chemotherapy and embolization is alive with disease. One patient died of disease.

Conclusion: Surgery is curative in most tumors but it may not be effective in removing paragangliomas due to site or invasion of adjacent structures: post-surgical long term sequelae may affect these patients. Genetic tests should always be considered in individual with these tumors, and genetic counselling be offered to their families.

IPSO: SESSION 5: LIVER TUMOURS AND GERM CELL TUMOURS

O-168 | Post-Text III and IV Hepatoblastoma: Extended Hepatic Resection Avoids Liver Transplantation in Selected Cases

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Background/Objectives: Primary liver transplantation has been advocated as surgical treatment approach for children with hepatoblastoma (HB) involving 3 or 4 liver sectors at diagnosis. However, in some cases tumors seem resectable after chemotherapy through aggressive use of nontransplant surgical procedures. Our aim was to analyze the outcome of HB patients presenting with POST-TEXT stages III and IV undergoing extended hepatic resection after neoadjuvant chemotherapy.

Design/Methods: Data of 27 HB patients were reviewed, undergoing extended liver resection for POST-TEXT III or IV tumors after chemotherapy between 1992 and 2015. Median follow-up was 58 months (range, 9-188).

Results: Median age at surgery was 18.2 months (IQR, 10.8-32.5). Staging of the children after chemotherapy revealed POST-TEXT III in 21 and POST-TEXT IV in 6 cases. In 2 children the hepatic resection was performed under cardio-pulmonary bypass because of extended vena cava thrombosis; in 2 patients a simultaneous sternotomy was performed for resection of bilateral lung metastases. The 5-year overall survival rate was 80.7%.

Conclusion: Aggressive surgical resection is a successful approach in selected patients with POST-TEXT III and IV HB who otherwise would be candidates for liver transplantation. These children should undergo central review and should be surgically managed at centers of excellence for paediatric liver surgery. Despite challenging surgical procedures and complex clinical courses the patients benefit from avoidance of morbidities of organ transplant. However, preparation of backup liver transplantation should be considered in selected cases.

O-169 | Evaluation of Biopsy Approach for Children with Hepatoblastoma

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Background/Objectives: The histopathological assessment of paediatric liver tumors at diagnosis is critical. The purpose of this study was to evaluate complications associated with approaches to liver biopsy, specifically clinically significant post-procedural hemorrhage requiring transfusion.

Design/Methods: Children with hepatoblastoma were enrolled on Children's Oncology Group Study AHEP0731 between 9/1/2009 and 4/1/2012. Demographic, tumour, biopsy characteristics, procedural reports, and pathology records were prospectively collected. This analysis evaluated patients who had advanced stages of disease and underwent a biopsy procedure at diagnosis. The primary endpoint was clinically significant post-biopsy hemorrhage, defined as requiring blood product transfusion.

Results: We identified 122 children (Pretreatment extent of disease [PRETEXT] staging I [n=0], II [n=35], III [n=58], and IV [n=24]) who underwent open (n=76, 62%), laparoscopic (n=18, 15%), or percutaneous (n=28, 23%) biopsies. All biopsy procedures yielded sufficient tissue for diagnosis, although information on the adequacy of tissue for biological and/or molecular studies is not known. Median age at the time of biopsy was 18.2 months. There was a non-significant trend between older age (median, IQR) at biopsy and percutaneous (23.4, 15.1-32.5 months) approach, compared to open (16.6, 8.2-25.2 months) or laparoscopic (17.7, 10.6-33.9 months) techniques (P=0.07). Post-biopsy hemorrhage requiring transfusion occurred after 25% (n=31) of biopsies. Need for blood product transfusion most commonly occurred following open (n=26/76, 34%) and laparoscopic (n=4/18, 22%) biopsies, compared with percutaneous (n=1/28, 1%) biopsies (P<0.01). There was no difference in age (P=0.27) or PRETEXT stage (P=0.57) between patients who had or did not have require post-biopsy transfusion. Patients who had post-biopsy hemorrhage requiring transfusion had a longer but statistically non-significant interval (median, IQR) before beginning treatment (5.0, 4.0-7.0 days vs. 4.0, 3.0-7.0 days; P=0.23).

Conclusion: Pre-treatment percutaneous biopsy of paediatric liver tumors yielded the lowest rate of clinically significant hemorrhage requiring blood product transfusion, without sacrificing diagnostic accuracy.

O-170 | Irinotecan as Salvage Therapy for Recurrent Hepatoblastoma

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Background/Objectives: To evaluate the outcome of children with recurrent hepatoblastoma (HB) treated with irinotecan as salvage chemotherapy.

Design/Methods: Retrospective review from the records of all children with recurrent HB from 2007-2015, treated with irinotecan. Re-evaluation after 2 cycles to assess resectability of the recurrence was done. Overall response to Irinotecan treatment and the outcome of patients was evaluated. Kaplan Meier survival estimates for a 2 year overall survival(OS) was done.

Results: Thirteen children in the age range of 9-36 months (median 18) were enrolled. They were 1 (8%), 3(23%) and 9(69%) patients of PRETEXT 1,2 and 3 stages respectively. Four(31%) were standard risk(SR) while nine(69%) were high risk(HR). Recurrence occurred during adjuvant chemotherapy in 4(31%) and after completion of chemotherapy in 9(69%) from 5-36(mean 11) months from diagnosis. The recurrences were local in 7(54%) and pulmonary in 6(46%). Overall, 12 received Irinotecan before resection of recurrence and of these 4 showed partial response(1 died on therapy before resection, 2 resected, 1 waiting pulmonary metastatectomy). Surgery for the recurrence was done in 6(2 local; 4 pulmonary), one is awaiting resection, while the other 6 could not be resected (2 died on therapy; 4 progressive disease). Of the 6 resected, 4 are alive and disease free while 2 re-occurred and developed progressive disease. Overall 10 of 13 were alive (2 yr OS 48%) for 7-131(mean 39) months. However, only 5 are alive (4 disease free and 1 awaiting pulmonary metastatectomy). Five had progressive disease and later discontinued follow-up.

Conclusion: Irinotecan salvage therapy for recurrent HB resulted in partial response in 33% cases and disease free status following resection in 4/13(31%) of those receiving irinotecan for 7-131(mean 79) months. None of the patients in whom the recurrence could not be resected are alive.

O-171 | Haemorrhage is the Most Common Cause of Perinatal Death in Patients with Sacrococcygeal Teratoma

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Background/Objectives: Sacrococcygeal teratoma (SCT) is the most common neonatal tumour with a good chance of survival in most of the patients. However, a small percentage of neonates diagnosed with SCT dies shortly after birth from tumour haemorrhage. The incidence and risk factors associated with haemorrhagic mortality are unknown.

Design/Methods: A retrospective review included 235 children with SCT treated between January 1970 - December 2010 at the six paediatric surgical centres in the Netherlands. Factors possibly related to haemorrhagic mortality that were analysed included sex, prematurity,

Altman type, tumour-volume, tumour-histology, the necessity of emergency operation and the time of diagnosis. Associations between patient- or tumour related factors and haemorrhagic mortality were analysed with Chi-Square or Fisher's exact test if indicated.

Results: In total, 18 patients (7.7%) died at a median age of 163.5 days (range 1.7 – 973 days). Nine patients died of a malignancy. The others (3.8%) died perinatally (age 1–27 days), six of them within two days after birth. Seven patients died due to tumour haemorrhage and/or circulatory failure. Risk factors for haemorrhagic mortality were prematurity, tumour volume >1000cm³ and performance of an emergency operation. Sex, Altman classification, and tumour histology were not associated with haemorrhagic mortality.

Conclusion: Haemorrhagic mortality of neonates with SCT is relatively high (3.8%) representing almost 40% of the overall mortality in the neonatal period. High-output cardiac failure, internal tumour haemorrhage and perioperative bleeding were the most common causes of perinatal death and were all strongly associated with larger tumour sizes.

O-172 | Urodynamic Abnormalities in Follow-Up Patients of Sacrococcygeal Teratoma

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Background/Objectives: To assess the long-term follow-up patients of sacrococcygeal teratoma (SCT) using urodynamic evaluation (UDS) in addition to clinical and radiologic evaluation.

Design/Methods: A prospective cohort study on post-operative patients of SCT. The long term urological outcome was assessed using clinical, radiological (ultrasonography[US] and Micturating cystourethrography[MCU]) and urodynamic evaluation.

Results: Of the 57 patients included, 42 (73.7%) were females and 15 (26.3%) males. Thirty-five (62.4%) were following treatment for benign disease and 22 (38.5%) for malignant disease. Twenty-eight of the 57 (49.12%) patients had urological co-morbidity. Clinically evident urinary complaints were present in 21 (36.8%) patients and included stress urinary incontinence in 14 (66.7%), enuresis (day time/night time/ both) in 9 (42.9%), poor stream or dribbling of urine in 6 (28.6%). US was performed in 51 patients, of whom 8 (15.7%) had abnormal findings. Three (37.5%) had contracted, trabeculated thick walled bladder, 3 (37.5%) bilateral hydronephrosis and 6 (75%) had significant post void residue (PVR). Out of 7 patients who underwent MCU, 5 (71.4%) had abnormal report; significant PVR in 4 (66.7%), small trabeculated bladder 3 (42.8%), reflux 2 (28.6%) and a large capacity bladder 1 (14.3%). Out of 27 patients in whom UDS was done, 18 (66.7%) had an abnormal UDS. These abnormalities included a small capacity and raised pressure in 8 (44.4%), normal capacity but high pressure in 4 (22.2%), a small capacity but normal pressure in 4 (22.2%) and large capacity in 2 (11.1%). Abnormal UDS was detected in 6 (22.2%) patients who did not have any clinical abnormalities and 10 (37%) patients without any ultrasonographic abnormalities.

Conclusion: Urodynamic abnormalities were detected in 6(22.2%) patients who had neither any urinary complaints nor an abnormal USG. It is therefore suggested that UDS should be an integral part of urological surveillance in follow-up patients SCT to detect hidden abnormalities early.

O-173 | Perioperative Management and Surgical Intervention for Retroperitoneal Teratomas in Children

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Background/Objectives: Retroperitoneal teratomas (RTs) are rare among germ cell tumors and predominantly occur in infants. Surgical resection constitutes the mainstay of therapy. However, RTs are often difficult to manage by perioperative management, and the surgery remains challenging due to its anatomical features. In this study, we retrospectively reported our experience with RTs at a single institution, and reviewed the literature focusing on the perioperative considerations.

Design/Methods: 70 patients with germ cell tumors were treated from 1989 to 2015 in our institution. 14 patients had RTs (3 boys and 11 girls). The median age at diagnosis was 5.5 months (range, 0 - 64), and 3 were antenatally diagnosed.

Results: All except one patient underwent total tumour excision. They exhibited dense adhesions with major vessels, and ligation of the splenic and gastroduodenal arteries was required in 2 patients. Injuries of PV and renal artery occurred in 2 patients. IVC injury in a neonate with a giant mass caused circulatory failure and brain death occurred postoperatively. Other major complications included injury of the diaphragm and bile duct. An infant whose tumour compressed the superior mesenteric artery on 3D-CT developed enteritis while waiting for surgery and non-occlusive mesenteric ischemia, resulting in massive intestinal necrosis. The perioperative complication rate was 50%.

Conclusion: RTs are rare neoplasms that are diagnosed incidentally or after the tumors have grown to vast proportions. Although patients with successful complete resection have an excellent prognosis, surgery for RTs remains challenging. A preoperative evaluation of the vascular anatomy is crucial because of the high complication rate. 3D-CT angiography is mandatory for the preoperative evaluation of RTs. Additionally, in cases with suspected arterial compression and hypoperfusion due to RTs, pre- and intraoperative fluid management is important to avoid any unexpected fatalities.

O-174 | Malignant Ovarian Germ Cell Tumour in Children: Judicious Usage and Timing of Surgery

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Background/Objectives: Malignant Ovarian germ cell tumours (GCT) are uncommon heterogeneous group of tumours in children and adolescents. The aims of this study were to analyse the impact of primary surgery or excision of residual disease after incomplete surgery but following chemotherapy on the outcomes and secondly to evaluate the role of preoperative chemotherapy in patients with advanced stage disease.

Design/Methods: The records of 54 patients with malignant ovarian GCT treated from June 2005 to December 2014 were reviewed and analysed for clinicopathological characteristics and survival.

Results: Median age of the patients was 12 years (range, 9 months to 18 years). Thirty-four patients had a primary presentation; 16 received preoperative chemotherapy and 18 were operated upfront. Tumour rupture and significant blood loss occurred in 4 and 2 patients in the upfront group. Twenty patients had incomplete surgery and all except two patients had residual disease in the abdomen on imaging. All patients with residual disease received chemotherapy followed by delayed surgery. At a median follow-up of 43 months the 5 year overall (OS) and event free survival (EFS) for the entire cohort is 86% and 78% respectively. The OS and EFS after adjusting for stage in patients with primary presentation were similar for patients with upfront surgery or surgery after preoperative chemotherapy. Similarly there was no difference in OS and EFS after adjusting for stage between primary and residual group.

Conclusion: Pediatric ovarian GCT has favourable outcomes. Although the outcomes are similar with upfront surgery and preoperative chemotherapy, the latter may reduce the surgical morbidity associated with resection of large tumours. Complete surgical excision may avoid the need of second look surgery.

IPSO: SESSION 6: RHABDOMYOSARCOMA AND MISCELLANEOUS

O-175 | Evaluating Urologic Outcomes in the Survivors of Rhabdomyosarcoma Bladder Prostate: 14 Year Experience at a Tertiary Care Centre

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Background/Objectives: Majority of parents of our children with rhabdomyosarcoma of the bladder-prostate (RMS-BP), who achieved partial remission with neoadjuvant chemotherapy, refused surgery because of non-acceptability of likely incontinence and need clean intermittent catheterization. This decision was influenced by socio-religious and/or financial constraints. This study was to evaluate the impact of multimodality therapy, in this scenario, on urologic outcomes among the survivors RMS-BP.

Design/Methods: All patients received chemotherapy with radiotherapy+surgery. Micturating cystourethrography(MCU), radionuclide studies and urodynamic studies (UDS) were done as required.

Results: Eighteen survivors of RMS-BP treated between 1999 and 2013 with a mean follow-up period of 96.2 months after completion of therapy were evaluated for urinary symptomatology. Primary tumour site was bladder base/prostate-12; bladder-5; bladder dome-1. Five children underwent bladder-conserving surgery followed by external beam radiotherapy (EBRT) in three of these. One of these three, had nocturnal enuresis. Another child had dribbling with fecal incontinence and UDS revealed small capacity, high pressure system (54% of mean expected for age) which responded to Imipramine therapy. Two, who did not receive EBRT, had no symptoms or imaging abnormalities on follow-up.

Thirteen of 18 were not operated. Of these, 12 received EBRT while one had chemotherapy alone. This child had frequency but normal UDS and upper tract studies. Of the Twelve who received EBRT, six (50%) were symptomatic on follow-up. Three of these actually had recurrence or disease progression with one showing upper tract dilatation. One child had developed a bulbar urethral stricture. Overall, eight of fifteen (53.3%) children who received EBRT were symptomatic, while only one of the three (33.3%) who didn't receive EBRT was symptomatic.

Conclusion: Fifty percent of the RMS-BP survivors had urinary symptoms with or without UDS abnormalities. The incidence of urinary symptoms were more among those who received EBRT (53% vs 33%). Therefore, substituting EBRT for surgery may not be advantageous.

O-176 | Massive Resection of Lung Metastasis for Survival of Patients with Osteosarcoma in Instituto Nacional De Pediatría

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Background/Objectives: During years, the massive resection of lung metastasis in patients with osteosarcoma was controversial in our community. In this study we will show that it is feasible to improve the survival of patients with osteosarcoma with this approach.

Design/Methods: A single institution, ambispective, cohort study. All patients under 18 years who were treated in our hospital with metastatic osteosarcoma were included in the review. The cardinal criteria were a number of 15 or more pulmonary nodules. The exclusion criteria were primary lung nodules or metastatic disease by other cancer.

Results: 92 patients with metastatic osteosarcoma were treated with massive osteosarcoma resection in our hospital during 2011-2015. 20 patients were synchronous and 72 were metachronous. We perform 102 thoracotomies in all the patients mention before, 62 clamshell thoracotomies, 36 posterolateral thoracotomies and 4 anterior thoracotomies, and follows like in patients and out patients during 2-5 years (mean 2.5 years). The nodules size were between 5-125 mm. The number of metastasis were no related with the overall survival. We related the grade of necrosis, total resection and response of the primary tumour to chemotherapy with the survival. The overall-survival for 2 and 5 years was 52% and 36% respectively. 15 of our patients are in medical surveillance.

Conclusion: The massive resection of lung metastasis would provide quality of life, less resistance to treatment and improve curative rate in patients with metastatic osteosarcoma. However we suggest a multicentric study to define position to patients with multiple pulmonary metastasis.

O-177 | Paediatric Gastrointestinal Post-Transplant Lymphoproliferative Disorder: Incidence, Clinical Characteristics, and Impact of Surgical Intervention Upon Overall Survival

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Background/Objectives: Post-transplant lymphoproliferative disorder (PTLD) is a significant complication of solid organ transplantation. A common site for PTLD development is the gastrointestinal (GI) tract. The purpose of this study was to evaluate the incidence, clinical features, and overall survival (OS) of paediatric patients with GI-PTLD, and to assess whether surgical intervention increased mortality.

Design/Methods: With Ethics Board approval, records of paediatric transplant patients who developed GI-PTLD between January 2000 and June 2015 were retrospectively reviewed at a single institution.

Results: Thirty-nine out of 795 patients (5%) who received solid organ transplants developed GI-PTLD, including heart (40%), liver (38%), lung (10%), small bowel (7%), and kidney (5%). Lung transplant had the highest incidence of GI-PTLD (9%). The shortest mean time to GI-PTLD onset was 11±0 months (kidney). Sites of disease included the colon (28%), jejunum (26%), gastro-duodenum (23%), and mesentery (21%), while 56% of patients had multi-site involvement. Epstein-Barr viral (EBV) loads >1000 copies/μg of DNA were reported in only 41% of patients, while 33% of patients were EBV(-). The mean time to develop GI-PTLD for patients that were EBV(+) was 56±31 months, and 20±23 months for patients that were EBV(-). The commonest histological subtypes were polymorphic B-cell (36%), Burkitt lymphoma (18%), and plasmacytic B-cell hyperplasia (15%). Medical therapy included reduction or withdrawal of immunosuppression (85%), antivirals (59%), chemotherapy (51%), and monoclonal antibodies (46%). Surgery was required in 28% of patients, related to bowel obstruction and perforation. OS for these patients was 73%, compared to an OS of 64% for all patients.

Conclusion: The highest incidence of GI-PTLD was in lung transplant patients, and the shortest mean time to disease development in kidney transplant patients. GI-PTLD complications required surgical intervention in a relatively large subset of patients. Despite multi-modal therapy, OS remains poor. However, surgical intervention does not appear to result in a lower OS.

O-178 | Detection of Biomarkers in Blood Macrophages Via EDIM Blood Test in Patients with Rhabdomyosarcoma

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Background/Objectives: Rhabdomyosarcoma is the most common paediatric soft tissue sarcoma and the third most common extra-cranial solid tumour of childhood. So far, a biomarker for rhabdomyosarcoma has yet not been described. A sensitive and specific liquid biopsy test of diagnosing tumour occurrence within the peripheral blood could possibly contribute to an improved prognosis of affected patients. Different reactions of the immune system to tumors have been observed so far; these reactions include as a very early step phagocytosis of tumour cells by macrophages. The Epitope Detection in Monocytes (EDIM blood test) allows detection of intracellular tumour-protein epitopes in peripheral blood macrophages after phagocytosis of tumour cells or even compounds.

Design/Methods: We analyzed blood samples from eight patients with rhabdomyosarcoma and nineteen healthy blood donors without pathological levels. CD14⁺/CD16⁺ macrophages from peripheral blood were analyzed by use of flow cytometry and assessed for the presence of intracellular epitopes of tumour proteins Apo10 (proliferation defect) and TKTL1 (activation of aerobic glycolysis) using the EDIM test.

Results: Incorporated tumour proteins Apo10 and/or TKTL1 were detected in the CD14⁺/CD16⁺ macrophages of all analyzed patients. A correlation to upregulated Apo10 and/or TKTL1 expression in tumour samples from patients with rhabdomyosarcoma was observed in comparison to healthy blood donors without pathological levels.

Conclusion: In summary, these results provide evidence that this new and innovative EDIM blood test might serve as an additional tool for risk stratification at initial diagnosis, for monitoring of the treatment course, and for an early detection of tumour relapses.

O-179 | Has Propranolol use Eliminated the Need for Surgical and/or Laser Intervention in Infantile Haemangiomas Treatment? Over 6,5 years of Experience

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Background/Objectives: Haemangiomas are most common vascular anomalies in children. The paper aims at presentation of over 6,5 years of experience in Propranolol use in haemangiomas' treatment, and subsequent need for surgical and/or laser intervention.

Design/Methods: In Poland propranolol was initiated for the treatment of haemangiomas in Gdansk in March 2009. From III 2009 to XI 2015 oral Propranolol was introduced in 278 children; aged between 4 weeks and 5,5 years. Majority of lesions were in the proliferative phase 265(95,3%). The response to treatment (growth inhibition, shrinkage in size, healing of ulcerations) was observed in 272 (97,8%). Final assessment was mainly focused on patients' appearance, and the need for subsequent surgery or laser therapy.

Results: The treatment was completed in 235 (84,5%) patients and lasted fmean 11,7 months (4-28). Lesions with an unsatisfactory response to pharmacotherapy (3) were removed surgically. Three patients were lost to follow-up. Rebound effect was observed in 27 patients (9,7%) with a good response to reintroduction of propranolol in all. 11 patients experienced multiple relapses. 41 patients were operated on: 49 excisional procedures performed (8 operated while still on propranolol). 38 patients had laser therapy (57 procedures) 21 patients await surgery and 35 - laser treatment. In summary, 135/235 patients (57,4%), who had completed the systemic propranolol treatment, required or would require in future additional invasive procedures, such as surgery or laser. There was only one significant adverse reaction notified - a hypoglycemia.

Conclusion: Although, systemic Propranolol seems to be a method of choice among patients with clinically significant infantile haemangiomas with a small number of lesions resistant to treatment. Noticeably, more than a half (57,4%) of pts. still require an invasive procedure upon completion of therapy. Early introduction of treatment offers the best chances for a good result. Our 6,5 years experience confirms the safety of this form of therapy.

O-180 | Abdominal and Pelvic Rhabdomyosarcoma: The University of Texas MD Anderson Cancer Center Experience

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Background/Objectives: Approximately 30% of rhabdomyosarcomas (RMS) occur in the abdominal/pelvic cavity. While certain subgroups have an excellent prognosis, such as vaginal botryoid RMS, pelvic RMS does poorly. The objective of this study is to present our institutional experience of 30 patients with abdominal/pelvic RMS and to evaluate the association of survival outcomes with clinical covariates.

Design/Methods: Retrospective record review of 30 patients from 1991 - 2014 treated at the University of Texas MD Anderson Cancer Center. Recurrence-free survival (RFS) and overall survival (OS) probabilities were estimated using the Kaplan-Meier method. Log-rank test was used to compare outcomes between subgroups.

Results: Sixteen patients (53%) were female, and the median age at diagnosis was 4 years (range 0 - 27 years). Embryonal RMS was the most common histologic subgroup (n = 26; 87%). Of 6 patients tested for fusion status, 2 were FOXO1 positive. The most common primary tumour site was the bladder/prostate (n=15; 50%) followed by uterus/cervix (n=5; 17%). Stage 3 (n=11; 37%) and Group 3 (n=13; 43%) were the most common staging characteristics encountered. Median follow up time was 5.4 years (95% CI: 2.3, 10.1). The 5 - year RFS was 49% (95% CI: 31% - 76%), and OS was 62% (95% CI: 42% - 87%). Patients older than 10 years had worse outcome for both RFS (P = 0.009) and OS (P = 0.0006). Surgery, radiation therapy, and surgical margin status were not statistically significant for RFS or OS. Eight patients died of disease, and one died of secondary malignancy. Of the patients who died of disease, 6 had ERMS and 4 had metastases at diagnosis while 1 had nodal involvement.

Conclusion: Despite predominance of ERMS histologic subtype, abdominal/pelvic RMS has a worse clinical prognosis than expected. Local control did not significantly impact RFS or OS. Alternative therapies are needed for abdominal/pelvic RMS.

NURSES: FREE PAPERS SESSION 1: QUALITY OF LIFE AND QUALITY OF NURSING CARE IN PAEDIATRIC ONCOLOGY

O-181 | Development of a Valid Instrument to Assess Baseline Standards for Paediatric Oncology Nursing Care

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Background/Objectives: Baseline standards for paediatric oncology nursing care in low- to middle-income countries were developed by the SIOP PODC Nursing Group and published in 2014. The six standards reflect the elements of quality nursing care essential to promote

optimal outcomes for children with cancer. A valid instrument with measurable criteria for each standard is needed to correlate quality of nursing care with clinical outcomes.

Objectives:

1. Establish measurable criteria for each of the six baseline nursing standards.
2. Develop and validate an instrument to accurately measure the baseline standards.

Design/Methods: A SIOP PODC Nursing task force convened to develop an instrument that will measure the six baseline nursing standards as indicators of quality nursing care. Once consensus on the criteria were reached by the task force, a separate panel of eight nursing experts representing all six WHO geographical regions was consulted to validate the instrument. The panel rated how well each criterion measured the corresponding standard, using a four point scale. A content validity index (CVI) was obtained by using the percentage of total standards given a score of "3" or "4" by the experts.

Results: The six standards were rated by each expert, resulting in a content validity index (CVI) of .98. CVI measures the degree to which an instrument measures what it is intended to measure. A CVI of > .80 is recommended for a newly developed instrument. Based on the panel's recommendations, minor modifications were made to the survey.

Conclusion: A valid instrument is needed to consistently measure the baseline standards for paediatric oncology nursing care. This instrument will allow for future research on the effects of nursing standards on clinical outcomes, including mortality and abandonment of treatment, with the potential to influence health policy decisions and improve nursing support in low and middle income countries.

O-182 | Evaluating the Acceptability and Efficacy of An Educational Intervention to Enhance Healthy Behaviors and Healthy Lifestyle in Childhood Cancer Survivors: A Randomized Controlled Study

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Background/Objectives: Completing treatment can be joyful as well as frightening for patients and families. The health promotion is an ongoing health precautions and planning for off-therapy for survivors of childhood cancer. The study was to evaluate the feasibility and efficacy of an educational program to enhance healthy behaviors and healthy lifestyle after children completing cancer treatments.

Design/Methods: It was a mixed method study design. Participants completing treatments were recruited and randomly assigned to two groups from January 2014–December 2015 in Taiwan. The intervention group received an educational intervention in addition to standard care, while the control group received only standard care. Each participant was assessed using the healthy behavioral efficiency (HBE) and healthy promotion lifestyle (HPL) at two time points (baseline, and four months after interventions). The t-tests were used to estimate the effects of intervention. Qualitative findings were analyzed using content analysis to determine the feasibility of the intervention.

Results: The experimental group reported a significantly higher score of HBE after participating in the education program ($t = 3.4, p < .01$). The score of each HBE subscale in the experimental group was significantly enhanced from baseline to four months, except in the exercise dimension. HPL significantly increased over time in two groups. Qualitative results reported participants evaluated the intervention positively, especially regarding how to take care of themselves after completing treatments.

Conclusion: The educational program administered was acceptable for childhood cancer survivors and was found to enhance healthy behavioral efficiency. Healthcare professionals may adapt the educational program for providing support to increase children's healthy behavioral efficiency, and explore the effects of the educational intervention on psychological outcomes.

O-183 | The Impact of Cancer and its Treatment on the Physical and Psychological Well-Being among Chinese Children in Mainland China: A Descriptive Study

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Background/Objectives: Cancer and its treatment adversely affect children's physiological and psychological well-being. Although several similar studies have been conducted in the West and Hong Kong, cultural discrepancies make these findings inapplicable to Mainland China. This study aimed (1) to compare the quality of life and physical activity levels between children hospitalized with leukaemia and their healthy counterparts; (2) to describe the impact of therapy-related symptoms on the physical and psychological well-being of children with leukaemia; (3) to examine the coping strategies adopted by children hospitalized with leukaemia.

Design/Methods: A cross-sectional study was conducted. A total of 125 children undergoing leukaemia treatment and 243 healthy children were invited to participate in the study. Their physical activity level and quality of life were assessed and compared. Data of therapy-related symptoms and coping strategies used by children with leukaemia were collected. Furthermore, 15 children with leukaemia were purposively selected to attend an individual semi-structured interview.

Results: An independent sample *t*-test showed a statistically significant decline in physical activity levels and quality of life among children with leukaemia. The results of regression analyses showed that physical activity levels, number of therapy-related symptoms, and the mixed coping strategies made statistically significant contributions to children's quality of life. In addition, results of semi-structured interviews revealed that fatigue, unawareness of physical benefit of regular activities, and advice for more rest from parents and healthcare professionals were the main reasons preventing children with leukaemia from engaging in regular physical activity.

Conclusion: This study reveals that cancer and its treatment can result in declining physical activity levels and quality of life among Mainland Chinese children with leukaemia. Moreover,

results showed that children with leukaemia having a higher level of physical activity and using mixed coping strategies reported better quality of life.

O-184 | Decreased Central Line-Associated Bloodstream Infection (CLABSI) Rate after Implementing Custom Made I.V System, Needle Free Connector and Intensive Training of the Nurse Staff

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Background/Objectives: Central venous lines are an essential instrument in treating paediatric hemato-oncology patients. Preventing and decreasing CLABSI is a major challenge.

To decrease the high rate of CLABSI in a paediatric hemato-oncology department action was taken by profound reorganization of the IV system, an intensive training of the nurse staff and by introducing the MicroClave[®], a needle free connector.

Design/Methods: In 2012 it was clear that the number of CLABSI in the paediatric hemato-oncology department was too high in comparison with similar centers: 7.6 CLABSI/1,000 tunneled catheter days (National Healthcare Safety Network (NHSN) mean 2.3) and 5.74/1,000 port-a-cath days (NHSN mean 1.7).

To reduce this high rate of CLABSI an action plan was worked out: implementation of the Clear MicroClave[®], a needle free connector system; implementation of a custom made closed IV system, with less risk of introducing infection in the system and intensive training session of the nursing staff.

As there was already a lot of experience with the needle free connector in the intensive units in the hospital and as the system meets the recommendations, as published in the recent guidelines of CDC, the choice for the MicroClave[®] Clear system was obvious.

The whole process was intensively supported by the infection control department. Besides an intensive training of the whole nursing staff was set up, also at the end, all nurses mandatory had to pass a test.

Results: These actions resulted in a dramatic decrease in CLABSI, from 7.6/1,000 tunneled catheter days to 0 at the end of 2015, and from 5.74/1,000 port-a-cath days to 0 at the end of 2015.

Conclusion: Intensive staff training, introduction of a new IV prepared system and the introduction of a needle free system resulted in a dramatic fall of central line infections on a paediatric hemato-oncology ward.

O-185 | When Values Collide: Family-Centred Care Vs. Family-Driven Care

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Background/Objectives: Family-centred care is acknowledged as best practice in many paediatric healthcare settings worldwide. A family-centred care framework ensures that the family retains control over their own choices. However, conflict arises when the family's choices challenge the clinical judgment, behaviours, and decisions of the healthcare team. When family demands are perceived as unreasonable, this creates an unbalanced relationship leading to *family-driven care*. This relationship is characterized by dissension, mistrust, and untold stress.

Design/Methods: Our healthcare team was challenged with how to respond when these difficult situations arose. We implemented several interventions, including support sessions for nursing, team debriefings with the team psychologist, assertiveness training, education sessions for the healthcare team on building resilience, boundary setting and how to have difficult conversations. In addition we held regular family meetings with the core healthcare team and family to create a mutually agreed upon care plan. Daily check-ins were held with the nurse leaders and social work to address any immediate concerns with the family. Family advocates were involved in building a covenant of care.

Results: The healthcare team experienced distress and felt challenged in balancing respect for family demands while upholding the team's clinical judgment. To help our team understand what contributed to conflict between the family and the team, we developed a framework to describe family-driven care. Increased understanding enabled the team to balance respect for the family's demands while optimizing goals of care for the patient.

Conclusion: Understanding the distinction between family-centred care and family-driven care is important in the paediatric oncology care context. Promoting family-centered care between the family and healthcare team is never predictable and the outcomes can be challenging when conflict arises. Our framework helped the team understand the nuances of family-driven care and to re-shift towards family-centred care.

O-186 | Biomarkers of Apoptosis are Increased During Central Nervous System Treatment and Associated with Decline in Cognitive Abilities among Children with Acute Lymphoblastic Leukemia

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Background/Objectives: One of the most challenging treatment-related sequelae experienced by children with acute lymphoblastic leukaemia (ALL) is decline in cognitive abilities. Aggressive central nervous system (CNS) -directed treatment prevents metastasis of leukaemia cells into brain tissue, but at least 40% of ALL survivors have problems with memory, attention, processing speed, and visual spatial skills. Knowledge about mechanisms of neurologic injury

is lacking, and greatly needed in order to develop novel neuroprotective interventions. The purpose was to investigate the potential role of apoptosis in neurologic injury.

Design/Methods: Children ($n = 59$) with newly diagnosed ALL were enrolled and followed for 3 years. Caspase (3/7, 8, and 9) enzyme activity was measured in cerebrospinal fluid samples collected in conjunction with diagnostic and therapeutic lumbar punctures. Changes in expression of miRNAs known to regulate apoptosis were measured in CSF from a subsample of 6 children. Cognitive abilities were assessed as soon as the child was medically stable and then every 12 months for 3 years.

Results: A significant increase in the activity of caspase 3/7 ($F = 32.72$; $p < 0.001$), caspase 8 ($F = 27.56$; $p < 0.001$), and caspase 9 ($F = 27.28$; $p < 0.001$) was observed across the phases of ALL treatment. There was also a significant fold change in 4 miRNAs measured prior to and during the most intensive phase of CNS-directed treatment. Declines in visual spatial skills, working memory, and attention/concentration were significantly associated with an increase in caspase 3/7 activity. Visual spatial and fine motor abilities were associated with miRNA expression fold changes.

Conclusion: Findings suggest that apoptosis may be involved in neurologic injury associated with CNS-directed treatment and biomarkers of apoptosis may identify children at risk for decline in cognitive abilities.

Funding for this project was received from Alex's Lemonade Stand Foundation Discovery Award.

NURSES: FREE PAPERS SESSION 2: EDUCATION FOR CHILDREN, PARENTS AND NURSES

O-187 | The Past, Present and Future: Siop Paediatric Oncology Developing Country Nursing Working Group

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Background/Objectives: The Pediatric Oncology Developing Country (PODC) Nursing Working Group is a vital contributor to the SIOP PODC Committee. Nurses from low-and middle income countries (LMIC) are often challenged by their limited resources, education and scope of their professional practice. The PODC Nursing Working Group has created a bridge between LMIC and HIC (high income countries) nurses to develop an understanding and promote collaborative efforts to improve outcomes for children with cancer. Past accomplishments included development of teaching modules and baseline nursing standards for LMIC. Current goals are focused on increasing membership, promoting collaboration, facilitating networking and creating member-led project groups for key activities.

Design/Methods: The PODC Nursing Working Group holds monthly meetings on the Cure4Kids Website. The meeting incorporates business and educational components. Project groups with co-leaders provide updates of current activities. The educational topics are determined by the members and include a discussion following the presentation. Meetings are recorded and both notes and slides are made available.

Results: Over the last 6 months, the membership has increased by 35% with 83 members representing 30 countries. There have been 4 educational presentations and informative discussions on abandonment of care, supportive care, writing abstracts, developing posters/presentations and infection control/prevention. Other significant achievements include the ongoing work of the SIOP PODC Baseline Nursing Standards, Pediatric Oncology Nurse Recognition Day, nurse education/training repository, nurse mentor list for abstract and grant writing and a membership directory. Internet connectivity and scheduling meetings during daylight hours across multiple time zones are ongoing challenges.

Conclusion: The restructuring of the PODC Nurse Working Group has created a sustainable community beyond the annual conference, meeting the needs of LMIC and HIC nurses. The numerous projects have fostered collaboration, created opportunities for membership involvement, encouraged professional growth and facilitated leadership development. Future directions include the expansion of LMIC nurses' leadership and advocacy skills.

O-188 | Education Program to Parents of Children with Cancer and their Impact in the Level of Knowledge, Perception of Hospital Care and Occurrence of Adverse Events

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Background/Objectives: Parents of children with cancer must receive information related with their child disease for an optimal care. The aim of this study was to determine the effect of an educational program to parents of children with recently diagnosis of cancer in the level of knowledge, perception of hospital care and occurrence of adverse events.

Design/Methods: Experimental, prospective and multicenter study in parents with children with recently diagnosis of cancer in two reference children's hospitals in Santiago, Chile. In one center, parents received educational intervention (experimental group) and the second center did not received intervention (control group). We evaluated through a test level of knowledge of child disease at day 1, 10 and 90, perception of hospital care at day 1 and 120 and occurrence of adverse events during one year.

Results: A total of 72 parents were enrolled between June 2014–November 2015 (36 in each group). At day 1, both group had the same number of correct answers, but at day 10 we observed a significant increase in correct answers in the experimental group ($p < 0.001$). At day 90, a trend toward a higher number of correct answers was observed in the experimental group. Perception of hospital care was similar in both hospitals; days of hospitalization because of fever (without neutropenia and not related with chemotherapy) was significantly higher in the control group ($p < 0.002$) as same as a trend toward a higher number of central venous catheter infection episodes.

Conclusion: Our results suggest that an educational program by the nurse to parents of children with cancer, increase the level of knowledge at the beginning of the disease and lower adverse events might be observed in this group. Implementation of systematic educational programs should be consider for parents of children with cancer in hospitals delivering care of this susceptible population.

O-190 | Sustained Paediatric Oncology Nurse Training in Botswana

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Background/Objectives: The majority of new paediatric oncology cases are diagnosed in low and middle income countries (LMICs), yet the survival rates lag significantly behind those of high income countries. This disparity in survival may be attributed to limited access to effective chemotherapy, late diagnosis, and lack of education amongst health care workers. Clinical in-service training in Botswana is typically centered around short workshops which rely heavily on didactics with limited bedside reinforcement. While this method has been effective for general topics, it may have limitations as a platform on which to increase lasting knowledge in subspecialty areas such as paediatric oncology.

Design/Methods: We assessed the effectiveness of a sustained paediatric oncology nurse education program at Princess Marina Hospital (PMH) in Gaborone, Botswana. Variables of interest included pre- and post-test scores, and satisfaction evaluations, of the course participants.

Results: The 16 week paediatric oncology nurse training course at PMH covered a broad range of topics including cancer presentations, treatment side effects and supportive care, oncology emergencies, and palliative therapy. Didactic sessions were reinforced with bedside rounds and case presentations. The facilitators included paediatric oncology physicians, oncology trained nurses, and the hospital dietician. A baseline knowledge assessment revealed an average score of 54% (32%–64%) and the average post-test score was 98% (96%–100%). A satisfaction survey of course participants revealed an average score of 4.3 out of a high of 5. The main suggestions for improvement amongst the participants were for an extension of the course length and the addition of a "hands-on" procedural skills session.

Conclusion: Sustained paediatric oncology nurse training at PMH resulted in an improvement in clinical knowledge and confidence amongst the course participants. We plan to increase the number of paediatric nurses participating in future training sessions and hope that this will translate into improved management of oncology patients on the ward.

O-191 | Usability Testing 'Help': An Online Information Intervention for Parents of Children with Acute Lymphoblastic Leukaemia

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Background/Objectives: Our previous research identified that parents of children with Acute Lymphoblastic Leukaemia (ALL) felt that they received minimal support to facilitate the acquisition of new knowledge, especially during the period closest to diagnosis. We developed an online intervention for parents named HELP (Harmonising Education about Leukaemia for Parents) to facilitate easy access to information about leukaemia. Our systematic approach to the development of HELP has been presented to delegates attending SIOP 2011, 2012 and 2014. Here we focus on the final stage of testing, usability testing, with parents of children currently undergoing treatment for ALL.

Design/Methods: The primary outcome of this stage was user-performance, which was assessed through parent's reports of the ease of use and ease of learning. Usability Testing was assessed over four discrete activities: Parents navigated HELP while thinking aloud; completed the System Usability Scale; took part in a semi-structured interview; and completed a demographic questionnaire. Sessions were filmed and audio recorded. Data were transcribed verbatim and analysed using NVivo. Usability Issues were identified using simple content analysis. These were grouped into four categories: content, functionality, user-interface and user-performance.

Results: Twenty-one families were approached. Eleven parents agreed to be contacted and seven (four women and three men, mean age 40.4 years) participated. Parents liked the inclusion of the voice of parents in videos on the website but felt clinician videos could be more engaging. Issues including case-sensitive passwords, embedding videos, missing content, the website background and colour-scheme were identified. Overall parents responded favourably to the website. Elements that could be added or amended were suggested. The mean System Usability Scale score was 80/100, suggesting that the website was 'acceptable'.

Conclusion: Usability Testing was a worthwhile, albeit time-consuming process. The HELP website is currently being refined using the feedback generated, ready for the launch later in 2016.

O-192 | The Nursing Oncopedia: A Five Year Update on a Global Nursing Education Initiative

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Background/Objectives: Eighty-four percent of paediatric oncology cases occur in low- and middle-income countries (LMIC), where resources are limited and chances of cure are very low. Knowledgeable providers and available, accessible, and completed treatment significantly contribute to treatment success in high-income countries (HIC), where more than 80% of children are cured. Trained nurses are an essential component in the care team; yet, many paediatric oncology nurses lack access to specialized in-person education due to time and financial constraints, or lack of locally available training opportunities. Thus, online learning provides an alternate resource for educating paediatric oncology nurses. In 2011, Cure4Kids launched Nursing Oncopedia, an interactive, online, open-access, peer-reviewed paediatric oncology resource. The purpose of this project was to evaluate the five-year impact of the project.

Design/Methods: Cure4Kids Nursing Oncopedia articles describe nursing management of paediatric hematologic and oncologic diseases and their complications. Articles were submitted for online peer review by disease specific nursing experts through a restricted discussion board. The articles' standard format included (a) an overview of the disease/complication; (b) specific aspects of nursing assessments; (c) administration guidelines of potential treatments; (d) guidance for patient and family education; and (e) links to related material on Cure4Kids.org.

Results: Between March 2011 and March 2016, a total of 61 articles were published; 20 were original English articles and 41 were translations in Spanish, Portuguese, Arabic, French, and Italian. Cure4Kids Nursing Oncopedia content acquired 8,129 hits by 2,352 unique users in 125 countries. The top two countries accessing the content were The United States and Mexico.

Conclusion: In congruence with its goal, Cure4Kids Nursing Oncopedia has successfully created a global paediatric oncology nursing network. This network allows education and knowledge sharing between nurses in HIC and LMIC countries alike. This initiative will continue and new submissions from all nurses are welcomed and encouraged.

NURSES: FREE PAPERS SESSION 3: DIFFERENT NURSING ROLES IN PAEDIATRIC ONCOLOGY

O-193 | Improved Compliance of Out Patient Visit with Use of Active Database Management and Help of Nursing Staff in Paediatric Cancer Patients

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Background/Objectives: Non-compliance is a frequent phenomenon in treatment of cancer, especially in resource poor countries and can be improved with use of patient database management & tracking system and help of nursing staff.

Design/Methods: We prospectively maintained a patient database and a tracking system in out-patient department (OPD) visits from Aug'2015 to Feb'2016 with help of data manager and nursing staff. We tracked down all patients who missed the scheduled OPD visit and tried to find out the possible causes of non-attendance and refusal of treatment. Those who couldn't be contacted through phone calls were traced down to their case files to find out the possible causes of non-attendance. We classified the causes of treatment refusals in three categories-patient related, hospital related and disease related factors.

Results: Patients visited 9,875 times (90%) out of the 11,011 scheduled OPD appointments. Out of remaining 1135 absent visits (10%), 817 times (72%) patients were contactable through phone calls. After the calls it was found that 103 patients were dead, 31 patients refused for further treatment and rest of the patients were re-scheduled for next OPD visits. Causes of treatment refusals were- hospital related factors in 12, family related factors in 13, disease related factors in 4, and cause not known in 2 patients. Case files were traced for remaining 144 patients (visits-318) and last status of those patients was- progressive disease (PD) on metronomic therapy- 17, PD on palliative chemotherapy-23, PD on best supportive care-19, treatment not started yet-38, patients on active curative treatment-29, off treatment-15, and others-3.

Conclusion: Compliance was good in our patients during OPD visits, and it was achieved with database management and surveillance system with help of data manager and nursing staff. Early emphasis should be given on the reasons of treatment refusals to improve compliance.

O-194 | Enhancing Safety through Correct Identification of Patients in Central America

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Background/Objectives: Correctly identifying patients is essential to ensure patients receive intended treatments and services, and to avoid potential harm. According to the World Health Organization, incorrect identification of patients is associated with errors related to drug administration, surgical procedures, diagnostic tests, blood transfusions, and placement of newborns with the wrong families. Although identification processes are regulated and well-integrated in many hospitals and nations, this is generally not the case in low- and middle-income countries (LMIC). In efforts to enhance patient safety at a paediatric oncology hospital in Central America, a quality improvement project was developed based on the Joint Commission International (JCI), International Patient Safety Goal: Identify Patients Correctly. The objectives of this project were to standardize patient identification processes from admission to discharge, and enhance identification of patients prior to medications, blood/blood products, specimen collections, and treatments/procedures.

Design/Methods: Project methods included review and amendment of a patient identification hospital policy, baseline audit of patient armbands and identification practices, education of staff, documentation, and continuous monitoring by nurse educators.

Results: Standardized patient identification practices were compared between patients evaluated in May and October, 2014. Preliminary results revealed a 53% (24% to 77%) improvement across inpatient and outpatient settings. As a result of this initiative, patient identification was adopted as a nursing-sensitive quality indicator at the institutional level.

Conclusion: Adopting a culture of safety through correct patient identification is instrumental to optimizing treatment and survival in paediatric oncology. Stakeholder buy-in and interdisciplinary collaboration is essential to promoting a culture of safety. Future implications include replicating this project at various hospitals in low- and middle-income countries.

O-195 | Integrating A Specialized Nurse Practitioner Role in a Paediatric Oncology Center in Karachi, Pakistan

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Background/Objectives: The role of a specialized nurse practitioner has been widely accepted and appreciated in many high-income countries as it provides continuity of care, patient satisfaction, reduced morbidity and mortality and cost-effective treatment. In paediatric oncology, the continuum of care is critical given children's critical health status. Unfortunately, in low- and middle-income countries (LMIC) this nursing role is normally not recognized. At Indus Children Cancer Hospital, we have identified the need for specialized nurses for better patient care. After a year of specialized training, seven nurses were assigned to multiple subspecialties as a pilot project to integrate the role of the specialized nurse practitioner.

Design/Methods: The Pakistan Nursing Council (PNC), a licensure body, approved a one-year specialization diploma in paediatric oncology. Eight candidates were shortlisted after the admission process (an entry test and interview).

Results: The candidates were trained for one year in a program of theory and clinical nursing practice. The local licensure body conducted an exit exam; all the candidates were successful. In the second phase, each nurse chose an area of specialization: lymphoma, leukaemia, solid tumors, pain and palliative care, or infection prevention and control. This has allowed for integration of the specialized nurse's role in our hospital's nursing model. The process of integrating the role of a specialized nurse practitioner in the hospital's existing model has just begun and plans are to evaluate the efficacy of this initiative after one year by evaluating mortality rates, length of stay and patient satisfaction survey.

Conclusion: This successful pilot will serve as a model to integrate the role of a specialized nurse practitioner for paediatric oncology in other LMIC nursing models. This program is expected to improve outcomes for children with paediatric cancers, patient and family satisfaction, a continuum of care and increased nursing research opportunities.

O-196 | Nursing Addresses Increase in Multidrug-Resistant Bugs in Paediatric Oncology Unit of a Tertiary Care Center in India

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Background/Objectives: Multidrug-resistant organisms (MDRO) colonization and infections are of serious concern for children with cancer and the nurses who care for them due to high morbidity and mortality. In a paediatric oncology unit in Mumbai with 2000 children/year diagnosed with cancer, a nurse-led investigation determined the temporal trends in antimicrobial-resistant bacteria isolates and correlated findings with antibiotic utilization and community colonization.

Design/Methods: The unit's infectious disease nurse audited the prevalence of extended spectrum beta-lactamase-positive gram-negatives (ESBL), carbapenem-resistant gram-negatives (CRE), vancomycin-resistant enterococci (VRE) and methicillin-resistant staphylococcus aureus (MRSA) in blood cultures isolates from inpatient laboratory records from 2005, 2011, 2012 and 2013. Antibiotic utilization was evaluated and correlated with MDRO trends.

Results: In 2005, 14.9% of 2,587 blood cultures were positive. Incidence of ESBL was 6.95% and VRE 0.77% and CRE was 0.51%. In 2011, 7% of 1,600 blood cultures were positive for MDRO: ESBL 18.75%, CRE 28.57%, and pan-sensitive bacteria 44.64%. In 2012, 6.98% of 1,589 blood cultures were positive for MDRO: ESBL 33.33%, CRE 13.51%, and 38.73% pan-sensitive. In 2013, 21.3% of 3,994 blood cultures were positive for MDRO: ESBL 56.9%, CRE 27% and pan-sensitive 16.5%. Correlation with antibiotic utilization revealed an increasing use of carbapenems despite increasing resistance and colistin (effective for Pseudomonas, Escherichia, and Klebsiella infections).

Conclusion: This study illustrates the growing MDRO epidemic (especially CRE) in this paediatric oncology unit reflecting antibiotic use by patients before diagnosis. Specific local nurse-led multidisciplinary efforts will be presented including strict hand hygiene protocols, active surveillance cultures (ASC), antibiotics stewardship, contact precautions and isolation to optimize patient outcomes. As the largest single profession caring for children with cancer in the unit, nursing is particularly well positioned to address this alarming increase in drug resistance in Mumbai and across the world.

NURSES: FREE PAPERS SESSION 4

O-197 | Symptom Experiences of School-Age Children with Cancer Portrayed Through Their Drawings

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Background/Objectives: Children receiving treatment for cancer report as many as 10 co-occurring symptoms that adversely impact their quality of life. Children's verbal and cognitive abilities, however, are common barriers for having their symptoms understood. Arts-based techniques offer alternative approaches for symptom reporting by guiding children to organize and represent their experiences. This study describes symptom experiences of children with cancer as expressed in their drawings. Data are guiding the development of a mobile technology-based symptom assessment app for children with cancer.

Design/Methods: The project used a cooperative inquiry design which engaged children as active participants. Children received a packet of art materials and participated in "draw and tell interviews" to relate both a "good day" and a "sick day." A constant comparative approach using content analysis techniques was used to analyze children's pictures and interview responses to describe symptoms and self-care strategies.

Results: Participants were 14 boys and 13 girls (mean 9.16 years; range 6.33 – 12.83 years; 93% White non-Hispanic) receiving cancer treatment. "Good day" pictures most frequently related being involved in enjoyable activities, particularly outside activities. "Sick day" pictures related restricted activity, frequently with the child lying down. Children's pictures and interviews related 25 different physical symptoms and 12 different psychosocial symptoms with sadness (n=20), nausea (n=15), fatigue (n=10), stomach ache (n=9), and pain (n=8) most frequently reported. Children's pictures and interviews also related 21 different coping and symptom self-management strategies with lying down (n=11), use of blankets (n=6), and support from another person (n=4) most frequently reported.

Conclusion: Data demonstrate the capacity of children to provide rich personal data related to their cancer-related symptoms as well as the strategies they use to self-manage these symptoms. Study results can support a more personalized approach to symptom management for children with cancer.

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O-198 | Implementation of Infection Prevention and Control Guidelines: A Challenge in Oncology Centers in Pakistan

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Background/Objectives: Infection control and prevention measures are essential components of quality healthcare and patient safety in health facilities; moreover infection control nurses play a vital role in implementation of infection control and prevention guidelines. Healthcare-associated infections are global issue for patient safety. Patients in low- and middle-income countries (LMIC) are at a higher risk for hospital-acquired infections[DFS1] due to a lack of resources for infection control e.g., infection-control teams, hand sanitizer, and robust infection control policies and practices. Implementation of infection prevention and control is a particular challenge in paediatric oncology populations due to children's treatment- and disease-related immunosuppression. The objective of this study was to identify the challenges of infection control for nurses working in paediatric oncology centers in Pakistan. Pakistan has 13 paediatric oncology centers [jc2] for >199 million inhabitants, 21% (>417 million) living on < USD1.25/day, and 38% (>75 million) are <15 years old.

Design/Methods: Telephone surveys were offered to Infection Control Nurses in 9 major Pakistani hospitals across the 4 provinces; 8 participated. The interview took 5 minutes with 6 open-ended questions.

Results: The majority of participants had similar challenges. The most common were: a lack of modified guidelines and policies, staff reluctance to comply to infection control efforts, a lack of structured educational programs for infection prevention and control, inadequate or shortages of infection control supplies, overburdened work responsibilities, and being an unrecognized sub-specialty. All participants reported no surveillance or audit systems in place in to monitor infection rates.

Conclusion: Infection control requires multidisciplinary efforts with expert physicians and nurses. In Pakistan, hospital-based policies need to be developed to ensure continuous monitoring, auditing and surveillance of the progress and outcome of implemented policies particularly in paediatric oncology units. Infection control nurses must be dedicated to promoting the safe care of children with cancer in these settings.

O-199 | Development of a Paediatric Oncology Fertility Preservation Program: Lessons Learned and Challenges Yet to Conquer

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Background/Objectives: Many children treated for cancer are at risk for sub-fertility. The loss of reproductive potential has been described in the literature as a major Quality of Life concern for cancer survivors. Survivors report a lack of information being delivered and potential interventions being offered at diagnosis. To address this gap in care the SickKids Fertility Preservation Program (SKFPP) was launched in 2014. Our mandate is to provide information regarding fertility risk and fertility preservation (FP) and to provide interventions as needed.

Design/Methods: Funding from the Garron Family Cancer Centre was secured for 2 years for a 1/2 time Nurse Practitioner(NP) to develop the SKFPP in conjunction with an; Oncologist, Urologist, a Gynecologist and Survivor. The success of our program was achieved by creating awareness of the need for FP information for providers and patients and developing close working relationships with stakeholders at SickKids including: Haematology and Oncology, Quality and Risk Management, IGT, Peri-Operative Services and Sinai Health Centre for Fertility and Reproductive Health. Services offered to patients with fertility risk include; counseling, sperm banking and oocyte preservation. Under the SickKids Innovation Program unproven, interventions such as ovarian and testicular tissue preservation are offered to patients at risk. We continue to develop clinical practice guidelines and policy and procedures to support the delivery of these interventions. We offer ongoing education to staff and have created tools for patient education including a website and educational materials. To describe future trends in FP and as a platform for research we have developed a Research Ethics Board approved database.

Results: Since 2014, the SKFPP has consulted with over 150 patients and organized over 75 procedures. The NP role has been extended by the GFCC for 2 more years.

Conclusion: Moving forward our challenge is to secure stable funding for; our program and FP interventions for our patients.

O-200 | Factors Influencing the Physical Activity Levels in Hong Kong Chinese Paediatric Oncology Patients

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Background/Objectives: Despite the numerous health benefits from physical activity, there is a growing concern about physical inactivity in Hong Kong Chinese paediatric oncology patients. Before developing appropriate interventions to promote the adoption and maintenance of regular physical activity for such children, it is of paramount importance to understand the factors that influence their physical activity levels. The objective of this study was to explore the factors that affected their adoption of regular physical activity.

Design/Methods: A qualitative, phenomenological approach was employed. A total of 25 paediatric patients (9- to 18-year-olds) undergoing active cancer treatment were purposively selected for semi-structured interviews. The sample size was determined by saturation of data in repeating themes. Each interview lasted for about 30 minutes and was tape-recorded and transcribed. Content analysis was used to analyze the qualitative data.

Results: The qualitative analysis identified four themes: (1) Perceptions of physical activity, (2) Physical condition, (3) Psycho-emotional aspects and (4) Social Influences. Nearly all of them complained that physical activity interrupted with recovery process, cancer and its treatment weaken their body condition, disturb their mood and suffer from social discouragement for physical activity. The findings revealed that the patients' physical condition, misunderstanding about physical activity by children, parents and healthcare professionals, emotional disturbances and social influences are four important factors disengaging these children from physical activity during cancer treatment.

Conclusion: The study identified the factors impeding paediatric patients under cancer treatment from physical activity. This study prompted the urge to develop appropriate strategies, aiming at tackling the factors to advocate physical activity for these children to enhance their physical and psychological well-being.

O-201 | The Usage of Central Venous Access Devices to Improve the Quality Care in Children, Treated with Intensive Chemotherapy

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Background/Objectives: The treatment plan for patients with solid tumors included innovative methods of anticancer therapy, supportive treatment and high quality of nursing care.

Design/Methods: The data were collected from patients who received the treatment for solid tumors at paediatric oncological department during 2013-2015 years. A central venous access device plays an important role in the management of cancer patients. They serve not only for safe administration of chemotherapy, but also for prolonged administration of fluids, blood and blood products, antibiotics, parenteral nutrition, and frequent blood sampling. Different types of central venous access devices are associated with different patterns of complications. There are different types of venous access devices, but totally implantable venous access ports (TIVAP) are now used most commonly because of their safety, cosmetics, low infection rates, ease of implantation, and usage. A proper TIVAP not only provides secure vascular access for all patients' therapeutic needs, but can also reduce the frequency of venipuncture for the purposes of native vessel protection. In this study, 75 patients at the age from 9 months till 18 years received port implantations.

Results: However, the procedure and its subsequent maintenance are not free of side effects – 14 (27%) TIVAP were removed prematurely due to complications. We had observed complications associated with TIVAP, such as thrombosis and blockage at 11 patients (21% cases), embolization at 2 patients (4% cases), and catheter fracture at 1 patients (2% cases). We do not observed important complications, such as infections, pneumothorax, hematoma.

Conclusion: Intravenous ports are very important for children with solid tumors. The complication rate has decreased not only with improved techniques and material, but also high quality of nursing care. With increasing experience and knowledge about TIVAP care, we hope the associated complications will decrease, resulting in improved patient safety and compliance with the device.

O-202 | Implementation and Preliminary Effectiveness of a Real-Time Pain Management Smartphone App for Adolescents with Cancer: A Multicenter Pilot Clinical Study

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Background/Objectives: Pain in adolescents (12-18 years) with cancer is common and negatively impacts health-related quality of life (HRQL). We developed the *Pain Squad+* smartphone app to provide adolescents with real-time pain management support using a phased approach (i.e., systematic review, consensus conference and vetting, iterative usability testing cycles). The present study aimed to evaluate the implementation of the app for testing in a future randomized controlled trial (RCT) and to obtain treatment effect estimates for health outcomes (pain intensity, pain interference, HRQL, and self-efficacy).

Design/Methods: This single arm study recruited 33 adolescents from 2 Canadian paediatric tertiary care centers. Baseline validated health-outcome questionnaires were completed and adolescents used the app at least twice-daily for 28 days, receiving algorithm-informed self-care advice dependent on their reports of pain. A registered nurse received email alerts in response to sustained moderate to severe pain and contacted adolescents to assist in pain care. Post-study questionnaires were completed and 20 adolescents participated in audio-recorded semi-structured interviews. Descriptive analyses, with exploratory inferential testing conducted on health outcome data, were used to analyze quantitative data. Qualitative interviews were transcribed and independently coded by 2 investigators. Content analysis identified themes emerging from interviews.

Results: The app was implemented with: 75% accrual rate; 3% withdrawal rate; 18% of participants experiencing technical issues; adherence to twice daily pain reporting of 69.0±40.8%; and highly-rated intervention acceptability. Improvements in pain intensity and HRQL were significant ($p < 0.05$), with effect sizes of 0.20 to 0.69. Participants were generally satisfied with the app but also provided data that will be used to refine the intervention and study protocol prior to a RCT.

Conclusion: A user-centered approach was used to develop and establish the implementation procedures for the *Pain Squad+* app. A RCT will be undertaken to examine the impact of the app on health outcomes in adolescents with cancer pain.

NURSES: FREE PAPERS SESSION 5: INFORMATION AND COMMUNICATION FOR CHILDREN AND PARENTS

O-203 | Can Age Appropriate Information and Routines for Children with Cancer Undergoing Radiotherapy lower Children's Anxiety and Need for General Anesthesia?

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Background/Objectives: Due to separation from parents, unfamiliar equipment and the importance to keep still radiotherapy is a challenging procedure for children with cancer, implying that several require general anesthesia. The aim of this study was to investigate if age appropriate information and routines for children with cancer undergoing radiotherapy can lower their anxiety and need for general anesthesia.

Design/Methods: In a quasi-experimental controlled clinical trial (CCT) feasibility and effectiveness of age appropriate information and routines for children undergoing radiotherapy was assessed. Primary outcomes were the number fractions and children who managed radiotherapy without general anesthesia and secondary outcomes were children's anxiety, measured by self-estimated anxiety and heart rate, and emotional behavior, measured by observation. Sixteen children, 3-18 years, participated in a control group receiving traditional care and 17 children in an intervention group receiving age appropriate information and routines prior and during radiotherapy. Data was collected during the child's first three treatments, every fifth treatment and the last treatment.

Results: Preliminary results indicated that children in the intervention group showed lower anxiety, both self-estimated and observed, compared to the control group.

Conclusion: If children with cancer receive age appropriate knowledge prior and during radiotherapy it may reduce anxiety, negative emotional behavior and the need for general anesthesia which in turn results in decreased anxiety for parents and lower costs for the healthcare.

O-204 | Can Seven Year-Old Children with Cancer Understand and Report their Symptoms?

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Background/Objectives: Literature on self-report of symptoms of children < 8 years of age is limited. We used cognitive interview (CI) methodology with 7 year-old children with cancer, to determine the understanding and reporting of potential symptoms. This was part of a larger, prospective, qualitative study, namely the Pediatric Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) Initiative.

Design/Methods: Seven North American paediatric research hospitals participated. Children receiving cancer treatment were evaluated on wording of items, response options and reference period the draft version of newly developed Pediatric PRO-CTCAE questionnaires using CI methods. Two rounds of CI were performed using an iterative approach. This analysis was restricted to 7 year olds.

Results: A total of thirteen (7 female) 7 year-old children were interviewed; 8 in Round 1 and 5 in Round 2. Nine 7 year-olds required all or majority of PRO-CTCAE questions to be read out loud by the interviewer. However, only one of these 7 year-olds rated PRO-CTCAE items a "little hard to understand" with others (n=12) rating it "somewhat easy" to "very easy". A major issue of understandability was the timeframe of reporting symptoms in "the past 7 days"; only 2/13 children were able to show understanding by counting back 7 days. Generally, symptoms that had not been experienced by the child were more difficult to understand; for example, "tingly or numb hands or feet", "swollen belly", "flashing lights".

Conclusion: Our data suggest that use of this questionnaire in its current form may not be appropriate among 7 year olds due to developmental limitations in reading, understanding of time, and possibly conceptualisation of the understandability rating itself. Continued efforts to include younger children in questionnaire validation and research are critical to ensure we capture their experiences and perspectives accurately by directly including their voice.

O-205 | Children and Adolescents Tell Us How They Want to be Involved in their Treatment Decision Making, "Having A Say, as I Need at this Time"

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Background/Objectives: Involving children and adolescents in decisions about their care is identified as best practice by professional organizations and governmental agencies despite a lack of strong evidence to inform interventions to include children and the outcomes associated with doing so. Previous researchers have studied child and adolescent treatment decision making (TDM) using combinations of child, parent and/or clinician voices that were often analyzed and reported together. It is therefore difficult to distinguish unique child and adolescent TDM perspectives. We therefore conducted this study to better characterize how children and adolescents viewed their involvement in TDM.

Design/Methods: Using an interpretive qualitative design we interviewed 29 children ages 9-17 about their preferences for being involved in their cancer treatment decisions. Using constant comparison, we analyzed verbatim transcripts. Findings from the first 20 children required that we shift our conceptualizations and change interview focus to validate emergent findings of a new, broader construct- Having a Say, as I need at this time ("Having a Say").

Results: 'Having a Say' represents child communication preferences and processes that includes their need for information and treatment discussion involvement. Communication preferences were context specific and influenced more by illness conditions at the time than age. Preferences ranged from wanting to choose treatment, to inclusion in treatment discussions, to not wanting to hear information. Participants identified both positive and negative outcomes that resulted from having (or not having) their communication preferences met.

Conclusion: 'Having a Say' represents a conceptual shift in child and adolescent TDM. Their voices require us to reconsider the shared TDM paradigm. It may not always be optimal to encourage child and adolescent participation in TDM. Our findings suggest a more nuanced process that might require in the moment assessment before such inclusion.

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O-206 | The Everyday Life of Young Children Through Their Cancer Trajectory

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Background/Objectives: The young child's experiences of living with cancer are crucial to providing evidence based care. The aim of this study was to explore and describe experiences of health and functioning in the everyday life of young children with cancer, over a three year period from diagnosis.

Design/Methods: Children and parents were interviewed at four time points and questionnaire data collected at five time points over a three year period from diagnosis. A qualitative content analysis to describe the child's experiences shortly after diagnosis and six and 12 months later. Mixed methods were used to identify a comprehensive set of ICF-CY codes describing everyday health and functioning in the life of the young child with cancer. These codes were then used to follow changes in everyday health and functioning over the study's entire three year period from diagnosis.

Results: The everyday life of young children with cancer changes over time and health care services are not always in phase with these changes. Children living with cancer want to be participatory in their care and to have access to their parents as protectors. They need access to and ongoing contact with peers and preschool. Although physical difficulties in living an everyday life with cancer reduce over time, new difficulties emerge as the child post cancer treatment re-enters society.

Conclusion: The results of this study reveal emerging issues of survivorship that need to be addressed as young children learn to live an everyday life with cancer and the effects of its treatment. A structured follow-up throughout the cancer trajectory and not just during active treatment is necessary. A child-centered philosophy of care would guide the child towards attainment of health and wellbeing.

O-207 | Parents Perceptions of Their Initial Hospital Education Related to Caring for Their Child: A Report of the Children's Oncology Group

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Background/Objectives: When their child is diagnosed with cancer, parents experience overwhelming distress and uncertainty. Within this context, they must learn vast amounts of information about their child's diagnosis, treatment and care at home. Best practices for delivering this information have not yet been established. The purpose of this study was to describe parents' viewpoints on timing, content and approach to information sharing they experienced during their child's initial inpatient admission.

Design/Methods: In this qualitative study employing constant comparative analysis we interviewed 20 parents of children newly diagnosed with cancer who received their diagnosis and initial treatment as inpatients. The sample consisted of 16 mothers and 4 fathers ranging in age from 21-51. Children were diagnosed predominantly with leukaemia and non-CNS solid tumors within the past 2-12 months. Parents participated in a single, semi-structured interview in a location of their choice.

Results: Parents described receiving diagnosis and discharge information with little reciprocity or actual learning. Learning occurred between these two time-points when parents described education as more interactive and easier to assimilate. As parents moved from passive receipt of information and were able to connect information to their child's condition they were better able to process the information. Parents reported the need for consistency, opportunities for active engagement, and attention to pacing of information delivery to become competent caregivers for their child. Social support and reassuring provider communication promoted learning.

Conclusion: Opportunities for more effective teaching interventions exist during the initial inpatient stay and after discharge. Diagnosis and discharge information was more of a "telling" than reciprocal education process. Attention to timing of education, received content and preferences for learning is needed to maximize retention during this stressful time.

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NURSES: FREE PAPERS SESSION 6: ETHICAL CHALLENGES FOR PARENTS AND NURSES IN PAEDIATRIC ONCOLOGY NURSING

O-208 | What are the Current Ethical Issues Encountered by Professionals Who Care for Young People

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Background/Objectives: Healthcare professionals often encounter ethical questions in their daily practice that are challenging due to moral uncertainty and differing perspectives. Ethical conflict may occur when there is a clash of values between individuals, or within an individual, concerning which of the possible options should be chosen. We sought professionals' views on ethical issues in cancer care to present a contemporary perspective on the current ethical concerns and challenges faced by those working with young people.

Design/Methods: We used personal contact, conference proceedings and published papers to identify professionals (n=25) working internationally in young people's cancer care. We received detailed feedback from 12 individuals, in response to a list of open questions that were based on a questionnaire used by Cecilia Bartholdson and colleagues from Sweden. Using descriptive qualitative analysis, the data were grouped into four themes.

Results: The themes included: 1. stopping or not stopping when treatment is futile; 2. delaying or avoiding difficult conversations, about cancer, around poor prognosis, or end-of-life care; 3. caught between competing obligations, such as family-centred care; patient choice and shared-decision making, when faced with treatment options and place of care, access to clinical trials/research, fertility options, or when refusing treatment; 4. tensions between a professional's personal moral compass, expectations attached to their role and conflict with team members.

Conclusion: The centrality of relationships between healthcare professionals was a theme running through the comments of all of our respondents. Facilitators to this were trust, mutual respect, open dialogue, professional competence in the care of young people, and intentional collaborations with them and their family members. Barriers included understanding the shifting roles within families, professional differences within clinical teams, and the often-ambiguous interpretation of the law regarding those considered a minor (where age varies in different countries).

O-209 | Ethics Case Reflection Sessions in Childhood Cancer Care – Conditions and Obstacles

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Background/Objectives: Previous research concludes different aspects that enable a good ethics case reflection (ECR) session. Among those aspects are; a structured model for ethical analysis; a trained facilitator and a good group composition. In a previous study we found that healthcare professionals clarify their professional views on the ethical issue at hand in order to be able to consolidate their care during ECR sessions in childhood cancer care. When professional perspectives are clarified, consequences like increased understanding, group strengthening and decision grounding occur. However, conditions and obstacles for ECR sessions were also identified. Knowledge about these circumstances can help/assist the implementation and facilitation of future ECR sessions. The aim of this presentation is therefore to present conditions and obstacles during ECR sessions in childhood cancer care.

Design/Methods: Data were collected by qualitative observations and interviews with healthcare professionals to explore their experiences from ECR sessions. A total of 35 healthcare professionals participated in 6 ECR sessions, and 10 healthcare professionals were individually interviewed afterwards. Data were analysed following grounded theory methodology.

Results: Two categories emerged in data. One of them includes conditions and the other is about obstacles in ECR sessions. Each category holds three subcategories. The conditions and obstacles for clarifying perspectives during ECR sessions were: "organizational conditions"—timing, structure and an open climate, and "team feature barriers"—medical dominance, ranging ethical skills and poor familiarization with the facts.

Conclusion: Knowledge about the importance of timing, structure and an open climate during ECR sessions creates opportunities to perform well-rounded ECR sessions. Awareness of the frequent emphasis on medical issues rather than over nursing issues could reduce the somewhat biased attention and contribute to a holistic multidisciplinary dialogue. When members of the team put aside their disciplinary differences and focuses on the patient, constructive interdisciplinary work becomes easier.

O-210 | Parent Interaction Behaviors with their Child During Cancer-Related Port Starts: A Longitudinal Analysis

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Background/Objectives: Parents play critical roles in supporting their child during painful and distressing cancer-related procedures in that parent caring behaviors relieve child pain and distress. Previous studies have described parent behaviors in a cross-sectional rather than a longitudinal way and not from a caring perspective. The purpose of this study is to examine the longitudinal change in parent caring behaviors over repeated cancer-related port starts experienced by their children.

Design/Methods: This study used a longitudinal and observational design. Two coders coded 104 video-recordings of port starts from 43 children being treated for cancer; 25 children had two video-recorded port starts and 18 children had three (T₁, T₂, T₃). The Parent Caring Response Scoring System derived from Swanson's Theory of Caring was used to code parent behaviors during their children's port starts. Three 3-5 minute slices were coded for each video. Mixed modeling with generalized estimating equations was used to analyze change in parent caring behaviors from T₁ to T₃. Friedman's test was conducted to explore the median differences in parent caring behaviors from T₁ to T₃.

Results: Only a few significant differences were found with respect to change in the parent nonverbal interaction behaviors from T₁ to T₃. Significant differences were found between T₁ and T₃ in: eye contact ($\beta=-1.05$, $p=0.02$), distance-close-enough-to-touch ($\beta=-0.81$, $p=0.03$), nonverbal comforting ($\beta=-1.34$, $p=0.04$) and availability ($\beta=-0.92$, $p=0.036$), suggesting that more parents used interaction behaviors at T₃ as compared to T₁. Parent burdensome or intrusive questions ($\beta=-1.11$, $p=0.03$) and nonverbal comforting ($\beta=-1.52$, $p=0.047$) increased from T₂ to T₃. The median values of parent interaction behaviors showed no significant change from T₁ to T₃.

Conclusion: Parents adjusted to use more caring behaviors as their child experiences additional port starts. Experimental studies should be designed to help parents use caring behaviors to better support their child during painful and distressing cancer procedures.

O-211 | Using a Humanoid Robot to Reduce Procedural Pain in Children with Cancer: A Pilot Randomized Controlled Trial

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Background/Objectives: Children with cancer often cite needle insertions into a subcutaneous port (SCP) as painful and frightening, even when the skin is numbed with topical anesthetic. Our group conducted a systematic review of interventions to manage paediatric cancer-related pain. Results indicated that, especially when capitalizing on engaging electronic modalities, psychological strategies that coach children through procedures decrease pain. We have developed a program for a humanoid robot that uses interactive movements and vocalizations to coach children through SCP needle insertions. Research objectives were to assess the feasibility of implementing the robot for effectiveness testing in a future randomized controlled trial (RCT) and to collect preliminary intervention effectiveness data.

Design/Methods: A pilot RCT was conducted in a large paediatric teaching hospital. Children with cancer (4-9 years) reported pain during previous SCP needle insertion and were randomized to receive either intervention (robot using pre-programmed series of coaching behaviours before, during, and after procedure) or active control (robot moving only) during needle insertion by a nurse. Following the procedure, acceptability data were collected and children reported pain intensity during the insertion. Implementation outcomes were: outcome measure completion, technical issues, child-rated acceptability, and nurse-rated impact on clinical workflow.

Results: Eight children (3 female; mean 6.4 years) were randomized in equal numbers across groups. All outcome measures were completed. Five easily rectified technical issues occurred. All children reported maximum satisfaction with the intervention and desired the robot at next needle insertion. Nurses rated the intervention as requiring an acceptable amount of time (3.7±0.6/4.0) and minimally impacting workflow (1.0±1.0/4.0). Mean change scores in child self-reported pain from previous to current needle insertion were clinically meaningful (intervention: -2.8/10; control: -2.5/10).

Conclusion: Implementation of this study protocol into a future RCT is feasible. If effective in a RCT, this intervention may decrease the negative impacts of invasive procedures on children with cancer.

PODC: FREE PAPERS SESSION 1

O-212 | **Essential Medicines for Childhood Cancer Treatment in Low- and Middle-Income Countries: An Ethiopian Example of the Reality, Implications, and Outcomes**

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Background/Objectives: Despite WHO's Essential Medicines List (EML) for Children (EMLc) 2015 revision, most low- and middle-income countries (LMICs) have frequent significant drug and chemotherapy shortages. A 2015 survey of the more limited 18 SIOP-recommended anti-neoplastic drugs in LMICs' national EML or reimbursable medicines lists showed availability in 7 low-income countries was (median) 7/18 and, for 37 African countries, 9/18. The Aslan Project supports two new paediatric cancer programs in Ethiopia (at Tikur Anbessa Specialized Hospital (TASH) in Addis Ababa since 2012 and at Jimma University Specialized Hospital in Jimma since 2015).

Design/Methods: An initial paediatric chemotherapy inventory was conducted on the TASH unit in 1/2014 (FY starts September). Chemotherapy purchases by the Aslan-supported TASH parents' group (TAPCCO) from 10/28/2015-2/11/2016 (with funds from a third-party donor) identified recent shortages.

Results: A 2014 inventory at TASH listed 15 drugs of the SIOP-recommended 18 with 3/15 out of stock. TAPCCO records showed purchases of drugs over 3.5 months from private pharmacies (USD1312) for 40 children. The most common were cytarabine, actinomycin, leucovorin, and carboplatin.

Conclusion: The Ministry of Health (MoH) is working with the TASH paediatric oncology department to scale up essential drug availability, which has improved. Drug procurement, importation, and management costs are challenging in all LMICs, but past efforts by Aslan and current efforts by TAPCCO and another local foundation to meet government shortages can only serve as a short-term solution. Moreover, the purchase of chemotherapy from private pharmacies precludes quality controls and price regulations; it is not assured that these over-priced medicines are even viable. In May 2016, the MoH, WHO, SIOP, Childhood Cancer International, Aslan, and other key stakeholders are conducting a workshop in Jimma to strengthen the national infrastructure for childhood cancer and address the challenge of equal access to essential medicines for children with cancer across Ethiopia.

O-213 | **Setting the Stage for Improving Childhood Cancer Outcomes in the Caribbean by Establishing Local Paediatric Oncology Registries through the Sickkids-Caribbean Initiative: Lessons for other Jurisdictions**

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St Lucia; ⁶Wendy Fitzwilliam Paediatric Hospital, Paediatric Oncology, Mount Hope, Trinidad and Tobago; ⁷Princess Margaret Hospital, Paediatric Oncology, Nassau, Bahamas; ⁸Milton Cato Memorial Hospital, Paediatrics, Kingstown, St Vincent and the Grenadines; ⁹Queen Elizabeth Hospital, Paediatrics, Bridgetown, Barbados; ¹⁰The Hospital for Sick Children, Infectious Diseases, Toronto, Canada

Background/Objectives: Childhood cancer outcomes in resource constrained, such as those in the English-speaking Caribbean (ESC), remain suboptimal when compared to high-income countries. The design and implementation of interventions to improve outcomes require accurate and comprehensive data on current treatments and outcomes. The SickKids-Caribbean Initiative, a partnership between SickKids Hospital (Toronto, Canada), The University of the West Indies, and various hospitals in the ESC, established a Registry Working Group (RWG) to provide accurate demographic, disease, treatment, and outcome data on children with cancer managed at each site by establishing hospital-based paediatric oncology registries.

Design/Methods: The RWG identified a core set of data variables, and selected the online database platform REDCap™ for entering and storing data. Following ethics approval from the relevant administrative bodies in each country, Data Managers were employed at each site and centrally trained. A site-specific alphanumeric identifier code per patient allowed the creation of seven separate but related datasets. Prospective and retrospective data collection is currently underway.

Results: Functional registries now exist in seven hospitals across six countries (The Bahamas, Barbados, Jamaica, St. Lucia, St. Vincent and the Grenadines and Trinidad & Tobago), with >300 cases registered to date. Data entry of complex cases are discussed during regular meetings between Data Managers and RWG leaders allowing for continued learning, team-building, and data comparability across sites. Other keys to success include limiting the number of data variables, stakeholder buy-in, Data Managers protected time, clinician validation, and clear data security and ownership agreements. Challenges include adaptation to settings varying by resources and patient volumes while maintaining data comparability and equity.

Conclusion: The establishment of hospital-based paediatric oncology registries in the ESC now allows for collection and analysis of data critical for designing future protocols to improve childhood cancer outcomes. Our experience can help guide other jurisdictions in creating networks of site-based paediatric cancer registries.

O-214 | **Centralized Pathology Review as a Reliable Option to Achieve Better Outcome of Children and Adolescents with Brain Tumours**

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Background/Objectives: Evidence-based medicine and personalized medicine are concepts of paradigm shift in medical practice as a result of technological advances and medical knowledge. Despite enormous benefits of these medical advances, allowing better survival and cure rates, economic reality partly explains the difficulty of implementing large scale in developed countries and its introduction in low or medium-income countries like Brazil. Genetic detection methods have become faster and more efficient, however, access to this type of technology is not universal, because they have a very high cost and require highly skilled and qualified professionals.

The central pathology review was created from an initiative of non-governmental organization "Associação de crianças e adolescentes com Cancer" (TUCCA) to provide a correct diagnosis and molecular exams for paediatric neuro-oncology.

Design/Methods: A specialized pathologist was incorporated to paediatric oncology team to review all cases. Business and research projects were written to gather financial support.

Results: 450 reviews were performed, 263 were CNS tumours, 80 were medulloblastoma, 50 low grade glioma, mostly pilocytic astrocytoma (25 cases), 10 high grade glioma, 42 ependymomas, 13 glioneuronal tumours, six atypical teratoid rhabdoid tumour, three pineal tumours, three choroid plexus carcinoma, one craniopharyngeoma, four germinoma and three meningiomas. Overall concordance was low (40%) but the rate of discordance was different across type of tumours. Medulloblastoma achieved high rate of concordance (96%) although only 28% was classified according 2007 WHO classification of CNS tumours. Gliomas represented the most discordant rate (65%).

Conclusion: Diagnosis concordance was low in CNS tumours but the rate variability was high across different type of neoplasia, which medulloblastoma reached high concordance and gliomas the lowest. The most frequent CNS disease was medulloblastoma followed by low grade glioma and ependymoma. Due to low diagnosis concordance, central pathology review brings high impact to patient survival and better treatment by correct classification of the neoplasia.

O-215 | **Destitution Level of Children with Burkitt Lymphoma and Effect on Adherence to Treatment and Follow Up**

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Background/Objectives: Burkitt lymphoma (BL) is the most common childhood cancer in Cameroon. Patients receive free treatment in Bansa Baptist Hospital (BBH) in northwest Cameroon. Parental support is provided for transport (CFA 10,000 or 20 USD) and meals during their child's hospitalization. Nursing care includes tracking patient adherence to treatment and following-up. This study aims to assess the degree of patient destitution and its effects on adherence to treatment and outcome for BL.

Design/Methods: This was a prospective cohort study including BL patients less than 15 years admitted in BBH from 2010–2014. A questionnaire was administered to assess household capacity; monthly income; access to food and basic commodities; and dependence on support from others for daily living. A destitution score was awarded on a scale of 1 to 10. Data was analyzed with IBM SPSS Version 21. Pearson's coefficient and Chi-square were used to assess correlations and associations.

Results: Of 140 respondents, 59% were male, and the mean age was 8.54 years. The majority (69%) were farmers, and 80% had a monthly revenue of less than CFA50,000 (USD 100). The mean social destitution score was 5.61 (SD 0.957). A 93% of the children completed chemotherapy, although 17% were delayed for their chemotherapy at least once. Over half (59%) were alive at the end of 2014, and 62% came for regular follow-up visits. There was no correlation between destitution score and adherence to chemotherapy schedules ($p=0.2$), nor remission ($p=0.2$). There was a significant inverse correlation between destitution score and post-treatment follow-up visits ($p=0.02$).

Conclusion: Adherence to treatment is appropriate, even when parents are destitute (93%). We believe this is probably due to financial support for transport and meals. A low destitution score may indicate which patients may abscond from follow-up visits. This may be attributable to a lack of access to transportation funding post treatment.

PODC: FREE PAPERS SESSION 2

O-216 | Cure4Kids Oncopedia: Review of An Interactive Educational Web Resource for Paediatric Oncology

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Background/Objectives: Cure4Kids.org is the leading web-based educational resource for paediatric oncology with more than 33,000 users worldwide. With the aim of enhancing its user interactive features, Cure4Kids launched Oncopedia in 2007.

Design/Methods: The Oncopedia section of Cure4Kids includes peer-reviewed, user-submitted interactive educational content on paediatric malignant neoplasms and hematological disorders. An international editorial board reviews and selects all Oncopedia published content and is responsible for posting relevant comments and moderating online discussions. A review of its content was performed, and usage preferences were analyzed. Data were obtained from the Cure4kids server.

Results: Oncopedia includes a variety of content formats: complex cases and images with specific open questions about patient management ($n=372$), polls about controversial topics ($n=73$), illustrative clinical, radiological, and histological images ($n=138$), disease-specific chapters ($n=73$), as well as links to selected full text publications from *Paediatric Blood and Cancer* (PBC). A dedicated section for nursing content was launched in 2010. Approximately 90% of the content is posted in English and the remaining in other languages (Spanish, Portuguese, and Arabic, among others); however, two of the top 20 most frequent accessed items were posted in languages other than English. As of March 31, 2016, Oncopedia content available on Cure4Kids was viewed 120,018 times by 12,605 unique users from 160 countries, and 713 unique users posted a total of 2,302 comments. One hundred forty six PBC publications were accessed 20,684 times. The top five countries in terms of usage of Oncopedia, were Mexico, Brazil, Argentina, United States, and Spain.

Conclusion: Cure4Kids Oncopedia is an interactive educational resource for paediatric haematology and oncology health care professionals. Use of Oncopedia content is more prevalent in Latin America and the USA. Multilingual content, while limited, is frequently accessed and should be expanded.

O-217 | The SIOP Africa /PODC Collaborative Wilms Tumour Project – Making Progress

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Background/Objectives: The Collaborative Wilms Tumour (WT) Africa Project is implementing a published consensus adapted WT treatment guideline in Malawi, Cameroon, Ghana, Zimbabwe and Ethiopia. A baseline evaluation of outcome was done in participating centres for children diagnosed in 2011 and 2012. Mean survival of 176 children at the end of treat-

ment was 39%; a quarter (26%) died during treatment and 31% did not complete ('abandoned') treatment. Treatment costs were considered an important cause of incomplete treatment. Overall 2-year survival was estimated at 25% based on the relapse rate after completion of treatment of children with a Wilms tumour in Malawi. The aim of the collaborative project is to reduce both incomplete treatment and death during treatment to below 10% and to increase 2-year survival to 50%.

Design/Methods: All participating centres obtained local IRB approval and implemented the adapted WT treatment guideline. The Collaborative helps fund treatment and associated costs such as travel to prevent abandonment.

Results: Patient enrolment started in 2014 and 108 patients have ended treatment. Eleven (10%) were misdiagnosed at admission; five of whom had a Burkitt lymphoma. Of the remaining 97 patients, 64 (66%) were alive and well at completion of treatment, 14 (14%) had abandoned treatment, 13 (13%) died during treatment, four children (4%) had unresectable disease and one (1%) had progression of disease during treatment. One child died during postoperative chemotherapy of another cause. Overall 2-year survival is estimated at 40–50%.

Conclusion: Relatively simple and low cost interventions have led to a significant increase of 27% of survival at the end of treatment with an estimated increase in 2-year survival of 15–25%.

O-218 | Impact of Integrated Services and Neoadjuvant Chemotherapy in Reducing Abandonment in Retinoblastoma

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Background/Objectives: Abandonment in patients with retinoblastoma is the highest amongst all childhood cancers. Availability of comprehensive care under one roof is associated with better compliance. Neoadjuvant chemotherapy may improve the acceptance for enucleation in our country.

Design/Methods: Records of all patients of retinoblastoma presenting at Dr Shroff's Charity Eye hospital, New Delhi between January 2010 and July 2015 were reviewed. Pediatric oncology services were introduced at the center in July 2014. Data on demography, treatment given, abandonment and outcomes was collated. The main outcome measures assessed were effect of integrated treatment at a single-center and impact of neoadjuvant chemotherapy in improving acceptance for enucleation.

Results: Medical records of 112 patients who presented in this period were analyzed. Of these, 24 patients were lost to follow up after the initial consultation or partial therapy. Of the 88 patients 30 were girls and the mean age was 2 years. Bilateral disease was seen in 34% and 65% had group E disease. Over half of the patients abandoned treatments before integrated services were provided at the center. This reduced to 10% after chemotherapy services could be provided on site. Six of the 10 patients (60%) who were advised primary enucleation in the initial phase refused surgery and were lost to follow while only 2 of the 26 patients (7.6%) who received neoadjuvant chemotherapy refused surgery.

Conclusion: The presence of comprehensive care under one roof in patients with retinoblastoma is associated with better compliance to treatment. Giving neoadjuvant chemotherapy is associated with better acceptance for enucleation as a treatment modality. The concerns regarding downstaging of disease leading to possible reduction in adjuvant treatment need to be balanced against the very high risk of abandonment in this disease in our setting.

O-219 | Factors Influencing Time to Diagnosis and Treatment among Paediatric Oncology Patients in Kenya

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Background/Objectives: Early diagnosis and start of treatment are fundamental goals in cancer care. This study determines the time lag and the factors that influence the time to diagnosis and start of treatment.

Design/Methods: Study participants were parents of childhood cancer patients diagnosed between August 2013 and July 2014 in a hospital in Kenya. Patient, physician, diagnosis, treatment, health-care system and total delay were explored using a questionnaire. Demographic and medical data was collected from the patients' medical records.

Results: Parents of 99 childhood cancer patients were interviewed (response rate 80%). Median total delay was 102 (9–1021) days. Median patient delay (4 days) was significantly shorter than health-care system delay (87 days) ($P<0.001$). Diagnosis delay (94 days) was significantly longer than treatment delay (6) ($P<0.001$). Lack of health-insurance at diagnosis and use of alternative medicine before attending conventional health services were associated with a significantly longer patient delay ($P=0.041$, $P=0.017$ respectively). The type of cancer had a significant effect on treatment delay ($P=0.020$). The type of health facility attended affected only patient delay ($P=0.03$). Gender, age at diagnosis, stage of disease, parents' education level or income, and distance from hospital did not have a significant effect on the length of any type of delay.

Conclusion: Training on childhood cancer should be included in the curricula for medical training institutes. In service workshops should be held for the health workers already working. Families must be obligated to get health insurance. Families should be encouraged to attend conventional health facilities and informed on symptoms of cancer through mass media.

PPO: HELP FOR THE PARENTS IS HELP FOR THE CHILDREN

O-220 | A Preliminary Examination of the Relationship between Parental Illness Uncertainty and Child-Reported Procedural and Treatment Anxiety

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Background/Objectives: Children with cancer undergo potentially painful and distressing procedures and treatments that may elicit anxiety for themselves, their parents, and their treatment team. The extant research supports the use of systemic interventions to target paediatric procedural and treatment anxiety. A relevant construct for targeting a child's procedural and treatment-related distress, is parental illness uncertainty, or the cognitive experience comprised of the ambiguity and lack of information, clarity, and predictability related to having a child with a chronic illness. Parental illness uncertainty has been associated with negative psychological adjustment outcomes for both children with chronic illnesses (e.g., depressive symptoms) and their parents (e.g., posttraumatic stress symptoms). Given the association between parental illness uncertainty and child adjustment outcomes, the current study examined the relationship between parental illness uncertainty and child-reported procedural and treatment anxiety in children age 7-16 years with a new (<6 months) cancer diagnosis.

Design/Methods: Twenty parents ($M_{\text{age}}=39.90$ years, $SD=8.79$) of children with cancer ($N=20$; $M_{\text{age}}=12.85$, $SD=2.76$ years) completed measures of illness uncertainty (Parental Perceptions of Illness Uncertainty). Children completed measures of procedural and treatment anxiety (Pediatric Quality of Life Inventory-Cancer). Participants completed measures as part of an ongoing, clinic-based study examining adjustment in children with newly diagnosed cancer and their parents.

Results: Parental illness uncertainty significantly predicted child-reported procedural anxiety ($\beta=-1.27$, $p=.03$), and explained 28.6% ($F(1,15)=6.01$, $p=.03$) of the variance associated with procedural anxiety. Additionally, illness uncertainty was a significant predictor of treatment anxiety ($\beta=-.87$, $p=.01$), explaining 34.4% of the variance ($F(1,15)=7.88$, $p=.01$).

Conclusion: Child adjustment outcomes have been consistently linked to parental adjustment, both in the general population and within paediatric chronic illness populations. Our preliminary results support this assumption and indicate that clinical interventions targeting parental illness uncertainty may function to decrease children's anxiety about their cancer-related procedures and treatments.

O-221 | Parental Contributions to Children's Coping and Involuntary Responses to Cancer-Related Stress During the Year Following Diagnosis

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Background/Objectives: Childhood cancer is a significant source of stress for children and families. Children's coping with cancer-related stress is a key predictor of emotional adjustment, but the determinants of children's coping are relatively unknown. This study examined parental contributions to children's responses to cancer-related stress (RTS), including children's volitional coping efforts and stress reactivity (i.e., involuntary stress responses). Parents' RTS and emotional distress were examined as predictors of children's RTS over time.

Design/Methods: Participants included 159 children (10-18 years-old; $M_{\text{age}}=13.56$, $SD=2.41$; 48% male) recently diagnosed with new (90.6%) or relapsed cancer and their mothers ($n=151$) and fathers ($n=79$). Diagnoses included lymphoma (34.6%), leukaemia (32.1%), brain tumour (4.4%) and other solid tumors (28.9%). Approximately two months post-diagnosis (T1), parents reported their depressive symptoms and RTS, including primary control coping (e.g., problem-solving), secondary control coping (e.g., cognitive-restructuring, acceptance), disengagement coping (e.g., avoidance), involuntary engagement responses (e.g., rumination, physiological and emotional arousal), and involuntary disengagement responses (e.g., emotional numbing, withdrawal). Children reported their RTS near diagnosis (T1) and one year later (T2).

Results: Parents' RTS and depressive symptoms were concurrently and prospectively associated with children's RTS. Over time, mothers' secondary control coping predicted decreases in children's involuntary engagement responses, whereas mothers' involuntary disengagement responses and depressive symptoms predicted increases in children's involuntary engagement responses. Fathers' secondary control coping predicted increases in children's secondary control coping and decreases in involuntary engagement responses. Fathers' disengagement coping predicted increases in children's involuntary disengagement responses. Fathers' depressive symptoms also predicted decreases in children's secondary control coping and increases in involuntary engagement responses.

Conclusion: Parents' functioning soon after their child's cancer diagnosis may shape how children cope with cancer-related stress and their stress reactivity (i.e., involuntary stress responses) over time. Parents' RTS and emotional distress may be important targets for interventions aiming to promote better adjustment in children with cancer.

O-222 | The Effects of Maternal Parenting Behaviors on Siblings' Coping and Adjustment Following A Child's Death from Cancer

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Background/Objectives: The death of a child from cancer is one of the most traumatic experiences a family can endure. As a result, parents may be overwhelmed by grief and unable to provide adequate emotional support to surviving siblings who are also coping with the loss. Research has indicated that supportive parenting behaviors are associated with adaptive coping strategies in adolescents. Therefore, we hypothesized that bereaved siblings would report more symptoms of depression relative to controls and that this difference would be partially explained by maternal parenting behaviors and sibling coping strategies.

Design/Methods: Bereaved families ($n=55$) were recruited from three paediatric hospitals following a child's death from cancer. Controls ($n=57$) were recruited from the classrooms of bereaved siblings and matched by gender, age, and race. Approximately 1 year post-death (T1), adolescents reported on their mothers' parenting (warmth, behavioral/psychological control). Two years post-death (T2), adolescents reported on their coping (primary control, secondary control, and disengagement) and symptoms of depression. Double mediation models evaluated the indirect effect of group status (bereaved vs. control) on sibling symptoms of depression via maternal parenting and sibling coping.

Results: Compared to controls, bereaved siblings rated mothers as less warm ($p=0.01$, $d=0.49$) at T1, but there were no significant differences for behavioral or psychological control. At T2, bereaved siblings endorsed significantly more symptoms of depression ($p=0.02$, $d=0.46$) than controls. Models indicated that there were significant indirect effects of group status on sibling symptoms of depression via lower maternal warmth and lower primary control (95% bias-corrected CI: 0.11-1.22), lower secondary control (CI: 0.05-1.00), and higher disengagement (CI: 0.04-1.15) coping.

Conclusion: Maternal parenting behaviors following a child's death from cancer may shape how surviving siblings cope, thereby affecting sibling adjustment. These findings underline the need for family-based interventions that can simultaneously target child and parent behaviors to promote family well-being.

O-223 | Implications of Barriers to Care and Illness Uncertainty in Parents of Children Newly Diagnosed with Cancer

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Background/Objectives: Parents of children newly diagnosed with cancer are faced with many new problems and stressors. Not surprisingly, this group of parents, on average, display higher levels of psychological distress compared to their peers. These parents face many novel challenges and multiple obstacles in navigating health care systems, learning to advocate for their child, and coping with the many uncertain implications of having a sick child. The present study aims to assess the relationships between parent-encountered barriers to care, their perceived uncertainty associated with their child's illness and its treatment, and psychological distress.

Design/Methods: As part of an ongoing study, 35 parents of children newly diagnosed with cancer ($M_{\text{age}}=37.76$ $SD=8.94$ years) completed a demographics questionnaire, Barriers to Care (BTC) Questionnaire ($M=87.21$, $SD=13.21$), Parent Perception of Uncertainty scale (PPUS; $M=69.09$, $SD=15.20$), and Brief Symptom Inventory (Global Severity Index was used: $M=.69$, $SD=.69$).

Results: Bootstrapped (to 5000) regression analyses revealed that BTC had an indirect relationship with parent psychological distress through increased PPUS, point estimate = $-.19$, 95% CI $[-.37, -.07]$, $\kappa^2 = .19$. There was no direct effect of BTC on parental psychological distress when controlling for PPUS, point estimate = $-.01$, 95% CI $[-.03, .02]$. The indirect effect accounted for 29% of parent's psychological distress variance.

Conclusion: BTC can be detrimental to the emotional health of parents of children newly diagnosed with cancer through its impact on their perceptions of illness uncertainty, and thus creating increased susceptibility for parental psychological distress. PPUS, an established predictor of many negative psychosocial outcomes, frequently heightens as illnesses become more severe. Although little can be done to target uncertainty resulting from disease severity, further analyses of BTC could inform the development of resources or accommodations which could target uncertainty in domains where control may be more likely (e.g., daily management, developing compensatory strategies around illness demands).

PPO: THE IMPORTANCE OF INTERVENTIONS

O-224 | Supporting Adolescent Oncology Patients: A Multidisciplinary Development Focused Perspective

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Background/Objectives: Background: In the Netherlands yearly around 550 children are diagnosed with cancer. From 2018 onward care will be centralized in one national center: the Princess Máxima Center for paediatric oncology. In anticipation of the opening of this new hospital, part of the Dutch patients are already treated in one hospital. In the center a developmental approach will be guiding all professionals involved in working with the children and their families. The focus on stimulating development is leading in care, part of psychosocial research and visible in the composition of the building. Key principles are reduction of medical traumatic stress, adequate communication and having a family focus. A quarter of diagnosed children are adolescents aged between 12-18 years. Adolescents present with unique challenges in the provision of care. Balancing between developmental needs and treatment related demands calls for a careful and tailored vision of provided support.

Design/Methods: Design/methods: Synthesizing current scientific knowledge, available best practice and stakeholder perspectives (patients, parents, health care providers and the national parent organization) in order to develop a program for adolescents.

Results: Results: An evidence based multidisciplinary informed program that supports adolescents and their parents during active treatment is being developed. Development on all domains (physical, emotional, social, cognitive, spiritual) is a central focus. Recognizing the adolescent's developmental stage and need for autonomy is important. Adjusting the physical environment of the building to represent the developmental focus is a unique addition to the support for adolescents. Examples of stakeholder perspectives, the incorporation of these perspectives in the provided support and plans for the future will be shown.

Conclusion: Conclusion: Adolescents have special developmental needs that can be supported by the program to optimize care in active treatment. Next step in the development is to evaluate the program in order to gain insight in clinical significant benefits.

O-225 | Further Development and Implementation of An Online Cognitive-Behavioral Intervention: On Track (Op Koers) in Paediatric Oncology

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Background/Objectives: In the Netherlands each year around 550 children are diagnosed with cancer. From 2018 onward care will be centralized in one national center: the Princess Máxima Center for paediatric oncology. In anticipation of the opening of this new hospital part of the Dutch patients are already treated in one hospital. In the center a developmental approach will be guiding all professionals involved in working with the children and their families. The focus on stimulating development is leading in care, part of psychosocial research and visible in the composition of the building. Key principles are reduction of medical traumatic stress, adequate communication and having a family focus.

Design/Methods: On Track (Op Koers in Dutch) is a group intervention that teaches coping skills using a cognitive-behavioral approach and has shown to have positive effects on psychosocial outcomes for children with chronic illness (CI) and childhood cancer (CC) survivors. Because of limited accessibility, the face-to-face version for children with CI and CC survivors was transformed into an online chat format (OK online).

Results: In the Princess Máxima Center, we are currently implementing OK online for CC survivors. Furthermore, we adapted the content and themes of OK online to be appropriate for siblings of CC patients/survivors. Since a CC experience can also be very stressful for parents, we are working on the development of a chat-course for parents. Besides these courses, we are exploring the possibility of developing separate modules for children with CC during treatment, for children in transition to high school and a course about the effects of dexamethasone for parents.

Conclusion: By empowering patients in their development and by also focusing on their parents and siblings, these interventions contribute to the mission of the Princess Máxima Center. We will investigate whether these interventions contribute to the development of children with CC and their families.

O-226 | Using A Developmental Approach in Paediatric Cancer Care: Implementing Patient-Reported Outcomes in Clinical Practice—The KLIK Method

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Background/Objectives: In the Netherlands yearly around 550 children are diagnosed with cancer. From 2018 onward care will be centralized in one national center: the Princess Máxima Center for paediatric oncology. In anticipation of the opening of this new hospital, part of the Dutch patients are already treated in one hospital. In the center a developmental approach will be guiding all professionals involved in working with the children and their families. The focus on stimulating development is leading in care, part of psychosocial research and visible in the composition of the building. Key principles are reduction of medical traumatic stress, adequate communication and having a family focus. A method to support systematic attention for children's development is KLIK (Dutch acronym for 'Quality of Life in Clinical Practice').

Design/Methods: KLIK is an effective method to monitor electronic patient-reported outcome measures (ePROMs). Before outpatient consultations, patients (aged 8-18 years) or parents (of patients aged 0-7 years): (1) register on the website and (2) complete physical/psychosocial ePROMs via www.hetklikeit.nu. Outcomes are being transformed into an eProfile and (3) discussed during the consultation with their healthcare professional.

Results: In June 2015 we started to implement KLIK as part of standard care in the newly formed Princess Máxima Center for paediatric oncology. Since then, 110 families (44%) registered on the website. In 74% of the cases ePROMs were completed before the consultation. In 56% of the cases, healthcare professionals explicitly referred to discussed eProfiles in the electronic record.

Conclusion: The KLIK method is an innovative and supportive tool in monitoring psychosocial consequences, which has been defined as a standard of care. The implementation shows positive results so far. Ongoing efforts and adaptations should be provided for a complete integration in the routine process of care and to overcome barriers for systematic implementation.

O-227 | Feasibility, Acceptability and Preliminary Efficacy of a Computerized Cognitive Training Program in Survivors of Paediatric Brain Tumors

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Background/Objectives: Survivors of paediatric brain tumors (SPBT) are at risk for attention and working memory deficits. *CogmedRM*, a computerized working memory intervention, has demonstrated promising results, primarily in survivors of childhood leukaemia. The present study evaluated the feasibility, acceptability and preliminary efficacy of *CogmedRM* in SPBT with working memory deficits.

Design/Methods: Potentially eligible SPBT (N=136), at least two years off treatment, were recruited. Fifty-one were never reached and 44 declined participation; 17 had no identified working memory deficits, resulting in a final sample of 24 SPBT (aged 7-15; M=10.9, SD=2.6). SPBT were scheduled to complete 25 *CogmedRM* sessions over 35 days, accompanied by weekly coaching calls.

Results: Thirteen participants (54.2%) completed all 25 sessions over 31-79 days (M=48.2, SD=12.8). Non-completers attempted 0-19 sessions (M=7.9; SD=7.6) over 49.6 days (SD=32.9) with 3 not completing any sessions. Non-completers had lower auditory attention abilities and more parent-reported working memory problems at baseline (t 's = -2.14 and 2.20 respectively, $p < .05$). Parents of completers were more likely to be employed (77% v. 36.4%) and have a household income over \$50,000 (75% v. 54.5%). Parents of completers endorsed survivor training-related boredom (69.2%) and frustration (100%) yet noted feeling very satisfied with training (76.9%) and survivors enjoying sessions (74.6%).

In paired samples t -tests, completers showed improvements in visual attention ($t = -5.86$, $p < .01$) and visual working memory ($t = -2.50$, $p < .05$) but not auditory working memory at immediate follow-up. Additionally, completers had significant improvements in parent-rated attention problems ($t = 3.37$, $p < .01$) and metacognitive abilities ($t = 2.37$, $p < .05$).

Conclusion: *CogmedRM* shows promise for SPBT with fewer attention and working memory problems with improvements primarily in visual working memory. Feasibility may be a barrier to the intervention for those with greater deficits or less family resources.

O-228 | Design and Rationale for Reboot Kids: A Parent-Targeted Behavioural Intervention to Promote Healthy Eating Habits in Children Recently off Cancer Treatment

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Background/Objectives: Childhood cancer survivors (CCS) are at higher risk of cardiovascular complications because of their cancer treatment. Despite these risks, CCS have poor dietary habits and a high proportion are overweight (29% to 69%). To overcome the limited availability of interventions targeting healthy eating habits in CCS, we have developed an evidence-based behavioural intervention for this at-risk group. The intervention's primary aims are to investigate whether a behavioural intervention i) is acceptable to parents of CCS, ii) is feasible to deliver, and iii) can increase fruit and vegetable (fv) intake in CCS.

Design/Methods: Parents of CCS aged between 2-12 years and less than 5 years off cancer treatment will be recruited at Sydney Children's Hospital, Australia. The intervention will include four weekly 45-minute sessions and a three-month booster session for parents, delivered by a psychologist via telephone. Sessions will focus on factors associated with increased fv intake in children including: (1) parent providing of fv (2) parent role modelling of fv, (3) home availability of ready-to-eat fv and (4) positive family eating routines. To support behaviour change, skills-based training for self-monitoring; goal setting; problem solving and gaining social support will be provided.

Results: We will assess the feasibility and acceptability of the intervention, parent attrition and parent satisfaction. A validated dietary questionnaire will examine changes in CCS fv intake.

Conclusion: A feasible and evidence-based parent intervention has the potential to reduce CCS risk of developing life threatening cardiovascular complications into survivorship.

O-229 | The Use of a Fitbit Intervention to Increase Physical Activity among Children and Adolescent Paediatric Cancer Survivors: An N-Of-1 Randomized Controlled Trial

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Background/Objectives: Although physical activity (PA) has been identified as improving health-related outcomes in paediatric cancer survivors (PCSs). Due to potential benefits, the American Cancer Society (ACS) recommends PCSs engage in 60 minutes of moderate to vigorous PA (MVPA) daily. Unfortunately, this population continues to engage in lower rates of PA than healthy peers. Interventions using FitBit devices have improved rates of PA among adults, but result have been mixed among children and adolescents. Furthermore, there are no studies examining the use of FitBits to improve PA among children and adolescents who are also PCSs. The purpose of this pilot study was to assess the use of a FitBit Flex™ as a low-intensity, low-cost PA intervention in PCSs.

Design/Methods: Utilizing a N-of-1 study design, 12 PCSs ($M_{age} = 13.91$; $SD = 1.92$) and one of their parents ($M_{age} = 42.36$; $SD = 6.31$) were randomized by day for 30 days to wear or not wear the FitBit Flex™. Randomization was completed through daily text-messages. MVPA was measured using actigraphy.

Results: Multiple degree-of-freedom F -tests revealed no intervention effect, $F(11,263) = 0.77$, $p = 0.67$. Results indicated no difference in minutes of MVPA from intervention ($M = 22.63$; $SD = 25.27$) to control days ($M = 21.02$; $SD = 21.67$).

Conclusion: This pilot study found that this low-intensity, low-cost FitBit Flex™ intervention did not impact rates of MVPA. Similar research among children diagnosed with Acute Lymphoblastic Leukaemia showed nonsignificant changes in PA. Unfortunately, participants did not meet the ACS PA guidelines of engaging in at least 60 minutes of MVPA daily. These findings are consistent with previous literature suggesting that approximately 50 percent of PCSs do not meet these guidelines. Future research should examine the use of low-intensity interventions such as this within the context of larger group and family-based health promotion interventions.

PPO: THE QUALITY OF MARITAL, PARENT-CHILD AND SIBLING RELATIONSHIPS WHEN A CHILD IS DIAGNOSED WITH CANCER

O-230 | Longitudinal Patterns of Marital, Parent-Child and Sibling Conflict in the First Year after a Child's Diagnosis of Cancer

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Background/Objectives: When a child is diagnosed with cancer, some families may experience considerable conflict as they renegotiate roles and make health care decisions. In normative populations, family conflict predicts child maladjustment. Yet, little is known about the degree and trajectory of family conflict following a child's diagnosis of cancer. In this study, we describe marital, parent-child and sibling conflict in the first year after diagnosis. We examined: (1) monthly levels of marital, parent-child and sibling conflict, (2) the number of families showing high conflict in each family subsystem at each time point, (3) key time points when families are at greatest risk for family conflict and (4) the trajectory of conflict across the first year of treatment.

Design/Methods: One hundred and sixty families with a 2-10 year old child newly diagnosed with any form of cancer or CNS tumour were enrolled ($M_{age} = 5.6$ years, 51% female). Primary caregivers completed monthly measures of marital, parent-child and sibling conflict in the 12 months post-diagnosis.

Results: Most couples were happily married. However, 18% of couples were in the maritally distressed range at Months 1, 2, 5 & 6. Marital adjustment remained stable over time. Parent-child conflict was relatively low on average. The greatest proportion of families (22.7%) reported high parent-child conflict at Months 5 & 6. Average level of sibling conflict was comparable to normative samples and increased over time. The greatest proportion of families (10.5%) reported high sibling conflict at Months 5 & 6. Growth models indicated considerable variability in starting points and rates of change in all aspects of family conflict.

Conclusion: Most families show low and stable levels of family conflict. A significant subset show (1) marital distress around diagnosis and at Months 5 & 6, and (2) parent-child conflict and sibling conflict at Months 5 & 6. Sibling conflict increased over time.

O-231 | Understanding the Perceived Influence of Childhood Cancer on the Parents' Relationship

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Background/Objectives: From the time a child is suspected of having cancer, parents are often faced with disruptions in daily routines and family life, including changing caregiver or spousal roles, threats to employment and financial strain, and emotional challenges that can significantly impact the cancer experience and the parents' relationship. This study objectives are to 1) explore how having a child with cancer impacts the quality of the parents' relationship; 2) describe the time points and events during the child's treatment when the relationship becomes most stressed and/or strengthened; 3) identify factors that help couples remain emotionally engaged throughout their child's cancer treatment; and 4) assess interest in interventions.

Design/Methods: This is a cross sectional, multi-center, mixed method study conducted via a semi-structured self-administered interview questionnaire that included The Revised Dyadic Adjustment Scale.

Results: 192 parents of children diagnosed between the ages of 1-21 participated (96% response rate). Over half of relationships reported as challenged. Over 40% felt their relationship moving in a negative direction. Relationship status before diagnosis predicted the relationship status after diagnosis. Diagnosis and relapse of disease were cited as the most stressful time points in the disease trajectory with hospitalizations and relapse most stressful to the relationship. Diagnosis was reported as the time participants felt most emotionally connected, with start of treatment and end-of-treatment the least emotionally connected. The majority of couples may be interested in counseling to address ways to support a marriage after the child's cancer diagnosis. Soon after diagnosis and during treatment appears to be the preferred time to administer these interventions.

Conclusion: This study identified specific events and partner behaviors that strengthen the couple's relationship during the childhood cancer trajectory that will inform the development of a couples intervention. Prospective research is needed to better understand how childhood cancer impacts caregiver's partnerships through survivorship and beyond.

O-232 | Stress and Sibling Conflict During Paediatric Cancer Treatment

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Background/Objectives: Sibling relationships can provide support for children undergoing challenging life experiences such as the diagnosis of cancer. However, little is understood about the effect of cancer on the sibling relationship. We examined the effect of stress on sibling conflict during the first year of paediatric cancer treatment. Four dimensions of stress were examined: cancer-related stress, general life stress, financial stress, and life threat/treatment intensity.

Design/Methods: Participating families ($N = 119$) had a 2-10-year-old child recently diagnosed with cancer ($M = 5.6$ years, 49% male) with at least 1 sibling. Primary caregivers completed monthly questionnaires through the first 12 months of treatment assessing sibling conflict and the four dimensions of stress. Using multilevel modeling, we explored the effects of stress on sibling conflict both at the within- and between-family levels to examine if changes in stress resulted in concurrent changes in conflict within an individual family, and whether greater average stress affected the trajectory of conflict across families.

Results: Three of the 4 stress predictors (cancer-related stressors, general life stressors, and financial stress) were associated with sibling conflict at the between-families level such that higher stress relative to the rest of the sample was associated with greater sibling conflict at the end of the first year of treatment. Financial stress was also associated with conflict at the within-families level such that an increase in financial stress from a family's typical level was associated with an increase in conflict concurrently.

Conclusion: Stress during cancer treatment may spill over into family relationships and contribute to increases in sibling conflict. Financial stress in particular may have both immediate and longer-term effects on siblings. Potential mechanisms through which stress affects the family will be discussed, as well as suggestions regarding interventions to promote positive sibling relationships during cancer treatment.

O-233 | Parent and Family Factors Associated with the Adjustment of Bereaved Siblings Over Time

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Background/Objectives: A child's death from cancer can place surviving parents and siblings at risk for many negative outcomes, including internalizing problems and disrupted family processes. However, little is known about the specific mechanisms by which poor adjustment is transmitted between family members. We hypothesized that bereaved siblings would experience greater internalizing problems than comparison peers and that this difference would be partially explained by parents' internalizing problems and the quality of parent-child communication and support.

Design/Methods: Following a child's death from cancer, families with a surviving sibling ($n=51$) and matched comparison families ($n=51$) were recruited from three institutions in the U.S. and Canada. Mothers and fathers reported on their own internalizing problems (Adult Self-Report) 1 year post-death (T1), while children reported on openness and problems in parent-child communication (Parent-Adolescent Communication Scale), social support from parents (Social Support Scale for Children), and internalizing problems (Youth Self-Report) 2 years post-death (T2). Sequential mediation models tested indirect effects of bereavement on sibling internalizing problems via parent internalizing problems and parent-child communication/support.

Results: Relative to comparison families, bereaved mothers, but not fathers, reported higher internalizing problems at T1 ($p=0.038$, $d=0.42$). At T2, bereaved siblings rated communication with mothers as less open ($p=0.021$, $d=0.47$) and reported higher internalizing problems ($p=0.028$, $d=0.44$) than comparison peers. Sequential mediation models found significant indirect effects of bereavement status on sibling internalizing problems via higher mother internalizing problems in combination with lower maternal open communication (CI: 0.05-1.28) and lower social support from parents (CI: 0.05-1.21).

Conclusion: Longitudinal data supported that poor sibling adjustment following a child's death from cancer can be explained in part by poor maternal adjustment which may impair open family communication and support. Considering this cascading impact of mothers' adjustment on siblings, it is critical that paediatric providers address maternal and family factors to enhance sibling well-being.

PPO: DEVELOPING PROGRAMS IN DEVELOPING COUNTRIES

O-234 | Stigma and Reactions of Family Caregivers to Childhood Cancers

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Background/Objectives: Family caregivers play significant roles in decisions to seek treatment and care of children with cancers. However, little is known on how their view of the cancer impacts on their treatment-related decisions and emotional well being. This study aimed to investigate Stigma and reactions to childhood cancers and their relationship with distress among family caregivers.

Design/Methods: A total of 65 adult family caregivers who consented were interviewed with a questionnaire designed to collect data on socio-demographic and treatment data, Psychological distress using General Health Questionnaire version 12 [GHQ-12], caregivers stigma and their reactions to the child's cancer. Data were analyzed using SPSS-20.

Results: The mean age of the participants was 37(±3.0) years, and were predominantly 53 (81.5%) made up of mothers. The mean age of the children was 6(±2) years and largely males 40(61.5%). Twenty (30.7%) family caregivers had significant psychological distress as they scored above the GHQ-12 cut-off score of three. The stigma score was positively correlated with psychological distress and duration of illness ($p < 0.05$). Again, those with behavioral reactions (that include denial, shock, depression, anger) to the children's cancers were more likely to report morbid distress, use alternative methods of treatment and report higher mean scores on the stigma scale in comparison with those who reported acceptance ($p < 0.05$).

Conclusion: Our study suggests that stigma and certain negative behavioral reactions may constitute explanatory factors for experience of psychosocial distress and poor treatment decisions among family caregivers of children with cancer. Psychosocial support, anti-cancer stigma strategy and improved public awareness may be potentially beneficial in paediatric cancers.

O-235 | Exploring Factors Influencing Health-Seeking Decisions and Retention in Childhood Cancer Treatment Programmes: Perspectives of Parents in Ghana

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Background/Objectives: Developing countries such as Ghana have very poor childhood cancer survival rates. There is a need to determine reasons for late presentation and treatment abandonment which are major causes of poor survival. Understanding these issues could inform effective strategies for childhood cancer control in resource constrained settings. The aim of this study was to explore factors influencing parental decision-making for children with cancer in Ghana, a low, middle income (LMIC) country, with regard to health seeking and retention in treatment, in order to provide information that will guide Public Health interventions for childhood cancer control.

Design/Methods: This exploratory qualitative study was conducted based on an interpretative epistemology using a social constructionist approach. Purposive sampling of parents attending the Paediatric Oncology Unit, Korle Bu Teaching Hospital in Accra, Ghana was undertaken. Twelve semi-structured moderate interviews and two small focus group discussions with a total of seven participants were undertaken. Data analysis was through thematic content analysis.

Results: Five major themes emerged. Knowledge and perceptions revealed a total lack of appropriate knowledge prior to diagnosis. Health-seeking behaviour was determined by interplay of individual and environmental factors. Orthodox medical treatment was largely perceived favourably. The impact of cancer on parents and children included psychological, physical and socioeconomic effects. Financial, spiritual and psychosocial support helped in coping. Parents recommended public education and health financing to address the major barriers.

Conclusion: Broad social determinants and experiences influence parental decision making for children with cancer. This implies health promotion strategies with multi-sectorial involvement will be required for effective implementation of cancer control strategies in LMIC settings such as Ghana.

O-236 | Impact of Counseling and Psycho-Social Support on Parents of Children from Rural Areas with Cancer

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Background/Objectives: During the treatment of cancer at a non-profit cancer hospital for children in Karachi, Pakistan, psychologists and counselors observed that most children with cancer and their caregivers undergo stress and hospital-related anxiety.

People frequent Indus Children Cancer Hospital (ICCH) even from remote areas, such as Afghanistan, Iran, Baluchistan and Interior Sindh provinces of Pakistan. The counselors at the Psychosocial Oncology Department (POD) at ICCH observed levels of stress and hospital-related anxiety to be higher in people who come from the aforementioned rural areas, and sought to test the hypothesis that there was a greater incidence of higher levels of stress and anxiety.

Design/Methods: A sample of N=100 parents was randomly selected from the hospital waiting area. On an average, every parent underwent at least three sessions of one-on-one counseling, and a detailed account of their struggles was obtained. The next step of this intervention was to offer psychosocial support to these parents, and increase familiarity with hospital staff, treatment teams, along with getting them in touch with the social services department, which looks after their expenses.

Results: It appears that stress and anxiety levels are indeed more intense in people who come from rural areas. Reasons for this included language barriers, relocation to a metropolis, lesser familiarity with hospital settings doctors' lingo, and financial constraints despite the treatment being free of cost.

Conclusion: It was observed over a two-year period, that there had been a positive effect of counseling and providing psycho-social support, which put the parents at ease, and facilitated their transition from rural settings. The implications of this study suggest that providing counseling and psycho-social support to families of children with cancer is vital to the process of a

child's treatment, because it familiarizes the family with the system, and informs them of what to expect and who from.

O-237 | Caregiver Burden and Psychiatric Morbidities Among Informal Caregivers of Children with Cancers in Lagos, Nigeria

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Background/Objectives: Childhood cancers are one of the most feared diseases; and can impact negatively on the wellbeing of the child and their caregivers. Unfortunately, there is dearth of information on the experiences of caregivers of children with cancers in Nigeria. This study was set to assess caregivers' burden and its relationship with anxiety, depression and posttraumatic stress disorders in paediatric oncology.

Design/Methods: Eighty family caregivers of children with histological diagnosis of cancer were recruited consecutively from two tertiary health institutions in Nigeria. The instruments administered included: sociodemographic and clinical questionnaire, the 12-item General Health Questionnaire, Zarit Burden Interview (ZCBI), and modules of the MINI International Neuropsychiatry Inventory were used to elicit generalized anxiety disorder, major depressive disorder, and posttraumatic stress disorder. Data were analyzed using SPSS-16.

Results: Of the total 80 study participants, 80% were females and 70% were the mothers. The mean age of the participants was 37.76 (±8.57) years while the mean age of their children was 6.19 (±4.22) years. The mean score of participants on ZCBI was 29.30 (±13.69) and 52.5% of the children were females. The predominant cancer diagnoses were leukaemia, retinoblastoma and Wilms tumour. Based on ZCBI, 52.5% had mild-moderate burden, 28.8% little-no burden, 17.5% moderate-severe burden, and 1.3% severe burden. Following dichotomization using ZCBI cut-off score of 40, 77.5% had low burden and 22.5% had high burden. The MINI interview showed that 16.05% had depression, 12.35% had generalized anxiety disorder, and 18.52% had posttraumatic stress disorder. The correlates of caregivers' burden include marital status $p=0.046$, depression $p < 0.001$ and posttraumatic stress disorder $p=0.002$.

Conclusion: Our study found that significant number of informal carers of children with cancers considered their roles burdensome and were found with certain psychiatric morbidities. Psychosocial support to address caregivers' wellbeing and further research are indicated.

PPO: NEXT STEPS - "WHAT ARE WE GOING TO DO ABOUT THIS?"

O-238 | Can the Theory of Planned Behavior Help Explain Follow-Up Attendance in Childhood Cancer Survivors?

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Background/Objectives: Childhood cancer survivors (CCS) are at high risk for late effects and regular long-term follow-up is crucial to monitor health and detect early cancer-related late effects. The Theory of Planned Behavior (TPB) was developed to predict a diverse range of health behavior. We investigated whether the TPB helps predicting attendance to follow-up care in Swiss CCS. We aimed to i) identify predictors for the intention to attend follow-up, and ii) examine associations between behavioral intention and actual attendance.

Design/Methods: We sent a questionnaire to CCS (diagnosed with cancer aged <16 years after 1990; aged ≥18 years at study, ≥5 years since diagnosis). We assessed the TPB predictors for behavioral intention (attitudes, subjective social norms, perceived behavioral control), behavioral intention to attend follow-up care and actual attendance to follow-up care. Additionally, fear related to late effects was assessed as a potential predictor. We used linear and logistic regression analyses.

Results: Of 716 eligible survivors, 299 (41.8%; 166 (55.5%) females) completed the questionnaire, and 145 (48.5%) participants reported regularly attending follow-up. Adjusting for socio-demographic and cancer-related characteristics we found that positive attitude (Coef. 0.22, CI: 0.07 – 0.36) and supportive social norms (Coef. 0.90, CI: 0.83 – 0.97) predicted the intention to attend follow-up, whereas perceived control and fear did not. Perceived control ($p=0.018$, OR: 1.53, CI: 1.31 – 1.80) and the intention to attend follow up were positively associated with follow-up attendance ($p < 0.001$, OR: 2.19, CI: 1.89 – 2.54).

Conclusion: The TPB strengthens our understanding of follow-up care attendance in Swiss CCS. Promotional interventions to increase intention for and actual follow-up attendance should focus on positive attitudes towards follow-up care, improve supportive social norms and enhance perceived control.

O-239 | A Study of Quality of Life and Psychosocial Status of Parents of Children Suffering from Malignancies in a Low Income Setting

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Background/Objectives: Prior research has emphasized on identifying parental psychosocial risk factors at cancer diagnosis in order to improve care and to reduce treatment abandonment, thus deliver the benefits of vastly improved therapeutic strategies in paediatric oncology. This study aimed to evaluate the impact of diagnosis of cancer on overall quality of life (QOL) and psychological status of parents in a low income setting and to correlate it with socioeconomic status.

Design/Methods: We conducted a comparative cross sectional study. Sixty parents of children diagnosed with haematological and solid malignancies were enrolled in study group and sixty well matched parents of healthy children were studied as a control group. World Health Organization QOL-Bref questionnaire and DASS scale was used for the assessment of the QOL and psychological status respectively. Socioeconomic status was classified as per Kuppuswamy scale.

Results: Mean score of QOL for study group in domains of physical health, psychological health, social relationships and environment was 47.3, 42.3, 44.9 and 39.8 whereas that of control group was 79.3, 76.2, 80.5 and 72.8 respectively. The difference was statistically significant ($p < 0.001$) in all domains. Mean depression, anxiety and stress score of the study group was 23.9, 20.06 and 24.09, whereas that of the control group was 7.1, 8.06 and 8.54 respectively and this too was statistically significant. Majority of our patients (76%) belonged to the low socioeconomic class. QOL of study group was similar for all socioeconomic groups. The correlation between socioeconomic status and QOL was statistically insignificant.

Conclusion: The study group had decreased scores in all domains of QOL and were significantly more depressed, anxious and stressed. Poorer QOL of study group was due to impact of the disease rather than the socioeconomic status. This study emphasizes the need for effective interventions to aid these families and thus improve the final outcome.

O-240 | The Basic Needs of Parents of Children Undergoing Cancer Treatment and Their Relationship to Parents' Psychosocial Adjustment Over Time

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Background/Objectives: Although children are surviving cancer at increasing rates, the challenges of paediatric cancer can create substantial needs for basic services among families of patients. This study examined (a) the extent to which the fiscal/material/social needs of families of children in treatment are met, and (b) the relationship of met needs to parents' psychosocial adjustment.

Design/Methods: Participants were parents (N=153, 81% mothers; 71% white; mean age=34) of children with cancer (60% male; mean age=6.56) who were receiving outpatient cancer treatment at two children's hospitals in the United States. Parents reported their trait anxiety, depression, and family resources at the time of study entry. At 3-month follow-up, parents reported their fiscal/material/social needs and whether they had been met; a ratio (%) was calculated between number of needs reported and number of needs met. Parents completed measures of psychological and post-traumatic stress symptoms at 3- and 9-month follow-ups.

Results: Seventy-eight percent of parents (n=119) reported having at least one need (mean=6.13; range=1-14). Of those, 29% reported having one or more unmet needs. The top 5 needs were: social work services, recreational/play activities, help with insurance to pay for medical care, educational/instructional activities to help children cope, and help obtaining medical services. When controlling for baseline parent depression and anxiety, percent of met needs at 3 months was significantly and inversely correlated with parents' somatic symptoms, anxiety, and global distress (but not depression) and PTSS hyperarousal at 9 months.

Conclusion: Parents of children with cancer have substantial need for basic services and the extent to which these needs are met is associated with their psychosocial adjustment. Parents with more met needs had lower levels of psychological distress over time. Unmet needs may be a psychosocial risk factor for patients and their families. Programs that address these needs may benefit the psychological adjustment of parents and their children.

O-241 | Health Behaviours in Survivors of Childhood Cancer: Modifiable Risk Factors for Developing Late Effects

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Background/Objectives: Childhood cancer survivors (CCS) are at risk of late effects and second neoplasms during survivorship. Health behaviours (such as exercising, sun protection, dental care) are important modifiable behaviours that may help to reduce the occurrence of late effects and second cancers. This study aims to explore the extent to which CCS engage with appropriate health behaviours.

Design/Methods: CCS and parents of CCS >5 years since treatment from 10 hospitals around Australia and New Zealand self-reported on current health behaviours. An age-matched control group was recruited to compare rates of behaviours.

Results: 327 CCS (average age 27years, SD=7.8; on average 19.7years since diagnosis, SD=8.8), 140 parents of CCS (child average age 12years, SD=2.2; on average 9.5years since diagnosis) and 640 healthy controls participated. Use of sunscreen, long-sleeved shirt, and a wide-brimmed hat were no different between CCS and controls, however, more CCS had undergone a skin check with a doctor in the last 24 months (42% v 21% $p < .001$). Rates of smoking were lower in CCS than controls (5% v 11%, $p < .001$). CCS engaged in fewer appropriate dental practices including flossing everyday (5% v 9%, $p = .012$). CCS and controls did not differ on average amount of exercise or alcohol consumption. CCS who were female ($p < .001$) and who engaged in more risky behaviours reported worse quality of life ($p < .001$).

Conclusion: Many CCS health behaviours are similar to or better than age-matched controls. However, dental practices among CCS are below that of controls and are an area for potential future intervention.

PPO: SLEEP AND NEUROCOGNITIVE FUNCTIONING

O-242 | Insomnia Symptoms and Memory Problems in Adult Survivors of Childhood Cancer

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Background/Objectives: Adult survivors of childhood cancer are at-risk of developing sleep and cognitive problems. No studies have examined the contribution of insomnia symptoms to neurocognitive function in this population.

Design/Methods: 642 adult survivors of paediatric cancer with mean[SD] current age = 34.5 years[9.2] and years since diagnosis = 25.9[9.1] completed standardized assessments of intelligence, memory, attention, and executive function. Age-adjusted z-scores were calculated using national normative data (M=0, SD=1). Insomnia symptoms were defined as difficulty falling asleep within 30 minutes and nighttime or early morning awakenings (>3 times per week). Functional impairment was defined as severe daytime fatigue or sleepiness. Multivariable regression models examined associations between sleep and cognition, adjusted for age, sex, age at diagnosis, and primary treatment exposures (cranial irradiation, methotrexate, anthracyclines, corticosteroids). Separate multivariable models were adjusted for emotional and physical late effects (psychological distress, pain, physical inactivity, obesity).

Results: 133 (21%) of survivors reported symptoms of insomnia; 61 (10%) reported insomnia symptoms and daytime fatigue or sleepiness. In multivariable models adjusted for primary cancer therapies, insomnia symptoms were associated with worse performance on multiple measures of verbal memory and learning; the magnitude of associations, approximately one-half standard deviation, was greater in survivors with insomnia and functional impairment: short-term memory ($\beta = -0.66$, 95% CI, -0.94 to -0.38, $P < 0.0001$); long-term memory ($\beta = -0.51$, 95% CI, -0.80 to -0.22, $P = 0.0003$); verbal learning ($\beta = -0.52$, 95% CI, -0.80 to -0.23, $P = 0.0003$); vocabulary ($\beta = -0.47$, 95% CI, -0.73 to -0.21, $P = 0.0006$). Similar associations were observed in models adjusted for emotional and physical late effects.

Conclusion: Survivors with symptoms of insomnia performed significantly worse on memory measures than survivors without such symptoms; observed risk exceeded that associated with cranial irradiation. Interventions targeting insomnia symptoms may confer cognitive benefit in survivors.

O-243 | Association of Dehydroepiandrosterone-Sulfate with Sleep, Fatigue and Neurocognitive Outcomes in Long-Term Survivors of Childhood Acute Lymphoblastic Leukemia (ALL)

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Background/Objectives: Dehydroepiandrosterone-sulfate (DHEAS) is an adrenal androgen used as a marker of glucocorticoid secretion, and is associated with arousal, fatigue and, potentially, sleep quality. We examined the association of DHEAS with sleep problems, fatigue and neurocognitive outcomes in long-term survivors of childhood ALL treated with chemotherapy only.

Design/Methods: Survivors of ALL (N=71, mean[SD] age 14.3[4.7] years; 7.4[1.9] years post-diagnosis) completed neurocognitive testing at ≥ 2 years post-treatment, and self-reported their sleep problems (Children's Sleep Habits Questionnaire/Adolescent Sleep Questionnaire) and fatigue (PedsQL Multidimensional Fatigue Scale) symptoms. Serum was collected concurrently and assayed for DHEAS. General linear modeling was used to assess associations among DHEAS, sleep duration, general and cognitive-fatigue, and neurocognitive function, adjusting for age at evaluation.

Results: Survivors performed worse than population norms on measures of executive function, processing speed and attention (all P 's < 0.05 adjusted for multiple comparison). Median DHEAS was 92.7 $\mu\text{g/dL}$ (interquartile range 47.0-139.2). Survivors with DHEAS levels within the lowest tertile of the cohort ($\leq 53.3 \mu\text{g/dL}$) displayed poorer performance than survivors with levels in the upper tertiles ($> 53.3 \mu\text{g/dL}$) on measures of inattention (adjusted Z-scores[95% CI] -1.08[-1.93, -0.23] vs -0.25[-0.77, 0.28]; $P = 0.05$), attention variability (-1.10[-1.80, -0.39] vs -0.14 [-0.58, 0.29]; $P = 0.009$) and response speed (-0.95[-1.64, -0.26] vs -0.10[-0.53, 0.32]; $P = 0.004$). Slower response speed ($P = 0.007$) and higher attention variability ($P = 0.01$) were correlated with longer sleep duration, which was also associated with more general ($P = 0.03$) and cognitive-fatigue ($P = 0.04$). Survivors who reported longer sleep duration, which may be associated with frequent night-time awakenings, had lower levels of DHEAS than those with shorter sleep duration ($P = 0.02$). Sensitivity analyses revealed that gender had no effect on the associations.

Conclusion: These results suggest that low-normal levels of DHEAS are associated with attention problems and potentially poor sleep efficiency. Future studies should evaluate the potential impact of adrenal insufficiency on sleep problems, fatigue and neurocognitive outcomes in survivors.

O-244 | Sleep Apnea Symptoms, Memory, and Quality of Life in Long-Term Survivors of Childhood Hodgkin Lymphoma

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Background/Objectives: To examine the association of sleep apnea symptoms with memory and health-related quality of life in long-term survivors of childhood Hodgkin lymphoma treated with thoracic radiation.

Design/Methods: Survivors of Hodgkin lymphoma (N=72, mean[SD] age 37.6[7.6] years, 22.9[7.5] years post-diagnosis) and age, gender, and race frequency-matched community controls (N=91) completed neurocognitive testing (i.e. California Verbal Learning Test-II), Short-form Health Survey (SF-36), and self/informant-report of sleep/sleepiness/fatigue. Sleep apnea symptoms were defined as "long pauses between breaths while sleeping" based on sleep-partner report (Pittsburgh Sleep Quality Index), combined with clinically elevated daytime sleepiness or fatigue from self-report (Epworth Sleepiness Scale, FACIT Fatigue). Group differences between those with sleep apnea symptoms and those with neither symptom were examined using chi-square and Wilcoxon rank-sum tests.

Results: A higher frequency of survivors (21%) compared to controls (11%) reported sleep apnea symptoms ($p=0.08$). No difference in body mass index (BMI) was identified between survivors and controls ($p=0.14$). Controls with sleep apnea symptoms had greater BMI ($p=0.02$) and neck circumference ($p=0.01$) than controls without symptoms. This pattern was not observed among survivors (BMI $p=0.49$, neck $p=0.71$). Survivors performed worse than controls on long-term free recall ($p=0.02$). While survivors with sleep apnea symptoms performed below population norms on long-term recall (z -score = -0.96 , $p=0.03$), survivors without sleep apnea symptoms demonstrated no difference (-0.19 , $p=0.26$). Neither controls with symptoms (-0.05 , $p=0.90$) nor without symptoms (0.20 , $p=0.07$) differed from population norms on long-term recall. Survivors with apnea symptoms reported lower mental health (-1.33 , $p<0.01$) compared with population norms. Survivors without symptoms and controls demonstrated no difficulties in mental health compared with population norms ($p>0.05$).

Conclusion: Survivors of Hodgkin lymphoma treated with thoracic radiation may be at higher risk for sleep apnea compared to community controls. Symptoms of sleep apnea appear to increase risk for long-term memory and mental health difficulties in survivors, but not controls.

PPO: ETHICAL CONSIDERATIONS

O-245 | Outcomes of Bereaved Parents Whose Child Did or Did Not Participate in An Early Phase Clinical Trial

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Background/Objectives: Phase I/II clinical trials may be offered to cancer patients where established treatment options had failed. Health professionals can find discussing early phase clinical trial participation challenging due to the potential to cause distress. This study evaluates long-term psychological outcomes of bereaved parents whose child has been offered and/or consented to participation in an early phase clinical trial.

Design/Methods: Parents >6 months post bereavement completed a questionnaire assessing whether an early phase clinical trial was offered and consented to. Distress, anxiety, depression, anger, grief, quality of life, and palliative care service use were assessed.

Results: Bereaved parents (n=119) who were on average 47 years old (SD=8.1), completed the questionnaire on average 5.6 years (SD=3.0) after the death of their child. Fifty-two percent of parents were offered early phase clinical trial participation for their child and 33% of parents consented to participating, 8% and 11% were unsure whether they had been offered or consented to an early phase clinical trial. Children diagnosed with non-Central Nervous System solid tumours were more likely to be offered clinical trial participation (OR=4.7, 95%CI: 1.3-17.0, $p=0.019$). Parents were more likely to consent to participation if their child was older at the time of relapse (OR=1.4, 95%CI: 1.0-2.0, $p=0.046$). There were no significant differences in psychological well-being or quality of life according to whether clinical trial participation had been offered or consented to. Similarly, there were no differences in timing or rates of referral to palliative care.

Conclusion: Discussing early phase clinical trial participation can be challenging in the context of incurable cancer for health professionals and families alike. Our results suggest parents' long-term emotional well-being and quality of life after the loss of a child to cancer is not influenced by whether their child has been offered or consented to clinical trial participation.

O-246 | Finding A Way to Promote Shared Decision-Making When Options are Limited: Doctors and Nurses' Strategies

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Background/Objectives: International Charter of Rights for young people with cancer states that they have the right to empowerment in making decisions thereby actively influencing their care (www.canteen.org). Likewise SIOP recommends that healthcare professionals support children's ability to participate in the decision-making process (Spinetta et al. 2003). This paper presents a secondary analysis of data from a larger study on triadic shared decision-making (SDM) in a cancer unit, to illustrate how healthcare professionals' assist with SDM, and the contextual factors which influence this process.

Design/Methods: With ethical approval from both university and hospital ethics committee, sixteen doctors and twenty nurses were purposefully sampled from one cancer unit in Ireland and interviewed face-to-face. The qualitative data were analysed using the constant comparative method and managed with the aid of NVivo.

Results: Decision-making focused on choices about care delivery and less so with treatment decisions. These were termed minor or small decisions usually associated with timing and delivery of procedures (e.g. medication, blood tests, IV dressings, nutrition). Older children could be involved in treatment decisions (sperm banking, sedation for procedure, research participation). Involvement was dependent on a child's characteristics, state of wellness, family dynamics, time pressure, and options available. Doctors' reported assistance mostly involved sharing information, instead of SDM. In addition to information provision, nurses' reported assistance included checking understanding, explaining options, bargaining, building trusting relationships and advocating for children's preferences. Eliciting children's expectations and preferred level of involvement in SDM were seldom reported.

Conclusion: Although professionals recognise the importance of children's involvement in SDM, their actions are constrained by the strict protocols and a life-threatening illness. Despite this, some professionals, generally nurses appear to offer children choices and involve them in treatment related decisions. Tools for assessing children's preferences for SDM and communication skills training are interventions that might help to increase professionals assistance with SDM.

O-247 | Spectrum of Psycho-Social Challenges in Childhood Cancer Care in a Developing Country: The Children's Hospital Lahore Pakistan Experience

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Background/Objectives: More than 80 percent of children with cancer live in low income countries with poor access to childhood cancer care. The purpose of this study was to elucidate the major psycho social issues faced by these families being managed in resource limited settings with lack of trained health professionals, paucity of paediatric oncology centers far from their homes and poor socioeconomic and educational background during this ordeal.

Design/Methods: The data was collected from 100 patients being treated in paediatric haematology and oncology department with the help of questionnaire and analyzed by SPSS16.

Results: Total 100 patients with age ranging from <1 to 15 years (43% <5 years and 57% >years old). M:F ratio was 1.2:1. Majority of these children had malnutrition with anemia (81% - Hb <10 gm%) and weight small for age in 63% cases at presentation. Majority of families had more than 3 children (71%), with youngest child <5 years in 80%. 95% families use public transport with 69% of them travelling 100-500 KM with 2-10 hrs duration to reach the primary treatment center. 80% had monthly income <150 USD. 58% had to borrow money for the trip to hospital (p -Value=0.003) and 70% had to take loan for the treatment course (p -Value=0.008). Only 48% had adequate knowledge about the disease. Education of siblings got affected in 51% of patients (p -Value=0.008) as parents are staying with children in 91% of cases and other siblings being taken care by grandparents in 65% and self care in 14% of cases. All of them were determined for treatment completion.

Conclusion: These major challenges lead to increased abandonment, morbidity and mortality in childhood cancer care in developing countries which can only be solved by capacity building in paediatric oncology, training of health professionals, intense psychosocial support and provision of loans by government/NGOs to facilitate the long treatment course.

O-248 | Dignity in Pain: How the Battle for Human Rights Made Morphine Constantly Available to Paediatric Oncology Patients in Senegal (West Africa)

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Background/Objectives: In Senegal, paediatric oncology patients arrive at the hospital at advanced stages of their disease with widespread tumors. In our context, both human and material resources are sparse. The availability of morphine was irregular. This study assesses the impact of the shortage of morphine on distress levels on the unit; the battle for access to morphine; and its outcome on patient care.

Design/Methods: Qualitative data from group and individual therapy sessions were reviewed. We've addressed pain management with patients, their parents and the medical staff. We had a sample of 24 children aged between 5 and 15 years, 10 parents, 3 doctors and 7 nurses. During therapeutic groups with children we've explored the impact of morphine and its lack thereof on pain and on their cancer experience. Subsequently, we've conducted directive interviews and focus groups with the parents, doctors and nurses. Additionally, we've contributed to a report of the Human Rights Watch exploring the medical and political causes to the morphine supply shortages, as well as its psychological repercussions on patient care.

Results: Reports have shown that morphine scarcity was agonizing for everyone on the unit powerlessly witnessing children in pain. Both children and parents were frightened, for they associated the intensity of pain with the severity of the illness. Doctors had developed avoidance mechanisms when incapable of justifying their inability to alleviate patients' pain, while nurses were depersonalizing when administering care. HRW concluded inaccurate estimation of needs due to miscommunication between the Ministry of Health and the prescribers was causal. Following the report's release, the government ordered ten times more morphine the following year. Morphine shortage became exceptional.

Conclusion: Adopting a collaborative approach between the medical and psychological teams, the government, and the civil society resolved an outstanding human right issue in cancer care; regardless of its occurrence in a low-income country.

PPO: IMPLEMENTATION OF PSYCHOSOCIAL STANDARDS OF CARE: BARRIERS AND FACILITATORS

O-249 | Psychosocial Standards of Care: State of Affairs in Three US Paediatric Oncology Centers

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Background/Objectives: The recently published, evidence-based Standards of Psychosocial Care for children with cancer and their families provide a unique opportunity for paediatric oncology programs to evaluate quality of their psychosocial care, identify areas for improvement, and address unmet needs. We aimed to use these Standards as a tool to assess psychosocial services currently provided to patients and families at three US paediatric cancer centers.

Design/Methods: Program evaluations were completed by psychosocial program directors at three US paediatric oncology programs. Program demographics were collected, and directors responded to prompts on how well their program met each standard (i.e., meets all aspects, partially meets, does not meet). Services provided to all patients/families via a standardized process were further classified as "well-developed", while services provided to some or none or implemented without standardization were classified as "less well-developed".

Results: Surveyed programs varied in size (150, 180, and 300 new diagnoses/year) and number of psychosocial providers (7, 23, and 15 FTEs, respectively). All 15 standards were reportedly met or partially met. The program with the most psychosocial FTEs fully met all but two standards, while the program with the fewest only fully met four. Across institutions, the most well developed services were systematic assessment of patients' psychosocial needs and psychosocial screening of long-term survivors. Less well developed services included monitoring for neuropsychological deficits and routine assessment of adherence. Patient access to psychiatry, parent access to mental health services, and opportunities for social interaction were cited as challenging.

Conclusion: This preliminary evaluation of psychosocial services revealed wide ranges of adherence to published standards, and all directors noted areas for improvement. Number of psychosocial providers may be related to capacity to provide recommended care. Ongoing evaluation of psychosocial programs can help centers identify and address gaps in care, facilitate implementation of best practices, and advocate for psychosocial personnel.

O-250 | Implementing Standards of Psychosocial Care for Children with Cancer - Single Slovakian Centre Experience

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Background/Objectives: There are three paediatric oncology centres in Slovakia. Number of newly diagnosed malignant diseases is around 140 – 150 per year. Approximately one half of this amount is treated in our centre. Specificity of people in our region is their focus mainly on somatic aspect of illness, not considering other-psychosocial aspects. This could be a reason why implementation of psychosocial standards of treatment is being protracted. In our cultural context it is connected with astonishment, negation either denial of psychosocial help. Relying on biopsychosocial approach we implemented some standards of psychosocial care. However there is still need of implementation of others according to relevant findings and published standards of paediatric oncology patient care.

Design/Methods: Preliminarily we succeed in implementing three tools as a standards – communicating diagnosis in different context as been used previously. Initial conversation about diagnosis is organised by psychologist. Senior oncologist, psychologist, child, parents and significant others for the family are involved. The second standard are regular weekly psychosocial meetings with presence of all members of caring team – doctors, head nurse, social worker, psychologist, teachers, physiotherapist, art therapist and member of parental organization. Third standard is the screening of families using tools as questionnaires, in depth interviews, clinical observations provided by medical staff. Main objective is more efficient care, better compliance, eliciting active coping of patients and their families and targeted support to families in need.

Results: Thanks standards we perceive improved co-operation between team members mutually and between patient and their families with medical staff. Obviously this process is struggling following small steps. Children's knowledge of disease is beneficial, brings them possibility of more active facing the disease.

Conclusion: Our experience with implementation of these psychosocial standards is positive, despite difficulties connected to process. The further evaluation with quantification of the impact of the standards are planned.

O-251 | Standards of Psychosocial Care in Paediatric Haematol-Oncology (PHO) Centres in Central and Eastern Europe

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Background/Objectives: To address inequalities in the availability and quality of childhood cancer care treatment and care across different European countries, SIOPE initiated a study of the current state and standards of PHO in Europe. At the conference in 2009, all involved stakeholders reached an agreement to create "European Standards of Care for Children with Cancer".

Design/Methods: SIOPE has launched in 2013 a Europe-wide survey in order to evaluate the implementation of the Standards. All Chairs of European NaPHOS have been contacted and experts from thirty four European countries provided comprehensive responses to the survey. Assessing the quality of treatment and care in different European states, we analysed separately implementation of psychosocial care standards in PHO centres in Central and Eastern Europe. Within psychosocial standards were analysed: 1. Patient's rights to be fully informed; 2. Access to psychosocial support; 3. Access to comprehensive palliative care; 4. Access to post-treatment support; 5. Collaboration with local parents organisation.

Results: 1. Patient's rights to be fully informed on cancer diagnosis and treatment are always followed in 66.6% of responding countries. In three countries, the aforementioned rights are perceived as mostly guaranteed. 2. Almost 80% of respondents stated that children with cancer have been offered with psychological support. 3. More than half countries (53.3%) have the possibility to provide terminally ill children with comprehensive palliative care through a multidisciplinary palliative care team. In Bulgaria, Ukraine and Czech this possibility occurs rarely. In four countries comprehensive palliative care is not available. 4. Only two countries do not guarantee post-treatment support to help patients reintegrate back into society. 5. Representatives of nine countries claimed that personnel rarely encourages collaboration with local parents' organizations

Conclusion: Five analysed standards of psychosocial care are implemented in most PHO centres in Central and Eastern Europe. The level of implementation varying between countries.

PROS: FREE PAPERS SESSION

O-252 | Does Post-Induction Chemotherapy PET/CT Response Predict Outcome in Young Adult Nasopharyngeal Carcinoma?: Prospective Study from CCHE

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Background/Objectives: To evaluate the predictive value of 18F-Fluorodeoxyglucose positron emission tomography (18F-FDG PET/CT), reflected in terms of disease free survival (DFS) and overall survival (OS), in paediatric patients received post induction chemotherapy for locally advanced nasopharyngeal carcinoma (LANPC), paediatric patients treated definitively with 3 courses of induction Platinum-based chemotherapy followed by concurrent chemoradiation (CRT) with simultaneous integrated boost intensity modulated radiotherapy (SIB-IMRT).

Design/Methods: This is a Prospective study included LANPC (stage II-III) paediatric patients treated definitively and consecutively between January 2008 and December 2014 with induction chemotherapy: cisplatin, and 5-fluorouracil (PF) followed by SIB-IMRT to a total dose 61.2Gy with utilizing weekly cisplatin. The volume of radiotherapy was based on tumour response to Induction chemotherapy. All patients had baseline pretreatment and post induction chemotherapy 18F-FDG PET/CT. Metabolic response of the primary tumour and LN was assessed using maximum standardized uptake value (SUV_{max}) that was correlated with treatment outcomes; OS and EFS.

Results: The study included 38 eligible paediatric LANPC patients. The 3-year OS and DFS rates were 84.6% and 79.5%, respectively. The median OS and EFS intervals were not reached. On a univariate analysis, the 3-years OS and EFS were significantly higher in patients with post induction metabolic regression of SUV max >65% for the primary and 57% for the nodal metastases (P=0.02). Furthermore, OS and EFS were lower in patients with initial high nodal metabolic activity (P=0.004) and (P=0.005) with SUV max cutoff values (14.5) and (6.9) respectively. Also Initial SUV-LN>SUV-Primary showed significant lower OS (P=0.004) and EFS(P=0.005).

Conclusion: In this study, the degree of metabolic regression in post-induction chemotherapy 18F-FDG PET/CT was a potential independent prognostic indicator for clinical outcomes in LANPC paediatric patients (treated definitively with PF induction chemotherapy followed by CRT). Further controlled clinical trials are worthwhile.

O-253 | Practice Patterns of Palliative Radiation Therapy in Paediatric Oncology Patients Amongst An International Paediatric Research Consortium

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Background/Objectives: Practice of palliative radiotherapy (RT) for paediatric oncology patients is based on extrapolations from adult palliative RT literature. We evaluated the

palliative paediatric RT practice patterns to highlight the various regimens employed and to assess opportunity for future palliative RT clinical trials.

Design/Methods: Five international institutions with paediatric expertise completed a 122-item survey evaluating patterns of palliative RT for patients < 25 years old from 2010-2015. Two of the five institutions have proton RT capabilities. Palliative RT was defined as treatment with the goal of symptom control or prevention of immediate life-threatening progression.

Results: Of 2,358 cases of RT for paediatric patients, 385 cases (16%) were delivered for palliative intent (range 4%-28% across institutions). Anesthesia was required in 12% of cases, most commonly in patients <5 years old. Palliation was required due to metastatic disease in 58% of cases. Common histologies included neuroblastoma (32%), osteosarcoma (17%), leukaemia/lymphoma (16%), rhabdomyosarcoma (12%) Ewing sarcoma (7%), and other (16%). Common indications included pain (40%), intracranial symptoms (24%), respiratory compromise (15%), abdominal distention (7%), and cord compression (6%). Common sites and regimens (total Gy/# fractions) included non-spine bone (38%; 20Gy/4-10fx or 8Gy/1fx), spine (12%; 30Gy/10fx or 20Gy/4fx), abdomen (16%; 30.6Gy/14fx, 30Gy/10fx, 24Gy/16fx, or 20Gy/5fx), head and neck (10%; 30Gy/10fx, 20Gy/5fx, 45Gy/20fx, 25Gy/10fx), lung/mediastinum (6%; 55.8Gy/31fx, 30Gy/4fx, 20Gy/5-10fx), primary brain masses (18%; 45Gy/25fx, 37.5Gy/15fx, 30Gy/10fx), and brain metastases (5%; targeted/radiosurgery: 35Gy/5fx; whole brain RT: 20Gy/5fx, 30Gy/10fx). Re-irradiation comprised 17% of cases. Common techniques were 3D-CRT (45%), IMRT (26%), and conventional RT (19%). SBRT and proton RT were employed in 25 and 4 cases, respectively, primarily for brain cases.

Conclusion: There is significant diversity of practice patterns in paediatric palliative RT. Research characterizing treatment response and toxicity is ongoing. Together, these data will inform the design of forthcoming clinical trials to establish effective regimens and minimize treatment time and toxicity.

O-254 | Magnitude of Respiration-Induced Diaphragm Motion During Radiotherapy: Is it Smaller in Children Than in Adults?

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Background/Objectives: Currently, in paediatric radiotherapy safety margins are based on adults' data. However, organ motion in children is most certainly smaller than in adults, which can have important implications for the safety margin sizes. The aim of this study was to quantify respiration-induced diaphragm motion and its variability among children during image-guided radiotherapy (IGRT) and to study the possible correlation with patients' height.

Design/Methods: This retrospective study is based on 102 abdominal-thoracic cone-beam CT (CBCT) scans of 15 childhood cancer patients (<18 years) with a mean height of 139cm (range 90-173cm). The cranio-caudal diaphragm dome position was manually detected in the CBCT projection images corresponding to the end-exhale and end-inhale phases of the respiration signal acquired during the CBCT. Peak-to-peak motion was quantified as the difference in diaphragm dome positions between end-exhale and end-inhale positions. Daily motion (intrafractional), day-to-day motion variation (interfractional) and inter-patient variability were quantified (averages and standard deviations (SD) of the peak-to-peak motion). Additionally, we investigated possible correlations between patients' average peak-to-peak motion and height.

Results: Over all patients, peak-to-peak diaphragm motion was on average 9.9mm (range 5-17mm). The peak-to-peak motion variability was 2.0mm and 1.1mm for respiration-induced intra- and interfractional diaphragm motion, respectively. Inter-patient variability was large (SD 3.1mm). Our results show smaller values in children than reported in adults (mean peak-to-peak motion 16.4mm) (Rit et al, 2011, DOI: 10.1016/j.ijrobp.2011.06.1986). Patients' average peak-to-peak motion correlated with height ($R^2=0.33$, $p<0.05$), and increased 0.8mm for every 10mm increase in height.

Conclusion: Respiration-induced diaphragm motion variability is larger within a daily treatment fraction than between fractions (day-to-day). Respiration-induced diaphragm motion in children was about half the magnitude of adults' data, suggesting smaller margins in children than in adults are advisable. Also, large inter-patient variability was found, suggesting an individualized approach is needed to define appropriate margins for paediatric IGRT.

O-255 | Navigating Radiation Therapy-An App for Children and their Families

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Background/Objectives: The Princess Margaret Cancer Centre sees over 130 children each year for Radiation Therapy and it is essential for these children and their families to have a better understanding of what will happen when they come to have radiation treatment.

Design/Methods: Patient education and understanding is an essential part of the Princess Margaret Cancer Centre and it was time to update our resources for this very special population. In 2013 we created the Paediatric Radiation Storybook to help the children and their families understand more about radiation therapy. It was also translated into French. In 2014 we started developing an APP and the end result was completed in the Spring of 2015 and available go all children and their families and it is called RADS4KIDS.

Results: The APP includes a game, a how are you feeling calendar, the storybook, and information for parents. Families are very busy trying to navigate the new world of cancer diagnosis and any ways to make it easier is always helpful. These families can download the APP and have it with them to read the information at their own pace and the children can play the game in comfortable surroundings. The interactive calendar gives us a better understanding of how the child is feeling during treatment.

Conclusion: The book and the APP were developed to be generic and is available worldwide. It could be utilized at any radiation centre worldwide.

O-256 | Clinical Outcomes of Palliative Radiotherapy for Paediatric Oncology Patients

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Background/Objectives: Limited data exist detailing paediatric palliative radiotherapy (RT) practices. Here, we characterize the practice, effectiveness, and toxicity of palliative RT for paediatric patients.

Design/Methods: All paediatric patients age < 25 years treated with RT with palliative intent, defined as goal of symptom control or prevention of impending, life-threatening progression, from 7/2009-1/2016 at a single institution were reviewed. Symptom response was assessed by patient report at post-RT encounters.

Results: Of 385 total paediatric patients treated with RT, 43 (11%) received palliative RT to a total of 76 separate sites at a median of 27.9 months (range 0.7-158.4 months) after diagnosis. Most common histologies included leukaemia/lymphoma (33%), rhabdomyosarcoma (18%), neuroblastoma (12%), retinoblastoma (9%), Ewings sarcoma (8%), osteosarcoma (5%), and other (15%). Common indications for palliative RT were: 63% pain, 8% cord compression, 8% intracranial symptoms, 8% respiratory compromise, 7% asymptomatic lesions risking impending symptoms, and 4% post-laminectomy. Common RT regimens were 3Gy x 10 (20%), 2Gy x 10 (16%), and 4Gy x 5 (11%). Of the 76 sites treated, 59 (78%) had response data with 74% experiencing symptomatic relief (44% complete and 30% partial response) with 36% responding prior to RT completion. Median time to response was 22 days (range, 2-96 days). Symptoms stabilized in 17%, and 8% clinically progressed. An exception was leukaemia and lymphoma—the most common histologies in this cohort—for which 100% of treatment courses led to clinical responses. Eleven percent of treatment courses were terminated early due to clinical deterioration. Median survival post-RT was 3.5 months (95% CI 1.2-5.9 months). One patient experienced RTOG grade 3 acute anorexia with 50 Gy in 25 fractions to a 15 cm pelvic sarcoma; otherwise the palliative regimens were well-tolerated.

Conclusion: Palliative RT is a useful, safe, and effective tool for paediatric oncology patients. Future research to minimize dose and number of fractions necessary for symptomatic relief in paediatric patients is warranted.

O-257 | Radiotherapy in Paediatrics: A Survey of International Patterns of Practice of Image Guided Radiation Therapy and Planning Target Volume

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Background/Objectives: Image guided radiation therapy (IGRT) is widely used in the treatment of various tumour types in both adult and paediatric patients and is intended to improve patient set-up. However, there are no international guidelines on its optimal use in paediatric radiotherapy. This study proposes to evaluate the current patterns of practice regarding the planning target volume (PTV) margin and IGRT policy in paediatric patients compared to adult patients through an international survey.

Design/Methods: A 9-item questionnaire was created to address IGRT protocols and PTV margins for paediatrics and adults in different tumour sites, Central nervous system (CNS), Head and Neck, Torso, Pelvis, and Others. International Paediatric Radiation Oncology Society (PROS) members were eligible to partake and were contacted via email.

Results: We received a completed response from 43 PROS members. Only 35-25% of centres have separate written IGRT protocols for paediatric and adult patients in different tumour sites. Only 38-32% of centres have a separate written PTV margin guidelines for adults and paediatrics in different tumour sites. For CNS as an example, 74% of participants stated that they use the same imaging frequency for both adults and paediatrics, 53% stated that they use the same scanning parameters for both adults and paediatrics and only 33% stated that they use different PTV margin in paediatrics.

Conclusion: Despite the extensive use of IGRT internationally, the majority of centres employ a series of site-specific protocols that fail to consider patient age or size. Given the desire to reduce radiation exposure in the paediatric patient cohort, further research is warranted to develop consensus guidelines on optimal IGRT use and PTV margin expansion.

O-258 | The Impact of Modern Technologies on Radiotherapy Toxicity in the Young Age. Review of a 10-year Literature

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Background/Objectives: Assessing the impact of modern radiation technologies in children and adolescents through literature with emphasis on the role of proton therapy (PT) in children, and adolescents.

Design/Methods: We performed an extensive review of published articles (A), from 01/2005 through 12/2015 through MEDLINE, according to the following key-words: Radiotherapy, English, Children, Toxicity (acute, late, sequelae), Novel technologies.

Results: 113 papers were selected, and classified in 3 groups: I] Pre-clinical studies: 37 A (dosimetrical: 15, mathematical models: 22). II] Clinical studies: 62 A, ranging from small (S<20 pts), to medium (M<50pts), large (L<100 pts), very large (VL<500pts), and extra-large (XL≥500 pts), totalizing 6,471 pts. III] Other studies: 13 A (economical: 3, general: 10).

In group I,II, and III, 73%, 50%, and 50% addressed the role of PT, respectively. In group II, most were retrospective (RE: 39/62), and of M size (20). None were randomized. All but a few pointed-out the superiority of PT, in terms of early/late toxicity. A subgroup of II, that

compared clinically, protons vs an alternative technique, represented 7 A, for a total of 1498 patients (pts): Mean/Mid F- up was 36 m in 6 A (1 group is NA). RE = 4/7 A. Brain ± Head & Neck: 5/7 A. Endpoints addressed were: Acute: 4/7 A, and late toxicity: 3/7 A. For acute toxicity, P > XR: 2 A, P=XR: 1A, P=C: 1 A. For late toxicity (neuro-psychological and K2): P > XR: 3/3 A. Unlike protons, the evaluation of other ion-species (such as carbon ions) in children remains anecdotal.

Conclusion: This literature review confirms the growing interest for modern RT technologies, esp. particle therapy, when toxicity is investigated. The proportion of clinical studies is becoming predominant compared with non clinical, although the proportion of comparative series with photon approaches remains low, and not in a randomized fashion.

O-259 | Facial Asymmetry in Head and Neck Rhabdomyosarcoma Survivors

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Background/Objectives: Radiotherapy is essential for achieving and maintaining local control in patients with head and neck rhabdomyosarcoma. However, radiotherapy may cause growth disturbances of facial bone and soft tissue, resulting in facial asymmetry (FA). The aim of this study was to develop a method to visualise and measure FA in survivors of head and neck rhabdomyosarcoma using three dimensional (3D) imaging techniques.

Design/Methods: Facial deformity was evaluated in a multi-disciplinary clinical assessment of 75 survivors of head and neck rhabdomyosarcoma. Local treatment consisted of the international standard: external beam radiotherapy (EBRT-based: London, n=26) or Ablative surgery, MOulage brachytherapy and REconstruction when feasible, otherwise EBRT (AMORE-based: Amsterdam, n=49). The clinical assessment of FA was graded according to the Common Terminology Criteria for Adverse Events. Individual FA was measured using 3D photogrammetry and expressed in a raw asymmetry index and a normalised sex-age-ethnicity matched asymmetry signature weight. FA was also compared between British and Dutch controls and between survivors and their matched controls.

Results: FA was more pronounced with increasing age (p<0.01) in British controls compared to Dutch controls (p=0.04). Survivors developed more FA than matched controls (p<0.001). The clinical assessment of facial deformity correlated with the raw asymmetry index (p<0.001). Survivors treated in the EBRT-based treatment group displayed more facial deformity than survivors treated in the AMORE-based treatment group (p=0.039) when assessed clinically.

Conclusion: 3D imaging can be used for objective measurement of FA in survivors of head and neck RMS. The raw asymmetry index correlated with a clinical assessment of facial deformity. Survivors of head and neck rhabdomyosarcoma exhibited more FA than healthy controls. However, comparisons between treatment groups seemed inappropriate given the differences in FA between British and Dutch controls. Possibly, pre-treatment images may serve as matched controls for post-treatment evaluation in future studies.

O-260 | A Comparison of PedsQL HRQoL Outcomes in Medulloblastoma Patients Treated with Modern Photon (XRT) or Proton Radiotherapy (PT)

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Background/Objectives: Comparative HRQoL outcomes in proton and photon treated cohorts are lacking. Here we compare the child-self-report (CSR) and parent-proxy-report (PPR) PedsQL HRQoL Core scores in contemporary (2004-2014) proton-treated (PT) and photon-treated (XRT) cohorts.

Design/Methods: In the proton cohort, medulloblastoma patients were enrolled on a prospective HRQoL protocol and assessed with PedsQL annually if NED; the latest available follow-up survey was used for analysis. In the photon cohort, medulloblastoma survivors were administered the PedsQL Core survey in a cross-sectional study design. Mean scores in both groups were compared using student's t-test. Then subgroups by age (<8 v. 8+), boost volume (TB v. WP), posterior fossa syndrome (PFS, yes/no), sex, and M-stage(M0v.M+) were compared between by modality.

Results: There were 73 patients (69 CSR, 71 PPR) in the proton cohort and 52 (45 CSR, 35 PPR) in the photon cohort. Median PT follow-up was 4.0 (1.0-10.0) years and median XRT follow up was 5.9 (1.3-11.6) years. Proton PPR report Total-Core-Score(TCS) of 69.3 and XRT PPR report scores of 53.1 (p<0.001). Proton children report TCS of 76.0 and XRT children report scores of 63.3 (p<0.001). Proton children report TCS of 7.8 points lower than US healthy control children (p<0.001); whereas proton parents report 13.4 points lower than controls (p<0.001). Photon children report TCS 20.6 points lower than UK controls (p<0.001); whereas parents report 31.5 points lower than UK controls (p<0.001). PedsQL subscores (physical/psychosocial) and affects of the clinical variables will be reported at the meeting.

Conclusion: In this comparison of contemporarily treated proton and photon children with medulloblastoma, TCS QoL outcomes appear better in children treated with proton radiotherapy in both child and parent proxy reports. However, both cohorts score lower than the US healthy control population.

ACUTE LYMPHOBLASTIC LEUKAEMIA

PD-001 | Components of the Metabolic Syndrome in Children with Acute Lymphoblastic Leukemia Treated with Dexamethasone

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Background/Objectives: Dexamethasone, a highly effective drug in the treatment of paediatric acute lymphoblastic leukaemia (ALL), can induce serious metabolic side effects. We prospectively studied the direct effects of dexamethasone administration on all components of the metabolic syndrome (MetS) in children with ALL, and investigated whether these side effects were dependent on dexamethasone levels.

Design/Methods: Fifty patients (3-16 years of age) with ALL were included, and were studied during one 5-days dexamethasone course (6 mg/m²/day) in the maintenance phase of the Dutch Childhood Oncology Group ALL-10 and ALL-11 protocol. Fasting insulin, glucose, total cholesterol, HDL, LDL, triglycerides levels, and anthropometric parameters were measured at baseline before start of dexamethasone (T1), and at day 5 (T2). Dexamethasone trough levels were measured at T2.

Results: Dexamethasone administration significantly increased median fasting serum levels of HDL (1.42 versus 1.55 mmol/L, P=0.00), LDL (2.55 versus 2.76 mmol/L, P=0.00), total cholesterol (4.20 versus 4.60 mmol/L, P=0.00), triglycerides (0.86 versus 1.09 mmol/L, P=0.04), glucose (4.4 versus 4.7 mmol/L, P=0.00) and insulin (25.2 versus 216.5 pmol/L, P=0.00). Insulin resistance (HOMA-IR>3.4) increased from 8% to 85% (P=0.00). Dexamethasone also significantly increased diastolic and systolic blood pressure SDS. Dexamethasone trough levels (N=24) were positively correlated with high glucose levels at T2, but not with other parameters.

Conclusion: We conclude that dexamethasone induces metabolic toxicity on all components of the MetS, already within four days of treatment. These findings, together with the wide variety of dexamethasone levels and its correlation with toxicity, suggest that further studies are needed aiming at individualization of treatment and dosing.

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PD-002 | Killer Cell Immunoglobulin Like Receptor (KIR) Polymorphism in Childhood Acute Lymphoblastic Leukemia: Homozygous KIR2DS4*FUL Has Susceptible and KIR2DS4*DEL A Protective Effect

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Background/Objectives: KIR via interaction with HLA-class-I ligands has a role in modulating the NK cell mediated immune surveillance and cytotoxicity. A role of KIR in pathogenesis of ALL is increasingly being reported; the association is varied and conflicting. An investigation of KIR gene distribution in ALL is presented.

Design/Methods: Patients (≤13-years) with ALL and healthy controls were enrolled. Genomic DNA was extracted from peripheral blood. KIR genotyping was performed by polymerase chain reaction using sequence-specific primer assay. The investigated KIR genes included: inhibitory (2DL1, 2DL2, 2DL3, 2DL4, 2DL5A, 2DL5B), activating (2DS1, 2DS2, 2DS3, 2DS4*FUL, 2DS4*DEL, 2DS5, 3DL1, 3DL2, 3DL3, 3DS1) and pseudogenes (2DP1, 3DP1*FUL, 3DP1*DEL). The frequency of KIR genes was obtained by direct counting and the significance determined by chi-square or Fisher's exact test. The significance was adjusted with Bonferroni correction.

Results: One hundred cases (B-ALL: n=92, T-ALL: n=8) and an equal number of controls were enrolled. Of the 19 KIR loci analyzed, a significant difference in cases as compared to controls was observed at 2DS4 locus. The homozygous KIR2DS4*FUL gene was upregulated in cases (p=0.0057). The frequency of KIR2DS4*DEL (homozygous as well as heterozygous) was reduced in cases (p=0.0019). No correlation was observed between KIR genes with age, white cell count, Day-14 bone marrow status or B versus T lineage ALL. Fifty-eight KIR genotypes were identified. None of the genotypes had a varied distribution except for BX-ID6, which was downregulated in patients (p=0.042).

Conclusion: The study highlights novel findings with respect to the role of KIR2DS4 locus in ALL. A susceptible and a protective effect of homozygous KIR2DS4*FUL and KIR2DS4*DEL allele, respectively was observed. Larger studies addressing KIR frequency in different ethnic populations are warranted to better define the role in leukaemogenesis. The association of KIR genes with childhood ALL will provide direction on developing therapeutic strategies for enhancing NK cell activity.

PD-003 | CDKN2A/CDKN2B as a Hotspot for Acute Lymphoblastic Leukemia Susceptibility in the Spanish Population

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Background/Objectives: Acute lymphoblastic leukaemia (ALL) is the most common childhood malignancy in children. A genetic basis of ALL susceptibility is supported by genome-wide association studies (GWAS) findings. Two GWASs independently identified variants in *ARID5B*, *IKZF1* and *CEBPE* genes associated with ALL risk, results that have been validated by several groups. A following work discovered an additional susceptibility variant in *CDKN2A/CDKN2B* locus. In this case, subsequent studies have also validated this result, but others were unable to replicate the association. In *CDKN2A/B* locus, other studies have found different variants in this locus associated with ALL risk. Thus, it is possible that different variants in the region are related to ALL risk. Therefore, the aim of this study was to determine the effect of SNPs at the *CDKN2A/CDKN2B* locus in a Spanish population.

Design/Methods: Blood samples of 217 paediatric patients with B-cell ALL in complete remission and 330 healthy controls of Spanish origin were analyzed. A total of 8 SNPs in this locus were selected. VeraCode GoldenGate platform was used.

Results: We studied a total of 8 SNP which give information of a total of 46 SNPs at the locus. From them, in a preliminary study, we found 3 SNPs significantly associated with B-ALL risk, rs2811712 located in *CDKN2B-AS1* ($p=0.0001$), rs3217992 in *CDKN2B* and *CDKN2B-AS1* ($p=0.009$) and rs2811709 in *CDKN2A* ($p=0.014$). rs2811712 and rs2811709 have been previously reported in association with B-ALL susceptibility in 4 studies.

Conclusion: These results provide evidence for the influence of genetic variants at *CDKN2A/CDKN2B* locus with the risk of developing B-ALL.

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PD-004 | Longitudinal Assessment of Neuropsychological Functioning in Children with Acute Lymphoblastic Leukemia (ALL) Treated Within the Children's Oncology Group

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Background/Objectives: Children receiving treatment for ALL are at risk for neurocognitive deficits, which can impact their overall functioning. Tracking and predicting neuropsychological change in individual patients can be difficult. Within COG, we are evaluating the combination of two assessment strategies to better characterize the onset and trajectory of cognitive changes during treatment for paediatric ALL: a brief, standardized, psychologist-administered battery (60-80 minutes); and a short (20-30 minutes) computerized monitoring battery (CogState) administered by medical staff in clinic.

Design/Methods: Children diagnosed with high-risk ALL at ages 6-11 years and enrolled on a COG phase III ALL trial (AALL1131) complete CogState and a parent-reported measure of executive functioning (BRIEF) at five (girls) or six (boys) time points from the end of Consolidation through one year off therapy. Children are also asked to participate in the psychologist-administered battery, administered 9-, 30-, and 60-months post-diagnosis.

Results: To date, 325 of 464 (70.0%) eligible patients from 155 sites have enrolled (47.1% female, mean age at diagnosis = 9.22 years). Over 550 medical staff have completed online training to administer Cogstate in clinic. Data collection averages 85.4% (range 77-94%) across time points. Of those evaluated thus far, 16% exhibit a deficit (> 1.5 SD below mean) in processing speed and 15% in sustained attention three months post-diagnosis ($n = 245$); those percentages increase to and 28% and 31%, respectively, among participants who have reached the fourth evaluation approximately two years later ($n = 75$).

Conclusion: Data suggest that a multi-site trial using computerized assessments of children by medical staff in clinic is feasible. The current approach may serve as a model for recruiting large, diverse samples, and for providing a cost-effective, low-burden method for ascertaining the trajectory of deficits and identifying emergent problems. Ongoing work is examining the feasibility of similar work with psychologist administered tests after treatment ends.

PD-005 | Posterior Reversible Encephalopathy Syndrome in Children with Acute Lymphoblastic Leukemia

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Background/Objectives: Posterior reversible encephalopathy syndrome (PRES) in children with acute lymphoblastic leukaemia (ALL) is an increasingly recognized clinicoradiological entity. Clinically, it is characterized by seizures, headache, altered mental status and visual impairment. Typically, it visualizes as bilateral, subcortical and/or cortical vasogenic edema in magnetic resonance imaging (MRI).

Design/Methods: Our aim was to describe the incidence of PRES in a population based series of paediatric patients with ALL ($n=643$) treated in Finland during 1992-2008. Patients received fairly similar first line leukaemia treatment. We identified the risk factors that predispose these patients to PRES, described the clinical features and determined the prognostic importance of PRES.

Results: Of the patients with ALL, 4.5% ($n=29$) developed radiologically confirmed PRES. Hypertension ($p<0.0001$), constipation ($p=0.006$) and long duration of alkalinisation ($p=0.001$) appeared to be significant and independent risk factors for PRES. Clinically, typical preceding symptoms were a triad of constipation, hypertension and hyponatremia. All patients presented with seizures. Over half of the patients experienced short-term seizures, one third developed epilepsy either directly or after a delay. Liver-inducing antiepileptic drugs were given to twelve patients. Relapses occurred significantly more often in patients with PRES and PRES ($p=0.003$) showed to be an independent risk factor for a relapse in multivariate analysis.

Conclusion: We found a slightly higher incidence of PRES than previously reported. The association between PRES and an increased risk of relapse is a new finding, and thus, further systematic prospective studies are needed.

PD-006 | Allergic-Like Reactions to Asparaginase: Atypical Allergies Without Asparaginase Inactivation

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Background/Objectives: Asparaginase is an important component of acute lymphoblastic leukaemia therapy in children. Unfortunately, this treatment is hampered by hypersensitivity reactions, which neutralize asparaginase activity. In general, allergic reactions cause complete inactivation of the drug, regardless of the severity. However, here we report atypical allergic reactions to asparaginase without inactivation of asparaginase, also called allergic-like reactions.

Design/Methods: We described patients with an allergic-like reaction to asparaginase, who were treated according to the Dutch Childhood Oncology Group ALL-11 protocol or the CoALL 08-09 protocol. The reactions were identified by continuous measurement of asparaginase activity levels. Clinical characteristics, including timing of occurrence, symptoms, grade and the presence of anti-asparaginase antibodies, were compared to those of real allergies.

Results: Fourteen allergic-like reactions occurred in nine patients. Five reactions were to PEGasparaginase, nine to *Erwinia* asparaginase. Allergic-like reactions occurred relatively late after the start of infusion (median, 25-75 percentile: 29, 12-47 minutes) compared to real allergies (2, 1-5 minutes) ($p<0.001$). Anti-asparaginase antibodies were absent in all but one patient with an allergic-like reaction while they were detected in all patients with a real allergy ($p=0.001$). Symptoms and grade did not differ between the groups. Asparaginase was continued with the same formulation in six patients of whom four finished treatment with adequate asparaginase levels.

Conclusion: In conclusion, allergic-like reactions occur relatively late without antibody development in most patients. Despite of these clinical differences, allergic-like reactions can only be distinguished from real allergies by continuously measuring asparaginase activity levels. If clinically tolerated, formulations should not be switched in case of an allergic-like reaction. Moreover, failure to recognize these reactions may lead to a less favourable prognosis when second line asparaginase therapy is terminated unnecessarily.

BONE TUMOURS

PD-007 | NKG2D Car Redirected T Cells Target Osteosarcoma Cells

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Background/Objectives: Metastatic osteosarcoma has a 5-year survival rate of less than 20%. Current combined surgical and neo-adjuvant chemotherapy are ineffective. One of the main NK cell activating receptors is NK cell group 2D (NKG2D). NKG2D receptor recognizes human MICA/ULBP1-6 ligands. These NKG2D ligands are expressed in osteosarcoma cells and constitute suitable targets for immunotherapy.

Design/Methods: Peripheral blood mononuclear cells from healthy donors were labelled with CD45RA microbeads and depleted using CliniMACS device. The HL20i4r-MNDantiCD19bbz lentiviral vector were derived from the clinical vector CL20i4r-EF1a-hgcOPT27 but contained the extracellular domain of NKG2D, the hinge region of CD8a and the signalling domains of 4-1BB and CD3-z. The cassette was driven by MND promoter. Viral supernatant was produced by transient transfection of HEK293T cells with the vector genome plasmid and lentiviral packaging helper plasmids: pCAGG-HIVgpc, pCAGG-VSVG and pCAG4-RTR2. To evaluate the *in*

in vitro cytotoxicity of NKG2D CAR expressing CD45RA⁺ T cells against 531MII osteosarcoma cells, conventional 4-hour europium-TDA release assays were performed. For the *in vivo* orthotopic model, 531MII YFP-luc osteosarcoma cells were used as target in NOD/scid IL2rgnull mice.

Results: Lentiviral transduction of NKG2D-4-1BB-CD3z markedly increased NKG2D surface expression in CD45RA⁺ T cells, which became consistently more cytotoxic than untransduced cells against osteosarcoma cell lines. NKG2D-4-1BB-CD3z expressing T cells had considerable antitumor activity in a mouse model of osteosarcoma, whereas untransduced T cells were ineffective.

Conclusion: Our results demonstrate NKG2D-4-1BB-CD3z CAR redirected T cells target NKG2DL expressing osteosarcoma cells both *in vivo* and *in vitro* and could be a promising immunotherapeutic approach for osteosarcoma patients.

PD-008 | Denosumab Treatment in Aneurysmal Bone Cysts: Evaluation of Eleven Cases

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Background/Objectives: Aneurysmal bone cysts (ABC) are benign bone tumors. Curettage followed by bone grafting is the common treatment which may, especially in certain locations, lead to severe morbidity. After its pathogenesis has become better understood, denosumab treatment has been reported in several ABC cases. Here, we report results of denosumab treatment in our ABC cases.

Design/Methods: Eleven patients treated with denosumab were evaluated retrospectively. Radiological and histopathological evaluation was performed in all cases. In four cases, denosumab was begun after other medical and/or surgical treatments while it was first line treatment in seven patients. A 70 mg/m² denosumab dose was used weekly in the first months, then monthly. Calcium and vitamin D maintenance were given throughout treatment. Clinical and radiological responses were evaluated every three months and side-effects were noted.

Results: There were seven boys and four girls with a median age of 142 (24-204) months. Most common symptoms were pain and swelling. Tumour location was vertebrae in three patients, pelvis in three, maxilla and mandible in three, femur and humerus in the remaining two. Longest axis of tumors varied between 3.7 and 15 cm (mean: 6.7±3.9). Denosumab was given in median 12 (9-15) doses. In all patients except one, clinical symptoms decreased in the first month and regressed within three months. Radiological evaluation revealed minor changes (sclerosis and reduction in cystic contents, contrast involvement and pathological signals) in six patients, 15%-60% reduction in size in five patients. There was no toxicity.

Conclusion: Denosumab, a monoclonal antibody that binds to RANK-ligand, inhibits bone resorption. It is used in the treatment of osteoporosis and recently in the treatment of giant cell tumors of bone. Our results showed that denosumab may be a treatment option especially in cases with spinal and pelvic tumors that might have high surgical morbidity.

PD-009 | Non- High Dose –Methotrexate (HD-MTX) Based, Dose-Dense (DD), Combination, Chemotherapy(CT) in 243 Non-Metastatic Osteosarcoma Patients: A Tertiary Care Centre Experience from India

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Background/Objectives: There is still no worldwide consensus on a standard chemotherapy approach in osteosarcoma. DD CT has proven superiority in other solid tumours. Considering, mandatory complex pharmacokinetic monitoring in in-patient setting, unpredictable toxicity and cost of therapy of HD-MTX, Non-HD-MTX based, DD, combination CT merits exploration.

Design/Methods: This prospective study evaluated OGS-12 regimen comprising DD-CT with Doxorubicin, Ifosfamide, & Cisplatin. Histological response (HR) to chemotherapy, survival and toxicity analysis was carried out for outcome measures. Baseline parameters were correlated with outcomes and toxicity.

Results: Between 2011-2014, 326 eligible patients were enrolled of which 243 (74%) were non-metastatic. Median age was 18 (6-65) years; 170 (70%) were males. The disease is biologically aggressive (mean LDH size = 11cm, 55% & 98% had high LDH & SAP); and nutritionally compromised population(at presentation, 74% had abnormal BMI, 54% were iron & 37% were vitamin-B12 deficient,38% anaemic).

Out of 214 analysable patients 124 (59%) had good histological response(100%=19%). At a median follow-up of 25(1-51) Months,median overall-survival(OS) and disease-free -survival(DFS) was not attained; mean OS & DFS were 47(45-48) & 40 (38-42) months respectively. Estimated 3 year OS & DFS is 87% & 68%. Median post relapse survival is 17 (13-20) months. The protocol was well tolerated; significant Grade 3/4 toxicity were febrile Neutropenia(FN)-27%, Thrombocytopenia-24%, anaemia-48%, cardiotoxicity-3%. There were 2/243(0.8%) chemotoxic deaths.

In Univariate analysis, ECOG performance status, lesion size, HR, baseline SAP, and albumin were significantly associated with OS; In uni & multivariate analysis, SAP, tumour site and HR were identified as independent predictors for DFS.

Conclusion: Non-HD-MTX based, DD, OGS-12 regimen has shown efficacy, feasibility and cost-effectiveness in nutritionally compromised and biologically aggressive osteosarcomas, without complex monitoring and inpatient treatment in real world scenario.

While conventional prognostic markers were re-established, identified novel prognostic markers like serum albumin, merits further exploration for reproducibility.

PD-010 | The Role of Mifamurtide in Chemotherapy-Induced Osteoporosis of Children with Osteosarcoma

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Background/Objectives: The bone metabolism is disturbed during therapy in children with osteosarcoma(OS), resulting in a reduced body mineral density (BMD) with respect to healthy controls. Since a reduced BMD predisposes to osteoporosis, specific attention and therapeutic interventions should be considered.

The immunomodulator mifamurtide (liposomal-muramyl-tripeptide-phosphatidyl-ethanolamine, L-MTP-PE) has given together with standard adjuvant chemotherapy in high-grade (OS) patients to improve outcome in this disease. L-MTP-PE acts activating macrophages and monocytes.

The aim of this study was to evaluate the role of mifamurtide on macrophage component of bone, the osteoclasts (OCs), during chemotherapy in children with osteosarcoma.

Design/Methods: OCs were obtained from peripheral blood mononucleate cells (PBMC) of healthy donors and OS patients at onset or during chemotherapy.

We studied the effects of L-MTP-PE on pro-osteoporotic [acid phosphatase tartrate-resistant (TRAP), phosphokinase-β-2 (PKCβ2), vanilloid receptor type 1 (TRPV1)] and anti-osteoporotic [cannabinoid receptor type 2 (CB2)] biomarkers of OCs by bio-molecular (qPCR), biochemical (Western blotting), and morphological (TRAP assay) approaches. Molecular and biochemical data are shown as means ± standard deviation. Categorical variables are evaluated by a chi-squared test. Continuous variables are evaluated by Student-Neuman-Keuls post hoc test. p < 0.05 is considered statistically significant.

Results: OCs from OS patients show an increase of pro-osteoporotic biomarkers and a decrease of CB2 respect to OCs from healthy donors.

This OCs hyperactivity is more evident in OCs from OS patients during chemotherapy.

L-MTP-PE reduces TRAP, PKCβ2, TRPV1 levels and increases CB2 levels in dose-dependent manner in OCs from healthy donors.

Moreover, L-MTP-PE reverts chemotherapy-induced effects on OCs activity markers.

Conclusion: Our data suggest a possible new therapeutic role for L-MTP-PE as anti-resorption agent in chemotherapy-induced osteoporosis in children with OS.

PD-011 | Cancer Predisposition in Diamond Blackfan Anemia (DBA): The Role of Ribosomal Protein (RP) Haploinsufficiency in Osteogenic Sarcoma

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Background/Objectives: DBA is an inherited bone marrow failure syndrome characterized by red cell aplasia, congenital anomalies and cancer predisposition. DBA is caused by haploinsufficiency of one of the small or large rp. We found one of the common malignancies in DBA to be OS. This led us to hypothesize that defective osteoblast formation, studied *in vitro* using a mouse embryonic stem (mES) cell model haploinsufficient for ribosomal protein Rps19, may be a selective pressure resulting in OS.

Design/Methods: The DBA Registry of North America (DBAR) was interrogated to quantitate the incidence of cancer. For *in vitro* studies, mES cells were differentiated towards osteoblasts using 1, 25-dihydroxy-vitamin D3, dexamethasone, ascorbic acid and β-glycerophosphate for 10 days. qRT-PCR and histologic stains assessed osteoblast production in wild type and Rps19^{+/−} cultures.

Results: The DBAR previously reported the cancer incidence with significantly elevated observed to expected ratio of 33 for OS. As of March 2016 (N=702), with a median patient age of 20yr7mo, 5 patients with OS are reported. The incidence of OS is highly significant. This in concert with the poor skeletal growth encountered in DBA patients led us to examine *in vivo* osteoblast differentiation. We observed reduced mineralization and bone formation from Rps19^{+/−} mES cells. Rp haploinsufficient cultures displayed a significant increase a marker for chondrogenesis; these results suggest that regulation of osteochondrogenic potential was altered. The qRT-PCR analyses revealed that Rps19 haploinsufficiency induced abnormal expression of the master transcription factors and p53 involved in osteoblast and chondrocyte development.

Conclusion: OS is a common cancer in DBA. The defective osteoblast differentiation demonstrated in our model is a likely selective pressure for malignant transformation. We have recently created a conditional Rps19 haploinsufficient CRISPR murine model, in order to clarify the contribution of both rp and p53 in the etiology of faulty bone formation and OS.

PD-012 | PET/CT or PET/MR in Paediatric Tumors?

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Background/Objectives: Reliable imaging is an essential requirement for the disease management especially in paediatric cancer patients. Hybrid imaging with (F-18) fluorodeoxyglucose (FDG) has been included in routine diagnostics and staging of many solid and hematologic tumour entities. In paediatrics, the goal of minimizing diagnostic radiation exposure is well acknowledged. The aim of the study was to evaluate the comparability of PET-CT and PET-MR in a cohort of paediatric and young adult cancer patients regarding lesion detection and radiation exposure.

Design/Methods: 23 patients (11 Ewing Tumour, 3 Osteosarcoma, 3 Synovialsarcoma, 3 Rhabdomyosarcoma, and 3 not classifiable sarcoma) were included in this study (17 male, 6 female; age 6 to 26 years at initial diagnosis; median 15 yrs). Patients underwent a single injection dual imaging protocol with F-18-FDG, followed by a PET-CT and PET-MR consecutively (PET/CT Siemens Biograph mCT[®]; PET/MR Siemens Biograph mMR[®]). 42 PET-CT and PET-MR examinations could be evaluated.

Results: PET-quality of both imaging methods (CT vs. MR) were comparable. Quantitative evaluation (5 point scale) showed a similarity between the suspicious lesions of the initial examinations with PET/CT (n=29) or PET/MR (n=26). Radiation exposure will be analyzed.

Conclusion: The study demonstrates that sensitivity of PET-MR in lesion detection is comparable with sensitivity of PET-CT suggesting that PET-MR represents a radiation-reduced alternative to PET-CT combining the high sensitivity of F-18-FDG PET to pinpoint areas with the dominant disease activity and the specificity of MRI for the detection and follow up of primary and metastatic lesions.

Authors Ginter and Schlegel contributed equally and the authors von Luettichau and Scheidhauer contributed equally.

BRAIN TUMOURS

PD-013 | The Ophthalmologic Recommendations for Standardized Visual Assessment and Treatment Indications within the Next Siop-Lgg (LOGGIC) Trial Including Children with Visual Pathway Glioma

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Background/Objectives: Visual function is the relevant functional measure in childhood visual pathway glioma (VPG). Lack of agreement on assessment methodology has resulted in incomplete/inaccurate SIOP-LGG 2004 ophthalmologic data.

Design/Methods: The next SIOP-LOGGIC trial will evaluate visual function as primary outcome in childhood VPG. Therefore it is essential to standardize assessment methods to obtain reliable data and compare treatment effects. We present results of multidisciplinary expertise defining recommendations (Ophthalmologic-LOGGIC).

Results: Visual acuity (VA) is the only mandatory parameter in childhood VPG. It should be tested monocularly, age-specific and under ideal conditions/corrections. Best & worst eye data should be reported in logMAR, ranging from normal (0.0) to no light perception (3.0).

At diagnosis, severe visual symptoms constitute additional criteria for starting treatment: either unilateral (severe deficit one eye) OR bilateral threat to vision (moderate deficit worst eye AND abnormal best eye). Non-functional (blind) eyes are not treated (unless bilateral threat).

After initial observation visual worsening is defined as unequivocal VA decline (logMAR increase ≥ 0.2), excluding refractive errors, amblyopia or other non-visual causes. Retest within 1-2 weeks is mandatory before treatment. Stable VA over time in young children (< 4 yrs.) may constitute lack of visual maturation and thus VA worsening. Visual fields (VF) are clinically relevant parameters. However poor collaboration (< 5 yrs.) and lack of instrument availability (Goldmann or Humphrey) may restrict their use. Optical coherence tomography (OCT) as objective tool to assess neuroretinal morphology and predict visual function should be prospectively validated. Other ophthalmologic parameters are recorded as exploratory. Visual related quality of life questionnaires (CVFQ) will be secondary outcome. Furthermore expert panel of ophthalmologists will be available to assist data interpretation.

Conclusion: Specific recommendations are composed for next SIOP-LOGGIC trial with potential consultation of an expert team in order to produce reliable visual data which can be related to effects of tumour and therapy.

PD-014 | Cribriform Neuroepithelial Tumour (CRINET): A SMARCB1-Deficient Non-Rhabdoid Tumour Sharing Molecular Similarities with the ATRT-TYR Subgroup but Showing Favorable Long-Term Outcome

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Background/Objectives: Rhabdoid phenotype and loss of SMARCB1 expression are characteristic features of atypical teratoid/rhabdoid tumors (ATRT). Rare non-rhabdoid brain tumors showing cribriform growth pattern and SMARCB1 loss have been designated cribriform neuroepithelial tumour (CRINET). Small case series suggest that CRINET may have a relatively favorable prognosis. However, the long-term outcome is unclear and it remains uncertain whether CRINET represent a distinct molecular entity or a variant of ATRT.

Design/Methods: Ten CRINET were clinically and molecularly characterized and compared with ATRT of each of three previously published molecular subgroups (i.e. ATRT-TYR, ATRT-SHH and ATRT-MYC) using Illumina Infinium HumanMethylation450 arrays, FISH, MLPA, and sequencing.

Results: Median age of the 6 boys and 4 girls harboring a CRINET was 20 months (range 10-129 months). On histopathological examination, all CRINET demonstrated a cribriform growth pattern and distinct tyrosinase staining. On unsupervised cluster analysis of methylation data, all CRINET examined clustered with the ATRT-TYR subgroup. CRINET mainly showed large heterozygous 22q deletions. As a second hit, SMARCB1 point mutations were encountered, their distribution across the nine exons of SMARCB1 being also remarkably similar to ATRT-TYR. An exon 9 missense mutation (c.1142C>G p.Thr381Arg), and an exon 6 duplication, respectively, were also demonstrated in the germline. Estimated overall survival of patients with CRINET was 125 months (95% confidence interval 100-151 months) and thus significantly longer as compared to 27 patients of the ATRT-TYR subgroup (Log-Rank P<0.05).

Conclusion: CRINET represents a SMARCB1-deficient non-rhabdoid tumour sharing molecular similarities with the ATRT-TYR subgroup, but has a favorable long-term outcome.

PD-015 | Incidence of Brainstem Injury in Paediatric Patients with Posterior Fossa Tumors

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Background/Objectives: Proton radiotherapy is commonly used in young children with brain tumors for their potential to spare late effects. However, some proton series report higher rates of brainstem injury (0-10.8%) than photon series (2.5-6.7%). Here we report the incidence of brainstem injury and risk factor analysis in paediatric patients with posterior fossa (PF) primary tumors treated with proton radiotherapy.

Design/Methods: 239 consecutive patients treated at our institution between 2000-2015 were included. Dosimetry was collected on plans after 2005 and was included for earlier plans when restorable. Grade 2-4 late brainstem toxicity was assessed by NCI CTCAE v4.0.

Results: Histologies include medulloblastoma (169, 70.7%), ependymoma (63, 26.4%), and ATRT (7, 2.9%). Median age at radiation: 6.7 years (range:0.5-23.1), dose: 54 GyRBE (range:46.8-59.4) and follow-up: 3.0 years (range:0.1-14.7) among 222 survivors. 80.8% received chemotherapy; 73.2% achieved GTR. The crude rate of injury was 1.3% in all patients, 1.8% in medulloblastoma, and 0%/0% in ependymoma/ATRT patients. The 3-year cumulative incidence of injury is 1.1% (95% CI:0.2-3.6%). Median brainstem dose in the whole cohort was D50: 53.6 GyRBE (range:2.6-56.8), Dmax: 55.1 GyRBE(17.7-58.3), mean: 50.4 GyRBE (10.1-56.7). In the three patients with injury, median D50: 54.7 (range:51.0-55.1), Dmax: 55.9 (55.0-56.2), mean: 52.9 (45.4-54.4). In two of three patients with injury, brainstem dose was in the highest quartile of the cohort. All patients with injury were older (age range:6.2-22.8), received chemotherapy and achieved GTR. Formal statistical analysis is limited by the minimal power due to the few events.

Conclusion: The incidence of injury of paediatric patients with PF tumors is consistent with previous reports in the photon setting and is relatively rare when D50 and Dmax is kept below 56.8 and 58.3 GyRBE, respectively.

PD-016 | Developing Risk-Based Selection Criteria for the Next SIOP Trial of "Sight-Saving Therapy" for Children with NF1-Associated Optic Pathway Glioma (NF1-OPG) – A Case-Based Consensus Survey

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Background/Objectives: In the 2014 SIOP-e NF1 OPG Nottingham Workshop clinical data from 9 European trial centres (Berlin, Copenhagen, GOS, Hamburg, Leeds, Nottingham, Padua, Paris, Vienna) identified 83 NF1-OPG cases which were studied to inform a consensus on imaging and visual function classification and a schematic for recording visual acuity results.

The objective is to develop a consensus questionnaire regarding eligibility criteria for a randomised trial of NF1-OPG patients, using age, visual acuity and anatomical site criteria to select cases by voting on their selection for suitability of either 1) immediate treatment with systemic chemotherapy; 2) 'watchful wait' with a treatment threshold of 0.2 LogMAR loss, or 3) randomisation between treatment and 'watchful wait'.

Design/Methods: The web-based questionnaire consisted of 10 cases requesting a management decision and justification from medical professionals in multi-disciplinary teams. The questionnaire was piloted in the European trial centres, and then distributed to members of the SIOP-E brain tumour group, European NF1 society and 25 institutions participating in a large NF1 OPG natural history study primarily based in North America.

Results: Ninety-six respondents (65 European and 31 North American) identified with $\geq 70\%$ agreement the selection of 5 cases for immediate treatment (2 cases < 2 years of age with unilateral vision LogMAR > 0.5 and 3 cases 2-5 years with bilateral vision loss LogMAR > 0.5). One case aged 5-10 years with bilateral LogMAR ≤ 0.5 for 'watchful wait'. Consensus was not achieved in four patients where up to 37% suggested they would be eligible for randomisation. Sub-analysis showed that there was no significant difference in treatment decision-making between European and North American respondents.

Conclusion: The identification of a consensus supporting immediate randomisation offers a new era of trial to study the case selection strategy for 'sight-saving' therapy as well as efficacy of the trial drugs.

PD-017 | Clinical Characteristics of Patients with Germline *SUFU* Mutations

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Background/Objectives: Germline mutations of the *SUFU* gene have recently been described in association to medulloblastoma. Only a few cases have been described in literature so far.

Design/Methods: We performed a retrospective review of the clinical and molecular data of all patients in whom a germline *SUFU* mutation had been diagnosed in Gustave Roussy and Institut Curie genetics laboratories.

Results: 21 probands had a germline *SUFU* mutation. Nineteen patients were diagnosed with a medulloblastoma at a median age of 18 months [range 1-35] (desmoplastic=9, extensive nodularity=6, classical=4). Two others patients were tested because of a familial history of medulloblastoma and criteria for a Gorlin syndrome without germline *PTCH* mutation. Macrocrania was frequently documented. Medulloblastoma in siblings or early death from brain tumour were described in several families. Mutations were inherited in 12/13 patients whose parents underwent genetic testing and de novo in 2 cases. Thirty-six healthy carriers have been identified.

Second malignancies were described in 3 medulloblastoma patients including basocellular carcinomas (CBC) (1pt), ovarian tumour and meningioma (1pt) and thyroid carcinoma (1pt). Several others cancers including early breast cancer and sarcomas were diagnosed in mutation carriers.

Conclusion: *SUFU* germline mutations predispose to medulloblastomas mostly of desmoplastic/nodular or extensive nodularity subtypes during the first 3 years of life, often associated with macrocrania. The incidence of CBC seems lower than in classic Gorlin syndrome. Due to incomplete penetrance, genetic counselling is difficult. International collaboration is necessary in order to better define the risk associated with these mutations and guidelines for surveillance.

PD-018 | High-Throughput Screening of Novel Histone Deacetylase Inhibitors for Epigenetic Therapy of Primary Brain Tumors

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Background/Objectives: Histone deacetylases (HDACs), key players of epigenetic and post-translational modification, represent a promising therapeutic target in cancer harboring distinct epigenomes from normal cells. In order to develop novel HDAC inhibitors (HDACi) as therapeutics, a unique in-house library of more than 200 HDACi was synthesized. To evaluate the antitumor effects of this library in brain tumour models, an optimal screening workflow was successfully established.

Design/Methods: The screening procedure was improved by automated dispensing of cell lines and reagents using the Multidrop Combi Reagent Dispenser (Thermo Scientific) and HDACi using the D300e Digital Dispenser (Tecan). We screened a panel of cell lines derived from different brain tumour entities (including 8 glioblastoma, 10 medulloblastoma and 6 atypical teratoid/hobbit tumour cell lines) and 5 normal control tissues. The HDACi were evaluated for their effect on tumour cell viability. Subsequently, corresponding dose-response profiles were generated using an in-house bioinformatics pipeline. Additionally, commercially available and clinically used HDACi (e.g. Vorinostat, Entinostat) were included as positive controls.

Results: The optimized pipeline allowed us to upscale the assay format from 96- to 384-well plates. Combined with additional modifications of the workflow, the overall throughput was remarkably increased, saving time and consumables, while generating accurate and reproducible results. We created a unique and comprehensive data set and could thereby identify various HDACi universally effective across brain tumors or specifically active in distinct tumour entities. Promising candidates are currently further characterized, including e.g. Panobinostat, which showed activity in the vast majority of brain tumour models at nanomolar concentrations.

Conclusion: HDAC inhibitors are increasingly evaluated in different tumour entities and clinical trials, with four HDACi already approved by the Food and Drug Administration for treating lymphomas and multiple myelomas. Our study demonstrates that HDACi are valid therapeutic agents and that selected inhibitors are promising candidates for future epigenetic therapy of primary brain tumors.

PD-019 | Adult Survivors of Childhood CNS Tumours: Self-Perceived Most Prominent Illness- and Treatment-Related Late Effects, Severity of Sequelae, and Surveillance Needs

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Background/Objectives: As part of the longitudinal Swedish childhood CNS tumour LIFE study, this study aimed at identifying self-perceived most prominent late-effects (SPLEs) among very long-term survivors (VLTSS), and the extent to which sequelae were experienced as disabling. SPLEs were examined in relation to self-perceived needs of, and current involvement in clinical follow-up.

Design/Methods: Study targeted the entire cohort of 706 Swedish 24-46 years old (mean=32) VLTSS diagnosed 1982-2001. SPLEs data were collected using a study-specific questionnaire in the second wave of data collection, while single predictor factor data emanate from prior wave, 7 years earlier. SPLEs were addressed in open-ended questioning format, for free unsteered information, and survivors' subjective perception of importance and severity of sequelae, aiming methodically at increased understanding of subject. Analyses were quantitative and qualitative.

Results: Three hundred thirty, 65.7%, of 507 data-providing survivors, reported prevalence of one to several SPLEs. Sixteen identified problem categories, experienced by >20 survivors, covered a range of SPLEs of medical, neurological, neurosensory, or neuropsychological origin. Most prevalent sequelae involved one or several of vision, balance, endocrinopathy, fatigue, hearing, pain, memory, and seizures/epilepsy. SPLEs were experienced as harmless by 7.4%; somewhat, clearly, very difficult by 33.4%, 28.5%, and 24.8% respectively; and completely disabling by 5.9%. Occurrence and severity varied with diagnosis age, gender, sub-diagnosis, and whether past cancer treatment included radiation therapy or not. Of 132 survivors with considerable to entirely disabling SPLEs, and who experienced need of surveillance/follow-up, 21% lacked access to such. As expected, health status 7 years earlier predicted later-life SPLEs.

Conclusion: A majority of CNS tumour VLTSS experience late effects that intrude upon quality of survival. Open-ended enquiry reveals subjectively experienced prominent difficulties, and informs about their perceived manageability, and surveillance needs. Today, as many as 1 of 5 studied CNS tumour VLTSS may lack required specialised surveillance in life-long follow-up.

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PD-020 | Ophthalmoscope, the Tools to Save Life, Eyes and Vision

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Background/Objectives: In Indonesia, retinoblastoma is the second most common type of cancer after leukaemia. Data from Dharmais Cancer hospital in Jakarta showed that almost 100% of children with retinoblastoma came already in a state of advanced stage. Given retinoblastoma is the only type of cancer in children that can be detected early, it is deemed necessary for all health workers in the front line to know it.

Design/Methods: 'Observation of see red' is the method used for early detection of retinoblastoma and ophthalmoscope is the tool required to perform such observation. There are currently an estimated 10,000 health centers spread throughout Indonesia. Since not all health centers have ophthalmoscope, Yayasan Anyo Indonesia - The Indonesian Anyo Foundation decided to help the government in the procurement of ophthalmoscopes for one-tenth of the existing health centers.

Results: Various attempts have been made, among others by organizing 'Anyo Charity Run' in the last 2 years. To support this program, educational video concerning retinoblastoma and how to perform 'observation of see red' has been made and published in YouTube. It is expected that the community, especially parents, more aware and have better knowledge on the early

symptoms of retinoblastoma and the health professionals can implement such early detection 'observation of see red' to children under five years in their workplace.

Conclusion: Hopefully this initiative, by *Yayasan Anyo Indonesia - The Indonesian Anyo Foundation* can reduce the occurrence of advanced retinoblastoma so that we can save not only lives but also the eyes and vision of children affected by retinoblastoma.

PD-021 | Nutrition Assessment on Admission of Paediatric Oncology Patients in a Specialized Treatment Center in Sao Paulo, Brazil

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Background/Objectives: The metabolic alteration caused by malignant neoplasm is already classified as a nutritional risk. It's estimated that at death all patients are malnourished, but still little is said about the nutritional status of these patients on admission by health services. Several studies have shown that nutritional status is a prognostic factor of major influence on the survival of cancer patients, so the evaluation and monitoring are essential throughout treatment. The objective of this study was to evaluate the nutritional status of patients from 0 to 19 years old, with malignant neoplasms, admitted by the nutrition service from January/2013 to January/2014 in a specialized treatment center in São Paulo, Brazil.

Design/Methods: This is a cross-sectional study, retrospective, descriptive, quantitative, with electronic medical record data collection. To classify the nutritional status were used Body Mass Index (BMI), Mid-Arm Muscle Circumference (MAMC) and recent weight loss. Data were tabulated and analyzed in Microsoft Excel.

Results: The sample consisted of 208 patients, 60.58% were male, 42.31% between 0 and 4 years old and 50% with leukaemia, central nervous system tumours or bone tumours. The mean time between admission and the first nutritional care was approximately 2.5 weeks. On admission 61.54% had normal nutritional status, but weight loss was observed in 50%, and it was serious in just over one third. Malnutrition was diagnosed in 8.66% with BMI and depletion of muscle mass at double (18.27%) with classification of MAMC.

Conclusion: In the face of what was found, it is concluded that the nutritional assessment should include several parameters in order to identify early nutritional risk for planning an effective intervention, because considering only the BMI we could have omitted the risk evidenced by the loss weight and classification of MAMC. So, stands out the importance of adequate nutritional assessment on admission by health services and throughout oncological treatment.

PD-022 | The Children and the Young Adults Involved in Childhood Cancer Awareness Campaign: The Nigerian Experience (Simara Children Cancer Foundation)

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Background/Objectives: The number of reported cases of childhood cancer in our hospitals is on the increase when compared to known cases, twenty years ago. Most often than not parents bring their children to the clinic/hospital for fever, rashes or other common symptoms unaware of what disease the child is suffering from. Some are unable to handle the shock of the news of cancer being diagnosed in the child, hence they are ill prepared to follow through with treatment. This prompted members of Simara Children Cancer Foundation (SCCaF) to embark on its first awareness campaign on 15th February, 2014 (Childhood Cancer Day) in the neighbourhood of SCCaF office with great results, and in October, 2014 a roadshow captioned 'Port Harcourt Cycles to Save a Child' which was used as a medium to create more awareness.

Design/Methods: Over one hundred and sixty-eight healthy children and young adults aged between eight years to twenty-seven years volunteered and participated in the cycling event. This activity involved the children riding a distance of two kilometers with the younger children leading and the skate-boarders bringing up the rear. It was a spectacular sight.

Results: The public were impressed that there was a visible difference as more parents brought in their children with early presentation to the hospital.

Conclusion: The healthy children wanted to show they cared and they did.

PD-023 | Lives of Korean Mothers of Children with Cancer : An Exploratory Study Using Photovoice

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Background/Objectives: Caring for a child with cancer can have profound effects on the parents, which in turn can affect the health and well-being of the ill child. Guided by the family resiliency model and using Photovoice methodology, we aim to describe mothers' lives post-diagnosis and their perceptions of how they have adapted to their child's illness.

Design/Methods: Photovoice, a participatory action research methodology, was used to better define the reality of the participants' lives from their own perspectives. Five Korean mothers of survivors of childhood cancer (currently aged under 12 years) voluntarily participated in five sessions of the Photovoice project. All participants were stay-at-home mothers aged 33 to 42 years. Their mean age of the child with cancer was 6.6 years and their mean time since diagnosis was 24.8 months.

Results: The participants took the initiative and ownership in theme selection, photo-taking, and group discussion on the group-decided weekly themes: *What I Want* (A break, Meeting with friends, Time for me and my family, and My career), *My Child And Food* (Whatever my child wants to eat and Love of family), *My Days for My Child* (Doing what my child wants to do, Being a playmate, and Changing for my child), and *Power Sources For Me* (Family, Courage of children, Mom is strong, and Hope).

Conclusion: This study enhances our understanding of mothers' perceptions of how their lives have been affected by cancer. Having a child with cancer greatly affects the mother's social lives, work lives, and emotional well-being. The mothers' daily lives appeared to be heavily influenced by the cultural norms in the society to which they belonged. The study helps clinicians develop programs for relieving parental stress and enhancing quality of life for families of children with cancer.

PD-024 | Cancer Treatment by Legal Prescription. Application of Legal Intervention for Abandonment of Treatment in El Salvador: Context and Reflections for other Teams and Settings

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Background/Objectives: Decreasing abandonment of treatment has been a main objective of the psychosocial team in the Salvadoran paediatric cancer program. Dealing with cases of potential or actual abandonment, the team found in the application of a law for protection of children welfare, a last resource to secure treatment for children. The law implies the duty of doctors to report parents that do not follow treatment for children affected with life-threatening conditions and the potential removal of parental custody.

Design/Methods: As part of a larger study on abandonment of treatment, observation, in-depth interviews and informal interviews were conducted with parents, doctors, social workers, and psychologists. Experiences of six cases considered for legal intervention are reported here.

Results: Six cases absent from treatment were reported to the governmental social services and enforced to comply with the therapy. The procedure entailed an upsetting and sometimes traumatic process for the families. Despite the initial confrontation that this action involved, the parents-doctor relationship was not severely affected. The parents did not change their view about the rightness of their decision or wish to abandon treatment; but they had no option other than adhere to the treatment, re-adapt to the situation, and assume the legal procedure as an external intervention not entirely in the hands of the doctors. The potential removal of parents' custody was dismissed by the legal system when the doctors assured that the children were back on treatment. Parents' feelings of being misjudged and surpassed as caretakers were mixed with the eventual recognition that the hospital team still offered a more understanding position compared to the one from the legal system.

Conclusion: The application of this resource must deem not only its efficacy regarding parents' following their child's treatment, but also a sensible use to diminish harmful consequences for the family and for the hospital team-parents' relationship.

PD-025 | CCLG PODC Paediatric Oncology Nurse Training Workshops—Chandigarh, Bangalore, Kolkata, Pune – Our Experience and Lessons Learnt

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Background/Objectives: Paediatric Oncology in Developing Countries (PODC) subgroup of Children's cancer and Leukaemia group (CCLG) UK is a voluntary group of doctors, nurses, parents and allied professionals working in paediatric oncology. Developing countries lack trained oncology nurses so 'nurse training' was adopted as a goal. The first workshop held in Chandigarh adapted the Royal Marsden foundation training course. Since then 3 further workshops have been held. The evaluation and feedback from each was used to modify and adapt the course to local needs. The developed programme and evaluations received is presented.

Design/Methods: International faculty (SV, MD) and national faculty (AT, SK) worked with local faculty to host workshops in India Chandigarh, Bangalore, Kolkata and Pune. The aim of these 2 day workshops was to provide foundation level training to nurses through lecture style teaching and hands on workshops.

Results: Over 200 nurses have attended. They represented paediatrics, paediatric oncology, BMT and adult cancer nurses from over 30 institutions. The course focussed on what is cancer, treatment modalities, identifying and managing toxicities, oncological emergencies, impact of cancer on the child and family and palliative care. Following feedback practical workshops on central venous access, infection control and safe handling of chemotherapy have been added.

Conclusion: Feedback from trainees and faculty, of the certified paediatric oncology training shows the workshops have created awareness of need for specialised care of children with cancer. It has also raised the profile of paediatric oncology nursing in the parent institutions concerned, increased confidence and knowledge and will help oncology nurses to remain on oncology wards and not to be transferred to other wards. Whilst two further workshops are planned in Delhi and Myanmar, we also want to do a survey of the trainees to find out what impact this training has had on practice.

PD-026 | A Non-Profit Global Consortium of Leading Childhood Cancer Charities to Accelerate Paediatric Oncology Drug Development

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Background/Objectives: Despite recent progress, a subset of children with cancer still face a very poor prognosis. While targeted and more effective drugs have been developed for adult indications, children have so far gained very limited benefit. Access to these new treatments is often delayed and specific drugs for childhood cancers are not developed by industry, because of the lack of sufficient commercial incentives. In order to save more lives we must accelerate the development of new agents to treat those forms of cancer with limited therapeutic options. Charities may be able to drive this process but a change of approach is needed.

Design/Methods: Charities should consider focusing their support on programmes that, despite their medical potential, would be otherwise stalled or abandoned by industry because of lack of commercial incentives. By filling this crucial investment gap more promising drugs may be further developed and brought to patients. Whereas a single charity may not have the required resources, a consortium of like-minded organisations contributing to a common fund may reach the needed critical mass and have a more significant impact.

Results: This project is driven by aPODD, a London-based charity founded by parents and drug development experts and the Medical Research Council Technology (MRCT), an independent life science medical research charity committed to drastically improving positive patient outcomes. Whereas aPODD brings along paediatric oncology expertise and links with the wider parents' community, MRCT has unique in-house expertise and deep knowledge of the drug development process.

Conclusion: This consortium may fund specific drug development projects up to pivotal clinical studies and will involve a number of leading childhood cancer charities across the world. It is believed that this approach will create powerful synergies and will bridge the current industry gap that delays the development of new treatments for children with cancer.

PD-027 | Sick Leave among Parents of Children with Cancer in Sweden – A National Cohort Study

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Background/Objectives: Due to increased care burden or psychological distress, parents of children diagnosed with cancer may face a higher risk of sickness absence from work. The objective of this study was to examine the short- and long-term impact of childhood cancer on parents' sick leave.

Design/Methods: The sample consisted of 3,635 parents of 1,899 children diagnosed with cancer during 2004–2009 identified by the Swedish Childhood Cancer Registry, and a matched reference group of parents (n=35,096) sampled from the general population. Sick leave was measured as amount of benefit payments and number of reimbursed days of sickness benefit. Annual individual data on sickness benefit were retrieved from the Longitudinal integration database for health insurance and labour market studies held by Statistics Sweden. Logistic and negative binomial regression models were used to compare outcomes with parents from the reference cohort.

Results: The average number of days with sickness benefit was 3.20 times higher for mothers of children with cancer than for referent mothers at year of diagnosis (95% CI, 2.91 to 3.52), and 4.54 times higher one year after (4.10 to 5.04). The increase in reimbursed days for fathers was 3.87 at year of diagnosis (3.40 to 4.42) and 4.61 at one year later (3.96 to 5.37). The increase remained statistically significant four years after diagnosis. Although the relative increase in relation to the comparison parents was higher among fathers than mothers, the average number of days in absolute numbers was higher among mothers than fathers for several years after diagnosis.

Conclusion: Both mothers and fathers of children diagnosed with cancer are at higher risk of sickness absence from work. The relative effect was more pronounced for fathers and the absolute effect was more pronounced for mothers.

PD-028 | The Utilisation of Modern Transport and Telecommunications Platforms to Assist in the Remote Provision of Paediatric Cancer Diagnostics in Tanzania

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Background/Objectives: The acquisition of a pathologic diagnosis represents a critical point in the management of children with malignant disease, allowing staff to plan a therapeutic pathway. In resource poor settings, diagnoses help to identify children who will benefit from the limited interventions available and those who will not. Access to timely diagnoses can be a challenge in low and middle income countries. While enhanced local laboratory capacity is the ultimate answer, interim solutions are needed to assist programs with existing deficits. Modern transport and telecommunications technology can facilitate this process.

Design/Methods: Muhimbili University, Dar es Salaam, provides a paediatric cancer program for Tanzania. As part of a formal twinning arrangement, laboratory staff in Dublin have provided interim diagnostic services while helping to develop local paediatric cancer diagnostic capacity in Tanzania. Samples are transported free via DHL[®] couriers. Preliminary reports are communicated to local clinical staff via WhatsApp with final reports scanned and e-mailed.

Results: Since 2008, almost 1000 cancer samples have been transported from Dar to Dublin. Transport time is two working days. In 92% of cases, a preliminary communication regarding specimen adequacy and provisional diagnosis was communicated via WhatsApp the day after receipt. In 90%, final diagnosis was proffered in 48 hours or less with average time to final report just 2.9 days. Marrow samples delivered in cellular antigen stabilising reagent (Transfix[®]) showed some loss of cytoplasmic antigens but sufficiently preserved membrane antigens to permit interpretation. Flow cytometric methods for leukaemia diagnosis are now established in Dar with technical and interpretative support continuing via remote access to local analysts from Ireland. Immunohistochemistry is being developed in Dar.

Conclusion: Rapid remote access to cancer diagnoses in resource poor settings is feasible using modern transport and communications platforms, providing a viable alternative while local capacity is under development.

PD-029 | Bringing Art and Volunteering Together to the Treatment of Life Threatening Diseases

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Background/Objectives: Chemotherapy, radiotherapy and surgical interventions in the treatment of cancer can impact the individual's quality of life and can lead to overall physical and mental deterioration (Graca, Figuerido & Fincham, 2012). Due to the unknown outcomes of treatment, patients are likely to experience feelings of anxiety and depression, and due to the invasive nature of therapy patients are likely to experience physical discomfort (Graca, Figuerido & Fincham, 2012; Elkis-Abuhoff et al., 2009). Several studies demonstrated that art therapy enhances the psychosocial treatment of cancer, including decreased symptoms of distress, improved quality of life and perceptions of body image, reduction of perceived pain, and general physical and psychological health (Monti et al, 2006; Nainis et al, 2002; Svensk et al, 2009). Studies also indicated a reduction of depression and fatigue levels in cancer patients on chemotherapy treatment (Bar-Sela, et al, 2007). Research by The National and Community Service in 2007 proved that volunteering promotes life satisfaction, lower mortality rates, greater functional ability, and lower rates of depression for the volunteers later in life.

Design/Methods: ART2CARE is the first art initiative within the Middle East regions using art expression, art therapy and art psychotherapy for paediatric oncology patients.

Results: In 3 major hospitals in Egypt, over 2,000 volunteers have been trained and provided with structured lesson plans aiming to: cultivate children's imagination, creativity, and expressive ability, reduce feelings of distress, sadness and anxiety, and mediate recovery after major treatment milestones.

Conclusion: ART2CARE brings together art and volunteering in a project to relieve those suffering from cancer. It aims to expand geographically and demographically, including all patients suffering from chronic diseases and providing training to introduce art therapy/psychotherapy to the region.

PD-030 | Clinical Risk Factors for Abandonment in Adolescents with Cancer. An Analysis of Five Institutions from Mexico

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Background/Objectives: Cancer is the second cause of death in adolescents after accidents and aggressions. Adolescents become a special group in the paediatric field due to their psychological, social and physical changes they are experiencing. Abandonment of treatment at this age is becoming a public health issue because it increases costs of treatment and risk of relapse and death. Social, economical and cultural factors have been associated to abandonment of treatment and have been widely discussed. Clinical factors, have not been clearly studied.

The objective of the study is to identify clinical risk factors such as secondary effects (nausea/vomit, alopecia, fever and neutropenia, anemia, pain, mucositis, neuropathy) and surgery (curative, exploratory, biopsy, amputation, palliative, sequel, port catheter) associated with abandonment of treatment in adolescents with cancer in Mexico.

Design/Methods: Five institutions participated. Clinical records from 2008 to 2014 were reviewed and every case was matched with one control regarding age, sex and diagnosis. Bivariate analysis was used to find variables associated with abandonment of treatment and then conditioned multivariate analysis with logistic regression was carried out.

Results: Forty-eight adolescents abandoned treatment and were matched with their control. Analysis of clinical factors as secondary effects and surgery showed only a slight though not significant (p=0.061) protector factor when secondary effects were present (OR -1.537, IC95% 0.043-1.074). The four principal factors associated with abandonment of treatment were nausea/vomit, and fever and neutropenia (protector, OR -1.247, p=0.018, IC95% 0.102-0.810 and OR -1.182, p=0.046, IC95% 0.096-0.980 respectively), and amputation and anemia (risk factor, OR 1.597, p=0.036, IC95% 1.112-21.914 and OR 1.578, p=0.016, IC95% 1.343-17.470 respectively).

Conclusion: The analysis of clinical factors associated with abandonment of treatment deserves attention in our country. More studies are necessary to create proposals to be employed in health institutions.

PD-031 | Making A Change for Childhood Cancer in Patna India Against All Odds - A Multipronged Approach

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Background/Objectives: CanKids...KidsCan is a support group working in 44 cancer centres across India. Creating awareness, advocacy and providing holistic support are critical components of our commitment to making a Change for Childhood Cancer in India. Cankids started working in MCVS, a not-for-profit cancer hospital in Patna in 2008. This centre caters largely to below-poverty-line families. The medical treatment was managed by a paediatrician and an overburdened Medical Oncologist. Cankids' support comprised of drug assistance, a social

worker and two parent support group members. However despite above provisions, outcomes continued to be poor with high rates of abandonment (50%), treatment related mortality (over 30%), treatment delays and high rates of relapse. All these led to poor long term outcomes.

Design/Methods: In March 2015, it was decided to review how best to improve the outcomes at the center. Root cause analysis was done and a number of factors were identified. Each of these factors was systematically addressed. Interventions included a monthly outreach clinic by a visiting Paediatric Oncologist, setting up of new adapted protocols for treatment and supportive care, enhanced support for drugs and diagnostics, providing a playroom and teacher, increased facilitation from governmental and non-governmental institutions and nutritional support.

Results: At the end of one year of these interventions the number of patients has doubled, the abandonment is less than 10%. The treatment related mortality is now less than 10%. Networks have been established with other units for services that are not locally available. The center is now contributing the largest number of patients to the first prospective paediatric oncology collaborative study in India. Outcome data is being prospectively collected.

Conclusion: With this one unit we have been able to create a composite model of Awareness, Advocacy and Medical Assistance which is a benchmark that can be replicated in other centers that share similar challenges.

EPIDEMIOLOGY

PD-032 | Health Related Quality of Life, Social Support and Social Capital of Mothers of Children with Cancer

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Background/Objectives: The diagnosis of childhood cancer is particularly stressful with adverse health effects for all the family. Social support and the wider social context can act as buffer, perhaps as long as the support provided is appropriate (stressor-specific hypothesis).

Aim: Investigate the health-related quality of life (HRQoL) of Greek-Cypriot mothers of children with cancer (MCC) and assess its association with perceived social support and social capital, as compared to mothers of healthy children (MHC).

Design/Methods: A descriptive comparative and correlational study of HRQoL (SF-36 survey) with 52 MCC (93% response) from the only paediatric oncology referral center on the island compared to 208 mothers of age/gender matched healthy children in the absence of population norms. In each group, the magnitude of the association of HRQoL with perceived social support (MOS-SSS) and social capital (SCQ) was assessed and compared in linear regression models.

Results: Significantly reduced scores on the SF-36 Mental Health Component and all four domains (effect sizes -0.4 to -0.7 SD, $p < 0.01$) were observed among MCC. While social support was positively associated with mental health among MHC (1.62 95% CI=1.02, 2.23 per 10 unit increase in social support score), no similar association was observed in MCC (0.08 95% CI=-1.16, 1.32); p for effect modification=0.03. A similar picture emerged in terms of social capital. In contrast, there was a strong association of social support and social capital with Physical Health in both study groups, and somewhat stronger among MCC.

Conclusion: Whilst in the general population HRQoL is positively associated with social support and social capital, the potential protective effect among MCC appears to be restricted to the physical, and not mental health, which is particularly poor. There is need to design and evaluate psychosocial programs targeted to the individual needs of these families in an integrated framework which combines professional and informal support.

PD-033 | Influence of Health-Insurance Status on Non-Hodgkin Lymphoma Treatment in Kenya

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Background/Objectives: Non-Hodgkin lymphoma (NHL) is the most common childhood malignancy in Sub-Saharan Africa. Survival rates for NHL are higher than 80% in high-income countries. This study explores treatment outcomes of children with NHL in Kenya, a Sub-Saharan low-income country, and determines the influence of health-insurance status at diagnosis on treatment outcomes.

Design/Methods: This was a retrospective medical records study. All children diagnosed with NHL from 2010 until 2012 were included. Data on treatment outcomes and health-insurance status at diagnosis were collected.

Results: Of all 63 NHL patients, 35% abandoned treatment, 22% had progressive or relapsed disease, 14% died, and 29% had event-free survival. Most patients (73%) had no health-insurance at diagnosis. Treatment outcomes in children with or without health-insurance at diagnosis differed significantly ($P=0.003$). The most likely treatment outcome in children with health-insurance at diagnosis was event-free survival (53%), whereas in children without health-insurance at diagnosis it was abandonment of treatment (44%). The event-free survival estimate was significantly higher in children with health-insurance at diagnosis than in patients without health-insurance at diagnosis ($P=0.003$). Age at diagnosis, gender, distance to hospital, duration of symptoms and stage of disease did not significantly influence treatment outcomes and event-free survival estimates.

Conclusion: Survival of children with NHL in Kenya is much lower compared to high-income countries. Abandonment of treatment was the most common cause of treatment failure. Health-

insurance status at diagnosis significantly impacted treatment outcomes and survival. Survival of children with NHL could increase if access to health-insurance would be improved.

PD-034 | An Integrated Pacific Children's Cancer Registry: A 5-Minute Cancer Registry to Improve Clinical Care for Children in the Pacific

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Background/Objectives: Like other PODC regions, Pacific Island countries including Fiji recognise the need for accurate and timely national cancer data to assess the development of child cancer services and measure improvements in treatment outcome. But a major barrier in many resource poor settings is the lack of clinician time and dedicated resourcing for sustained, timely and accurate data collection and analysis. We report the development of the Pacific Children's Cancer Registry (PCCR) – a 5 minute children's cancer registry.

Objectives

- 1) To describe Pacific Children's Cancer Registry, a simple and secure cancer registry
- 2) To describe the additional functionality within the registry to support clinical care and sustained data collection in a busy clinical setting.

Design/Methods: The registry was designed using a freely available open source MSQl database and the cloud based (Microsoft azure) web platform. It is configured for use on a desktop, tablet or smartphone. Fields are configurable for any country, region or centre. IACR confidentiality and registry development guidelines were used during development. All new cancer cases are registered by ICCC coding with additional data recordable on disease treatment, patient status, outcome, treatment completion and abandonment. Additional functionality includes the preparation of a diagnosis summary and treatment plan for inclusion in the clinical record. The program includes a panel of self-generating analysis tools and automated reports. All data can be exported in standard data formats for further verification and research.

Results: We have developed a simple 5-minute registry for the routine and accurate collection of childhood cancer registration, the preparation of treatment summaries and easy automated analysis. No additional training is necessary.

Conclusion: The PCCR is a generic simple children's cancer registry which can serve as a clinical record of care. This registry is adaptable to many any child cancer setting and should overcome the barriers to data collection and analysis.

PD-035 | Youth Vulnerability, Social Exclusion, Lag Time: Are there Influences on Childhood Cancer Survival in Sao Paulo, Brazil?

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Background/Objectives: This study aimed to evaluate the influence of socioeconomic conditions in the intervals first consultation-diagnosis and diagnosis-treatment among children with cancer living in the city of São Paulo, Brazil, as well as the impact of delays on 5-year overall survival (5y-OS).

Design/Methods: This is a retrospective cohort study including all cases of first primary cancers diagnosed among individuals < 20 years, registered in the Central Hospital-based Cancer Registry of São Paulo State in the period 2000-2010. Patients were classified according to two socioeconomic indices, based on the district of residence at diagnosis: the Youth Vulnerability Index (YVI) and the Social Exclusion Index (SEI). Five-year OS was obtained through Kaplan-Meier method and curves were compared using log-rank test. For all statistical tests, $\alpha=5\%$.

Results: During the study period, 2,756 cases were registered. No significant differences on intervals first consultation-diagnosis and diagnosis-treatment according to YVI were observed. However, a statistically significant difference on mean interval 1st consultation-diagnosis by SEI was found for individuals with bone tumors ($p=0.017$). Disparities in survival according to delay in diagnosis (days) were found for patients with CNS tumors (<8: 5y-OS=52.7%, ≥8: 5y-OS=67.2%, $p=0.013$), neuroblastoma (<7: 5y-OS=35.9%; ≥7: 5y-OS=51.6%, $p=0.033$), retinoblastoma (<13: 5y-OS=96.8%; ≥13: 5y-OS=66.7%, $p=0.016$), germ cell tumors (<7: 5y-OS=89.2%; ≥7: 5y-OS=74.1%, $p=0.041$), and carcinomas (<12: 5y-OS=73.6%; ≥12: 5y-OS=84.4%, $p=0.043$). Also, disparities in survival according to delay in starting treatment (days) were also observed for lymphomas (<18: 5y-OS=74.2%, ≥18: 5y-OS=84.4%, $p=0.013$), neuroblastoma (<7 days: 5y-OS=35.9%; ≥7 days: 5y-OS=51.6%, $p=0.011$), CNS tumors (<1: 5y-OS=63.9%; ≥1: 5y-OS=48.4%, $p=0.022$), bone tumors (<13: 5y-OS=40.6%; ≥13: 5y-OS=54.2%, $p=0.022$), and carcinomas (<13: 5y-OS=85.9%; ≥13: 5y-OS=71.1%, $p=0.019$).

Conclusion: SES did not have influence in access to diagnosis and treatment for children with cancer in São Paulo, Brazil. However, survival rates are strongly affected by delays in diagnosis and treatment.

PD-036 | Improving the Accuracy and Completeness of New Zealand Child Cancer Registration: The Benefit of Two National Registries

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Background/Objectives: New Zealand (NZ) has two childhood cancer registries; the Children's Cancer Registry (NZCCR), which receives comprehensive demographic, diagnostic and treatment information for patients referred to the two specialist paediatric oncology centres, and the population-based national Cancer Registry (NZCR). These registries collaborated to determine the accuracy and completeness of children's cancer registration.

Design/Methods: 2010-2014 registrations for children aged 0-14 years that met International Classification of Childhood Cancers (ICCC-3) inclusion criteria were obtained from each registry. Registration anomalies were reconciled using patient management systems, clinical summaries and laboratory reports.

Results: 794 unique cases were identified; 718 from the NZCR (incidence rate 157.9 per million) and 721 from the NZCCR (incidence rate 158.5 per million). The NZCCR provided an additional 55 non-malignant central nervous system tumours which are not registered by the NZCR and 14 Langerhans cell histiocytosis cases which were only registered from 2014. The NZCCR omitted 19 cases due to human error and 24 cases - predominantly melanomas and carcinomas - that had not been referred to either specialist centre, including 5 cases diagnosed at or around death. The NZCR erroneously registered 18 children from the Pacific Islands who came to NZ for part of their treatment and 5 non-malignant tumours. Errors were corrected for sex (n=4), age at diagnosis (n=15) and ICCC-3 diagnostic group/subgroup (n=25). Following the verification process, NZ's child cancer incidence rate was revised to 168.0 per million. Case completeness according to their respective registration criteria was 99% for the NZCR and 94% for the NZCCR.

Conclusion: This study highlighted improvements that can be made in the registration processes of each registry and identified gaps in NZ's child cancer referral pathways. With two national registries covering childhood cancers, NZ is uniquely positioned to undertake regular collaborative activities, thereby ensuring that highly accurate and complete data is available for research.

GERM CELL TUMOURS

PD-037 | Outcome of Extracranial Germ Cell Tumors in a Developing Country: The Children's Hospital Lahore Pakistan Experience

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Background/Objectives: The Children's Hospital Oncology department is a 45 bedded unit with over 700 new cases per year. Extracranial GCT accounts for 10% of new solid malignancy cases each year. The purpose of this study was to analyze its clinical manifestations, course and outcome in a resource limited public sector hospital.

Design/Methods: Retrospective review of 130 patients enrolled between January 2011 – December 2015 was done. Data regarding their age, sex, clinical classification, course of therapy, and outcome analyzed. The therapy comprised of 4-6 courses of JEB protocol.

Results: Total 130 patients with age ranging from < 1 to 15 years (64% < 5 yrs) were included. M: F Ratio was 1:1.8. 91% tumour had size > 5 cm and 70% stratified high risk (p-value=0.019). 52/130(40%) had yolk sac tumour, 12/130(9%) mixed malignant GCT, 8/130(6%) dysgerminoma, 22/130(17%) Mature teratoma, 10/130(8%) immature teratoma and 21/130(16%) unspecified GCT. Majority of these tumors originated from gonads 54/130(42%), Sacrococcygeal teratoma 44/130(34%) abdominal 25/130(19%) Head neck 4/130(3%) and mediastinal 3/130(2%). 59/130(41%) presented at stage IV, 58/130 (45%) with stage III and 18/130(14%) with stage II. Multidisciplinary team approach (MDT) was utilized in 93/130(72%) cases, (p-value=0.000) and surgery done in 111/130(85%) cases. Total 91/130 (70%) have completed treatment, 4/130 (3%) are on treatment, 16/130 (12%) left against medical advice (LAMA) and 17/130 (13%) expired due to progressive disease and sepsis. Regarding events 36/130(28%) had sepsis requiring hospital admission, 17/130 (13%) had recurrence after surgery alone, 6/130(12%) had obstructive uropathy, 6/130(5%) had neurogenic bladder and bowel and 4/130(3%) had relapse after surgery and chemotherapy (p-value=0.056). Alpha-fetoprotein was an important marker for diagnosis and follow up.

Conclusion: Overall survival of 91/130(70%) further can be increased and abandonment (16%) and mortality (13%) can be decreased by capacity building in paediatric oncology, training more health professionals including paediatric surgeons and strengthening MDT and social support and implementing infection prevention and control measures.

PD-038 | Urologic and Anorectal Dysfunction in Children with Sacrococcygeal Teratomas

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Background/Objectives: Late effects of oncologic treatment are very important. The aim of this study is to determine the incidence of urologic and anorectal late effects of sacrococcygeal teratoma (SCT).

Design/Methods: The records of patients with SCT between 1998-2013 were evaluated. Age, sex, Altman type, tumour size, histopathology, surgical procedures, renal functions, urodynamic assessment and rectal manometry results were evaluated. Bladder and bowel habits, urinary and fecal continence results were obtained with a questionnaire.

Results: There were 40 patients with SCT. (Female/Male ratio:2.3, median age 12 days (1 day-178 months)). 55% of the cases were newborn. 35% of the SCT cases diagnosed antenatally. Tumour size was larger than 10 cm (2-30 cm) in 35% of the cases. The Altman type of tumors were as follows: Type I 15%, type II 37.5%, type III 30%, type IV 17.5%. Tumour histology was mature teratoma in 70%, and immature teratoma in 12.5% and yolk sac tumour in 17.5% of the patients. Mean follow-up time was 78.5±44 months (26-206 months) after the surgery

urinary incontinence was seen in two cases and, gaita incontinence was also positive one of them. Constipation rate was 25% and abnormal rectal manometry rate was 5%. Hydronephrosis was noted in 15% of the patients. Vesicoureteral reflux determined in 17.5% of the cases. Abnormal urodynamic evaluation rate was 47%. Anticholinergic drug commenced in 35% of patients because of low detrusor compliance and sphincter dyssynergia. Chronic intermittent catheterisation is needed in 25% of group. One patient has predialysis chronic renal failure. Tumour size and Altman type III and IV was related with urologic and anorectal sequela in this study (p<0.056).

Conclusion: High incidence of urologic and anorectal dysfunction in children with SCT requires rutin urodynamic tests and rectal manometry in asymptomatic cases.

PD-039 | Paediatric Dysgerminoma: Results of the SFCE TGM Trials and Long Term Consequences on Renal, Hearing and Gonadal Functions

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Background/Objectives: Dysgerminoma (ovarian seminoma) are rare in children/adolescents with sparse data about long-term follow-up.

Design/Methods: French patients (≤18 years) treated between 1985 and 2005 were included in TGM-85, 90, 95 protocols based on primary unilateral oophorectomy with prophylactic iliac and lombo-aortic irradiation for localized diseases or platinum-based chemotherapy for advanced diseases (FIGO>Ic).

Results: 48 patients (median age 12.9 years) were included, 2 had a bilateral dysgerminoma. Six patients had gonadal dysgenesis. 28 patients had loco-regional dissemination (tumour rupture n=4, contiguous spread n=7, post-operative residue n=7, peritoneal spread n=10). 7 had para-aortic lymph nodes. None had distant metastases.

Primary surgery was performed in 47/48 patients (unilateral oophorectomy n=41, tumorectomy n=4, bilateral oophorectomy for gonadal dysgenesis or contiguous spread n=2). Complete resection (FIGO Ia-b) was achieved in 15 patients. Among these patients: 7 didn't receive adjuvant treatment, 6 had lymph nodes irradiation (20-24Gy) and 2 received chemotherapy. Among the 32 patients ≥FIGO Ic, 31 received chemotherapy, 1 with lymph nodes irradiation and 1 didn't receive adjuvant treatment. Staging was not available in 1 patient. Chemotherapy contained cisplatin (n=25) or carboplatin (n=8).

With a median follow-up of 14years, all patients are alive in complete remission. Five events occurred: 2 contralateral dysgerminomas (8m-2y after diagnosis), 1 peritoneal relapse (2y after diagnosis) and 2 second neoplasms (contralateral teratoma and melanoma).

Bilateral oophorectomy was necessary for 12 patients (6 dysgenesis, 6 other causes). A desire of pregnancy was expressed for 17/36 patients with unilateral oophorectomy, which succeeded in 13 cases (4 medically assisted). However, 2/17 had ovarian failure. The renal function was evaluated and normal on 25/41 patients treated with platinum, ifosfamide or irradiation. The hearing function was evaluated by audiometry on 17/36 patients treated with platinum: 11 Brock grade-0, 3 grade-1 and 2 grade-4.

Conclusion: Dysgerminoma has favorable prognosis with unilateral oophorectomy and adjuvant chemotherapy in advanced stages, with few long term complications.

PD-040 | Dysgerminoma in Children, Adolescent and Young Adults: A Report from the Malignant Germ Cell Tumour International Collaborative (MAGIC)

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Background/Objectives: Dysgerminoma is the most common malignant ovarian germ cell tumour (GCT) with its peak incidence during adolescence and young adulthood. It is highly curable even in the context of metastatic disease. Current standard of care for advanced stage dysgerminoma (ASD) consists of platinum-based chemotherapy (carboplatin(C) or cisplatin(P),

etoposide(E) and bleomycin(B)). Differing treatment strategies exist internationally between paediatric and adult practices. Our objective was to compare clinical outcomes across different therapies to facilitate recommendations for future trials.

Design/Methods: The Malignant Germ Cell Tumour International Collaborative (MaGIC) has warehouse data from seven GCT trials conducted between 1983 and 2009, from the United Kingdom (UK) Children's Cancer and Leukaemia Group (n=2), United States (US) Children's Oncology Group (n=2), and the US Gynecologic Oncology Group (n=3). Analysis of the pooled dataset identified 144 patients (paediatric trials: n=64, adult trials: n=80) with newly diagnosed stages I-IV pure ovarian dysgerminoma.

Results: Median age=16 years (range:4-46). Nine patients underwent surgery only and 137 received chemotherapy (JEB=66, PEB or Compressed-PEB=58, High Dose-BEP=13). The five-year event-free survival (EFS) and overall survival (OS) for all patients who received chemotherapy were 94.6% and 96.9% respectively. The outcomes were comparable between JEB (EFS=96.6%, OS=96.6%) and PEB (EFS=92.8%, OS=97.1%). Eight patients relapsed; of which two were alive at last follow up. All events occurred within the first 52 months after initial treatment, with a median of 5.7 months. The median follow-up of observed patients who did not experience an EFS-event was 9.2 years and for chemotherapy treated patients was 10 years.

Conclusion: Irrespective of chemotherapy regimen administered, patients diagnosed with ASD have an excellent OS. Clinical trial data from three large clinical trial organizations suggests that de-escalation of frontline treatment for ASD is warranted. Future treatment strategies should focus on risk-adapted tailoring of therapy to maintain these excellent outcomes while minimizing long term treatment related toxicities.

PD-041 | Preoperative Imaging and Surgical Outcome and Morbidity in Infants with Retroperitoneal Teratomas

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Background/Objectives: Retroperitoneal teratomas are uncommon tumors of infants and young children. Despite being typically benign, surgical morbidity is commonly encountered due to its huge size and distortion of major vessels. Perioperative deaths and major vascular injuries have been reported. We conducted a retrospective review of our institutional experience of cases with retroperitoneal teratomas in infants to access whether surgical outcome and short-term / long-term morbidity are predictable by preoperative imaging.

Design/Methods: Clinical and surgical details were collected through medical records and surgical reports on eleven procedures performed on nine patients under one year of age, including two procedures on recurrent tumors. Seven patients were girls and two were boys. All were pathologically diagnosed mature or immature teratomas.

Results: Age at surgery ranged from one to 370 days after birth. The aortic trunk was distorted in 3 cases. The vena cava was flattened in six cases. Renal arteries of either of the kidneys were extensively stretched in all but two cases, but encased in only two cases, of which one experienced postoperative renal infarction. Renal vein was flattened in all but two cases. Blood loss of over 15% estimated blood volume was seen in eight cases. Cases in which the aorta, vena cava and renal arteries were intact had a trend to loose less blood. There was one case that suffered postoperative chylous leak, of which a giant tumour extensively stretched and distorted the vena cava and the aorta. Tumour size did not correlate to post-surgical morbidity.

Conclusion: Surgeries for cases with distortion of the aorta and flattening of the vena cava tend to become more complicated and are prone to postoperative morbidities. Despite the extensive stretching of the renal arteries caused by the giant tumors. Unlike neuroblastomas in infants, renal atrophy seemed to be an uncommon sequelae.

IPSO

PD-042 | Rol and Biology of Cryosurgery in the Treatment of Osteosarcoma in the Paediatric Patient

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Background/Objectives: Cryosurgery is the use of therapy application of nitrogen (N2O) as a local therapeutic treatment of bone tumors which induces tissue necrosis as a form of ablative treatment. The surgical technique with tumour-free margins is extremely important, we propose the application of cryosurgery to level the tumour bed in all patients in order to stop further negative margins resection of the primary tumour and thus reduce the risk factor relapse secondary to microscopic residual disease.

Design/Methods: A retrospective, longitudinal study of patients diagnosed with osteosarcoma treated with cryosurgery in the service of the National Institute of Pediatric Oncology Surgery within 6 years conducted.

Results: Out of a total of 21 patients, 20 are alive, 4 current treatment with chemotherapy and two with methotrexate. They were 9 girls (48%) and 12 children (52%). The average age was 9 years. (5-17 years old). The most common site was the distal femur with 10 patients (48%), tibia with 3 patients (14%), pelvis with 3 patients (14%), humerus with 2 patients (9%), and 1 patient

clavicle, ulna, maxillary (5%). The most common histologic type was histologically with 17 patients (80%), type of surgery in the primary tumour was limb salvage in 18 patients (86%) and 3 patients with pelvic reconstruction. All patients were given and neo adjuvant chemotherapy. Patients received cryotherapy with N2O in the tumour bed and spinal canal where only one patient had relapsed.

Conclusion: The use of intraoperative cryosurgery is a tool in order to have local control in the tumour bed and medullary canal in children with osteosarcoma; with no evidence of vascular or nervous lesion nitrogen use.

PD-043 | Survival and Surgical Management of Hepatic Malignancies in Paediatric Patients Over A Period of 23 Years in a National Reference Center

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Background/Objectives: This study aims to characterize the hepatic malignancies, their surgical therapies and survival in a national referral hospital in Spain.

Design/Methods: Chart review of all paediatric patients with hepatic malignancies newly diagnosed and managed in Department of Pediatric Surgery from July-1993 to January-2016. Highlighting its characteristics, survival rates and surgical management.

Results: Among the 82 patients included, 61 (74%) developed hepatoblastomas with median age (MA) 29m (41M:20F, 9 deaths), 6 hepatocarcinomas MA 116m (4M:2F, 5-deaths), 7 embryonal-rhabdomyosarcomas MA 89m (3M:4F, 1-death), 2 cholangiocarcinomas MA 131m (2F, 1-death), 2 rhabdoid tumors (1M:1F, 1-death), 1 hepatic-lymphoma (1F), 2 infiltrating-neuroblastomas (1M:1F), and 1 infiltrating-Wilms tumour (1F). Patients with hepatoblastoma presented PRETEXT groups: I 2-cases, II 22-cases (3-deaths), III in 19-cases (2-deaths), and IV 18-cases (4-deaths); and segments involved were: I 21%, II 41%, III 39%, IV 62%, V 72%, VI 62%, VII 62%, and VIII 64%. Surgical treatment in patients with hepatic malignancies were: 9 biopsies, 8 atypical resections, 1 segmentectomy, 20R/7L-hepatectomy, 7R/3L-trisegmentectomy, 1 mesohepatectomy, 12 decesead-donor/16 living-donor liver transplants, and 1 multivisceral transplant. The survival rate of patients with hepatoblastoma was OS (91.4% 1y, 85.4% 3y, 85.4% 5y, 82.2% 10y), EFS (91.5% 1y, 85.1% 3y, 82% 5-10y); hepatocarcinoma OS (100% 1y, 80% 3y, 60% 5y, 0% 10y), EFS (100% 1y, 60% 3y, 40% 5y, 0% 10y); embryonal-rhabdomyosarcoma OS/EFS 85.71% (1-3-5-10y); cholangiocarcinoma OS/EFS 100% 1y, 0% 3y; rhabdoid tumour OS/EFS 100% (1-3y) and 50% (5y); and others tumors OS/EFS 100% (1-3-5-10y).

Conclusion: The results found in paediatric hepatic malignancies in our center are similar to those reported previously. Among patients with hepatoblastoma, the results have improved thanks to the liver transplantation program. Patients with hepatocarcinoma and cholangiocarcinoma have poor outcome, which requires analysis in future cases. The possibility of multivisceral transplant will require more development and analysis in highly selected cases.

PD-044 | Primary Orthotopic Detaenial Sigmoid Neobladder after Radical Cystectomy in 26 Paediatric Patients with Bladder/Prostate Rhabdomyosarcoma: 12 Years Experience in Zhujiang Hospital

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Background/Objectives: We present our experience with primary orthotopic detaenial sigmoid neobladder following radical cystectomy or proctocystectomy due to bladder/prostate rhabdomyosarcoma (RMS) in children resistant to chemotherapy and/or radiotherapy.

Design/Methods: Due to RMS of the bladder/ prostate, 22 boys and 4 girls underwent primary bladder substitution with U-shaped non-detubularized orthotopic detaenial sigmoid neobladder after radical cystectomy between August 2003 and December 2014. Early and late complications are documented. All patients underwent followup regularly including oncological result, functional data and growth status.

Results: Average operating time was 4 hours, including 2 hours for neobladder construction. Pelvic lymph node metastasis on left external iliac vessels were found in 2 boys. There was no perioperative mortality. Ileus was found 30 days postoperatively in one boy. Average followup was 40.7 months (range 12 months-12 years). Two boys died of recurrence or metastasis. Rest 22 patients were tumour-free. Daytime urinary continence was achieved in all patients 30-60 days after operation and one security pad was needed during nighttime. Average reservoir capacity was 150 ml in 9 months postoperatively. Slightly unilateral hydronephrosis was found in 3 patients and it is stable during followup. Severe hydronephrosis and intestinal disturbances were not observed. Severe metabolic acidosis were found in two patients and cured conservatively with indwelling catheterization and oral sodium bicarbonate intake. Urethrovicinal stricture was found in 2 boys and treated by endo-incision. Linear growth of patients was normal compare to peers. Patients went to school and had normal campus daily life when they were more than 7 years old.

Conclusion: Radical surgery may offer favourable oncological outcomes for refractory bladder/prostate RMS. The primary orthotopic detaenial sigmoid neobladder is safe and technically feasible, and offer satisfactory long-term functional outcomes and good quality of life with low morbidity.

PD-045 | Isosexual Precocious Puberty in Girls Due to Juvenile Granulosa Cell Tumour of the Ovary

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Background/Objectives: To evaluate the presentation, diagnosis, treatment and outcomes of girls with isosexual precocious puberty due to Juvenile Granulosa Cell Tumours (JGCT) of the ovary.

Design/Methods: All children less than 12 years who were diagnosed to have JGCT from 2005-16 were retrospectively evaluated.

Results: A total of 9 patients in the age range of 12-141 months (mean 70.8 months) were included. Vaginal bleeding along with breast enlargement was the most common presentation (77.8%). Five patients (55.6%) had an abdominal mass. Other presenting symptoms were appearance of pubic hair (55.6%), pain (22.2%) and generalised abdominal distention (11.1%). Diagnosis was made by raised serum estradiol levels (range 162-710 pg/ml) and presence of ovarian mass on imaging and confirmed histologically after resection. All 4 patients in whom inhibin A levels were done had raised levels. Alpha-fetoprotein and beta-hCG were normal in all. All patients underwent salpingo-oophorectomy on the affected side (1 laparoscopic, 8 open). All of them had Pediatric Oncology Group (POG) stage I tumour and none received adjuvant chemotherapy. Patients were followed-up with clinical examination, serum estradiol levels, serum inhibin A levels and serial ultrasonography. The symptoms of isosexual precocious puberty regressed in all. There was no recurrence during a mean follow up of 48.9 months (range 3-93 months).

Conclusion: Isosexual precocious puberty due to JGCT of the ovary in young girls presents with varied features with or without palpable abdominal mass. Complete excision of the tumour in these girls with POG Stage I JGCT has very good prognosis. Features of isosexual precocious puberty regress completely without any recurrence or need for chemotherapy.

PD-046 | The Rate of Kidney Salvage Following Nephron Sparing Surgery for Bilateral Wilms Tumour

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Background/Objectives: Although the nephron sparing surgery (NSS) is controversial in case of the unilateral Wilms Tumours (WT), it offers a chance to avoid dialysis and renal transplant in the bilateral ones. The survival expectancy highlights preventing the renal insufficiency and justifies maximal efforts to spare as much renal tissue as possible.

Aim of this review was to evaluate the rate of renal salvage, the oncological and functional outcome in patients with bilateral WT.

Design/Methods: Twenty-six consecutive patients were operated on for bilateral WT in a reference centre (2006-2015). Status of the renal vessels (primary and secondary branches – “encased or not”) supplying renal parenchyma to spare and the amount of this parenchyma (less than 1/3 or more) were the factors to decide on NSS or total nephrectomy (TN). An extra-renal and collective system invasions were considered less important as easy to resect and reconstruct.

Results: Renal salvage rate: Two of 26 pts underwent one sided NSS and TN on the opposite side due to the absence of the healthy renal tissue on the TN side. In 3/24 pts after both-sided NSS, one of spared kidneys became vanishing. Of 21 remaining with both functional kidneys, only 1 relapsed locally and died. Oncological outcome: Two of 26 patients developed relapses: one in the abdomen, another in the lungs. Both had anaplastic variant of pathology and both died despite re-treatment. Functional outcome: none of 24 children who are alive required dialysis or renal transplant, however 3 developed a moderate renal function impairment.

Conclusion: In our experience, the rate of both-sided, oncologically successful renal salvage in bilateral WT is high: 20/26 pts (77%) are alive and have both kidneys functional. The renal vessels encasement and a minimal or none renal parenchyma to spare were the contraindications to NSS going together.

PD-047 | Duodenum-Preserving Resection of the Pancreatic Head (DPRPH) for Pancreatic Head Tumour

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Background/Objectives: To investigate the indications and surgical procedures of duodenum-preserving resection of pancreatic head(DPRPH) for pancreatic head tumour.

Design/Methods: From Jan. 2004 to Mar. 2014, the clinical manifestations, operation methods and prognosis of 30 cases with pancreatic head tumour in children were analyzed retrospectively.

Results: We reported 30 cases of pancreatic head tumour that included pancreatoblastoma in 13 cases, solid pseudopapillary tumour of pancreas in 14cases and 3 cases of other type. Of them, 14 cases received pancreatoduodenectomy with digestive tract reconstruction, and 16 cases was performed DPRPH for pancreatic head tumour. 3 cases of the head of pancreas was wholly removed, and the conserved duodenum and bile duct.

15 months later following operation, 14 cases of enteron rebuild postoperative complications occurred in hemorrhage of digestive tract in 3 cases, 2 cases of chole-intestinal anastomosis had anastomotic stricture. In DPRPH, leakage of bile was postoperatively found in 3 cases, but all recovered after 3 months. Ten years follow-up showed that all patients are alive without relapse.

Conclusion: It is safe that duodenum-preserving resection of pancreatic head for pancreatic head tumour without invasion duodenal wall.

PD-048 | Transabdominal Left Medial Visceral Rotation – Application to Paediatric Left Sided Retroperitoneal Tumours

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Background/Objectives: Exposure of the retroperitoneum is vital when dissecting large left sided retroperitoneal tumours (LSRT). Left medial visceral rotation (LMVR) is a manoeuvre used extensively in trauma and vascular surgery because it facilitates excellent exposure of major vessels. We report the use of LMVR for LSRT in paediatric oncological surgery.

Design/Methods: All LSRT procedures by a single surgeon (1.9.2009 to 31.1.2016) were retrospectively reviewed for age, diagnosis, radiology, operative details and complications. The manoeuvre involves division of the postero-lateral attachments of the spleen followed by mobilisation of the tail/body of the pancreas. The mobilised segment, stomach and eviscerated bowel is placed in the right of the abdomen within a plastic bag to prevent drying. Following tumour resection the spleen is returned to the left upper quadrant.

Results: Of 69 patients with retroperitoneal tumours (29 right, 34 left, 6 central), 30 patients (median age 2.64 years (0.041 - 14.22); M:F 14:16) where LMVR was used for LSRT were identified (9 neuroblastoma (NBL), 18 Wilms, 1 mesoblastic nephroma (MN), 1 rhabdomyosarcoma, 1 clear cell sarcoma (CSS)). Median size of tumours was 876.44cm³ (4.52cm³ – 3,045.52cm³). The pancreas was displaced/compressed by tumour in 14; major vessel displacement/encasement was present in 22. Histological resection margins were positive in 11 patients (5 NBL, 1 MN, 4 Wilms, 1 CSS). In all cases LMVR significantly improved the exposure to the left diaphragm, crus and aorta. No complications were caused by LMVR. In all cases the follow up scans showed the spleen fixed back in the left upper quadrant.

Conclusion: LMVR provides a safe means to improve exposure to the retroperitoneum and avoids traction on the pancreas or spleen without increasing morbidity. Though this approach has been described, it is not routinely taught to trainees in paediatric surgical oncology. Intra-operative photos will be used to demonstrate the increased exposure.

PD-049 | Nephron-Sparing Surgery for Unilateral Wilms Tumour: The Price of Success

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Background/Objectives: Growing evidence suggests that nephron-sparing surgery (NSS) for unilateral Wilms tumour (UWT) is oncologically safe and has a renal function advantage over nephrectomy. Main concern refers to the risk of additional chemotherapy and abdominal radiotherapy required in children with positive surgical margins after NSS. We report our experience with an emphasis on the treatment of NSS complications in children with UWT.

Design/Methods: Of 45 children with UWT who underwent surgery at our Institution between 1992 and 2015, 7 children with UWT, and 1 with renal oncocytoma underwent partial nephrectomy; 5 children with WT and 1 with Beckwith-Wiedeman syndrome underwent tumour enucleation. Pre-operative chemotherapy was given according to SIOP protocol.

Results: Two children following partial nephrectomy and 1 following enucleation presented positive margins and were successfully treated with multi-drug (2 cases), or two-drug (1 case) chemotherapy. Radiotherapy was omitted in all 3 cases. Following partial nephrectomy one child developed local recurrence and underwent completion nephrectomy, involved pericaval lymphadenectomy, abdominal radiotherapy, and multi-drug chemotherapy. Kidney remnant was tumour free. At a mean follow-up of 14.75±6.76 years overall survival was 100%, and event-free survival was 92%. Following NSS all patients presented two-kidney eGFR values.

Conclusion: In our experience, partial nephrectomy and enucleation for unilateral WT appear to be oncologically safe at a reasonable therapy price. Collaborative studies are required to investigate whether positive surgical margins without lymphonodes involvement in children with intermediate risk UWT may be treated with Vincristine and Actinomycin and no abdominal irradiation.

PD-050 | Transscrotal Extracapsular “En Mass” Orchiectomy in Giant Testicular Tumours

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Background/Objectives: The standard surgical procedure in the treatment of testicular tumour is the high radical orchiectomy. At puberty, the first medical exam often detects giant size advanced tumors, when the standard groin incision needs long scrotal extension giving poor cosmetic results. If the tumour broke through the testicular capsule or tumour spillage happens further scrotal skin resection should be performed. The simple inguinal skin crease incision with high transection of the vas followed by scrotal crease incision and transscrotal extracapsular orchiectomy including the “en mass” removal of tunica Dartos and cremaster muscles may provide accurate tumour removal and better cosmetic results.

Design/Methods: We retrospectively analyzed the children underwent transscrotal extracapsular orchiectomy in our unit since 2010, focused on the feasibility of the procedure and the cosmetic results.

Results: Eight patients, 5 had germ cell tumour, 3 had paratesticular rhabdomyosarcoma. The follow up is 3 years 2 months in average. All the patients underwent high vas dissection and transscrotal extracapsular “en mass” orchiectomy. All had unilateral disease, in 2 cases retroperitoneal lymph node metastasis, in 2 cases multiple pulmonary metastases were observed at the time of diagnosis. The patients with retroperitoneal lymph node metastasis underwent radical retroperitoneal lymph node dissection, all the pulmonary metastasis disappeared during the treatment. 3 had significant scrotal hematoma. All the patients have almost invisible scars both on the groin and scrotum. Since the scrotal skin has been barely resected the size of the remained scrotal skin is enough for the testicular prosthesis implantation in all cases.

Nor local nor distal recurrence has been observed on the follow up.

Conclusion: The experience with transscrotal extracapsular “en mass” orchiectomy following high vas dissection is limited, but the preliminary results suggest that the procedure is feasible,

provides excellent cosmetic result and adequate oncological radicality and completely prevents the intraoperative tumour spillage.

PD-051 | Lymphatic Leakage (LL) after Neuroblastoma Surgery – is it Really a Rare Condition?

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Background/Objectives: LL is considered to be a rare condition after abdominal or thoracic paediatric surgery. While there are definitions for LL in adult patients, there is none for paediatric patients.

Design/Methods: We investigated our own patient cohort treated for neuroblastoma (NB) for duration of LL, amount of fluid drained in 24 hours, INSS, extend of surgery (complete macroscopic resection vs incomplete/ nearly complete resection and biopsy only) follow-up-Status (CR, SD, PD, DOD) and treatment modalities for LL. Here we defined LL as lymphoid secretion lasting more than eight days after tumour resection.

Results: Between 2003 and 2014, we performed surgery for NB in 205 patients. Follow-up Status was available in 191 patients (range six months-five years, median 30 months). Among these, 78 patients had abdominal or thoracic drainage with lymphatic excretion for more than eight days and up to seven weeks. The Duration of Drainage vs extend of surgery was statistically significant ($P=0.0001$). Treatment modalities for LL included total parenteral nutrition, medium chain triglycerides for oral nutrition and the i.v.-administration of somatostatin. However, there was no significant statistical difference regarding the treatment modalities and the duration of drainage. None of our patients received further surgery because of LL. In comparison, follow-up-Status vs LL was considered statistically significant ($p<0.000$).

Conclusion: LL is a common complication after extensive retroperitoneal Tumour resections. Observation and supportive measures are sufficient for Treatment of even prolonged LL in most cases.

PD-052 | Minimally Invasive Surgery Biopsies in Paediatric Oncology

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Background/Objectives: Minimally invasive surgery (MIS) is an accepted surgical technique for the treatment of a variety of benign diseases. But the use of MIS in paediatric cancer is a matter of debate. The diagnostic role of MIS was evaluated in our study in children with malignancies.

Design/Methods: Diagnostic accuracy, complications, conversion rate and time before specific treatment after MIS biopsy was estimated.

A retrospective analysis was performed involving 72 patients who underwent MIS for biopsy in our clinic from 2013 to 2016: 32 laparoscopies and 40 thorascopies.

Results: Sample size was more than 2 cm³ – 50 cases, less than 2 cm³ – 22 cases. More quantity of tissue did not provide growth of diagnostic accuracy.

Average intraoperative hemorrhage was 29 ml, ranged from minimal about 5 ml to maximal 1000 ml.

The duration of the procedure ranged from 20 minutes to 2.5 hours (average time 92 minutes).

The average time before specific treatment or outpatient treatment was 6 days.

The conversion rate was 5.5%. Intraoperative complications occurred in 4(5,5%) patients: in 2 cases - lesion of colonic wall by the coagulating, in 2 – continuing bleeding.

Postoperative complications had place in 6 children: the perforation of colonic wall in 2 children required open operations, in 1 case the postoperative wound did not heal over for a long time because of soldering of omentum at the edge of wound, in 3 patients with previous lung disease respiratory insufficiency required prolonged AVL.

The diagnostic accuracy of MIS biopsies was 94.5%.

Conclusion: Thereby MIS techniques in paediatric oncology and haematology are enough safe and reliable as a diagnostic tool. Using of MIS for biopsy can reduce the time before specific treatment. MIS techniques can be the method of choice for biopsy in view of interdisciplinary evaluation of possible risk for each patient.

PD-053 | Extent and Timing of Surgical Resection of High-Risk Neuroblastoma

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Background/Objectives: The impact of primary tumour resection, as well as its timing and extent in patients with high-risk neuroblastoma is a matter of medical debate.

Design/Methods: Medical records of children treated for high-risk neuroblastoma in a single paediatric surgery center between 2000 and 2014 were analysed. The extent of primary tumour resection before and after chemotherapy was correlated with outcome.

Results: A total of 51 patients with high-risk neuroblastoma were included in this study. Before chemotherapy, 11 patients underwent complete resection of a primary tumour and 40 patients underwent biopsy. No statistically significant difference was found between biopsy and complete resection as an initial surgical procedure before chemotherapy stated in terms of mortality of patients ($p=0.557$) using Fisher's exact test. In the group with pre-treatment biopsy, 25

patients underwent complete resection, 7 partial resection and 8 underwent no surgery after chemotherapy, with overall survival rates of 72%, 71% and 38%, respectively. We observed significant association between the mortality rate and different kinds of resection (complete, partial and no resection) after chemotherapy ($p=0.046$). No statistically significant difference was found between complete and partial resection in patients who underwent interventional procedure after chemotherapy ($p=0.272$).

Conclusion: The extent of the surgical procedure prior to chemotherapy in patients with high-risk neuroblastoma has no influence on the outcome. In patients who underwent initial biopsy, surgical resection of a primary tumour after chemotherapy for high-risk neuroblastoma is associated with better outcomes, while the extent of such resection is not.

PD-054 | Elevated Pre-Operative Neutrophil-Lymphocyte Ratio is Predictive of Poorer Prognosis in Paediatric Solid Tumours

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Background/Objectives: An elevated neutrophil-lymphocyte ratio (NLR) has been shown to indicate poorer prognosis in adult patients who undergo resection of solid tumours (with curative intent). This potentially represents an independent, universal adjunct prognosticator. There are currently no such prognosticators for paediatric solid tumours. NLR has not been assessed in the paediatric setting. The aim of this study was to determine whether NLR was prognostic in paediatric solid tumours.

Design/Methods: This was a retrospective study on prospectively collected data. All patients under the age of 18 years who were diagnosed with a solid tumour at our institution and underwent multimodal therapy were included. The exclusion criteria were patients with a diagnosis of retinoblastoma, patients who did not undergo resection with curative intent and patients who did not have a full blood count within one month of surgery. Data collected was analysed and compared across groups of five year overall survival and two year event free survival using univariate and multiple regression analysis.

Results: There were 444 patients diagnosed with solid tumours in the study period. 146 patients did not meet the inclusion criteria. There were 298 patients included in the study. The median age at diagnosis was 3.9 years (IQR=8.5). The most common tumours were neuroblastoma ($n=83$), Wilms tumour ($n=63$) and osteosarcoma ($n=41$). The NLR was statistically significantly higher in the group of overall survival less than five years compared to that greater than five years ($p=0.001$). Upon multivariate analysis, the NLR retained a significant difference across groups of overall survival ($p=0.010$). Log-rank comparisons of Kaplan-Meier plots confirmed an association between a high NLR value and both lower overall survival ($p<0.001$) and lower event-free survival ($p=0.014$).

Conclusion: An elevated NLR is prognostic of poorer prognosis in paediatric solid tumours and potentially represents an independent, universal adjunct prognosticator in such cases.

PD-055 | Unexpected but Obvious Complications Associated the Site of Port-A-Cath Placement

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Background/Objectives: In the paediatric oncology the port-a-cath is placed usually infra-mammary by cosmetic reason. Within the inframammary line there are 3 options for port placement, the medial, the midclavicular or lateral. The aim of the study is to detect the site related complications of port-a-cath placement.

Design/Methods: A review of the port-a-cath insertions from 2003-2015 was performed. The complication of long care and the reasons of port change or early removal were studied.

Results: All together 725 port-a-cath placement were performed in the examined period in 648 patients. 109 medial, 67 midclavicular and 549 lateral insertions were found.

The highest rate of port change and early port removal was found at the medial placement (35%). 2 patients had cardiac arrest with CPR; when the chest compression blocked the line while the resuscitation, made insufficient medicine administration through the line. The medial placement of port-a-cath never been used any more. There are no differences found in the midclavicular and lateral positioned placement in the thrombotic or infection complication, more mechanical failure happened at the lateral position group. ($p<0.001$). In the medial and midclavicular position made difficult and at least 4 times impossible to carry out cardiac US examination. No port-a-cath have been removed or changed due to this reason.

Conclusion: The medial inframammary localized port-a-cath has a major disadvantage with unusable for CPR. The midclavicular position directly covers the heart apex making difficult the cardiac US. Despite the lateral position has more mechanical failure, we suggest this localization for port-a-cath placement.

LATE EFFECTS

PD-056 | Time Trends in Hearing Loss after Childhood Cancer

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Background/Objectives: Hearing loss is a common adverse event of childhood cancer treatment, especially after platinum chemotherapy or cranial radiation. Treatment regimens have been modified over the last decades. Platinum chemotherapy is widely used for the treatment of childhood cancer, and today the less ototoxic carboplatin often replaces cisplatin. Radiation techniques also improved and result in lower doses to the cochlea. It is unknown if these changes in treatment affected the burden of hearing loss over the last decades.

Design/Methods: Within the Swiss Childhood Cancer Survivor Study, we sent a questionnaire to all Swiss ≥ 5 -year survivors aged ≤ 16 years at cancer diagnosis. We estimated cumulative incidence of hearing loss for different treatment groups (platinum chemotherapy, cranial radiation, both) and for different periods of cancer diagnosis (1976-1985, 1986-1995, 1996-2005).

Results: We included 2,061 survivors. Median (IQR) age at survey for survivors was 21 years (6-46) and median time since diagnosis was 15 years (5-36). For all survivors, incidence of hearing loss increased since the introduction of platinum compounds in the 1980s, but did not further increase in 1996-2005 ($p=0.017$). For survivors with cranial radiation, incidence of hearing loss increased in 1986-1995, and tended to decrease again in 1996-2005 ($p=0.092$). For survivors with platinum chemotherapy, incidence of hearing loss decreased in 1996-2005 compared to 1986-1995 ($p=0.017$). The incidence in survivors who had received both cranial radiation and platinum chemotherapy remained stable over all periods of diagnosis ($p=0.163$).

Conclusion: The burden of hearing loss increased with the introduction of platinum compounds, but did not further increase in recent decades. This could be due to adapted treatment regimens with less ototoxic radiation and carefully dosed platinum chemotherapy.

PD-057 | Where have all the Fat Cells Gone? A Comparative Analysis of Adiposity Patterns in Paediatric Brain Tumour Patients and Non-Cancer Controls

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Background/Objectives: Brain tumors are the most common solid tumors in children. Technological advances have increased survival rates in these children over the past three decades. However, this emerging group of survivors of childhood brain tumors (SCBT) have premature mortality and morbidities that can negatively impact their quality of life and lifespan. While adiposity has been identified as a major risk factor of cardiometabolic disorders in the general population, adiposity patterns in SCBT have not been determined. This study aims to investigate the adiposity patterns differ between SCBT and non-cancer controls, and to determine if lifestyle and treatment factors may contribute to these patterns.

Design/Methods: SCBT ($n=59$) and non-cancer controls ($n=108$) had sociodemographic and lifestyle details collected using standardized tools to assess diet, physical activity, and sleep. Brain tumour type, location and treatment details were obtained from medical records. Total adiposity was determined using bioelectrical impedance, and visceral adiposity was determined by waist-to-hip and waist-to-height ratios. Regression analysis was used to determine the factors associated with adiposity.

Results: SCBT have significantly higher total fat mass ($26.1 \pm 10.5\%$ vs $22.8 \pm 10.4\%$, $P=0.047$), waist-to-hip ratio (0.87 ± 0.08 vs 0.82 ± 0.09 , $P<0.0001$), and waist-to-height ratio (0.48 ± 0.08 vs 0.45 ± 0.08 , $P=0.007$), in the presence of similar body mass index in both groups. Female SCBT who received radiotherapy and/or chemotherapy had higher adiposity. A dietary pattern of white bread and fried foods with low dark bread was positively associated with adiposity. Lower physical activity levels, but not sleep duration, were associated with higher adiposity.

Conclusion: SCBT have higher total and visceral adiposity than non-cancer controls.

Sex, chemoradiotherapy, high fat diet, and physical inactivity can contribute to these adiposity patterns. These results provide multiple points of entry to design interventions that reduce adiposity, and may improve long-term outcomes in SCBT.

PD-058 | Potential Neurotoxicity of Non-CNS-Directed Chemotherapy During Childhood: A Neuroimaging Study of Brain Structure and Function

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Background/Objectives: Chemotherapy has been associated with neurocognitive sequelae in patients with leukaemia and brain tumors. However, for survivors of childhood solid non-CNS tumors treated with multiagent chemotherapy, evidence remains limited. This study aims to explore structural and functional brain connectivity for attention-related networks and white matter (WM) integrity in survivors of solid non-CNS tumors.

Design/Methods: We acquired magnetic resonance (MR) brain images of survivors of solid non-CNS tumors ($n=25$) and healthy age-matched controls ($n=25$). Patients were treated with chemotherapy only (no radiotherapy). MR-scans included functional imaging during rest, i.e. resting state fMRI (Rs-fMRI) and Diffusion Weighted Imaging (DWI), which characterizes the WM structure.

(1) For Rs-fMRI, functional networks were calculated by using independent component analysis. We used the neuroimaging tools SPM8 and FSL. Attention-related networks were selected for group comparisons, being the default mode network (DMN), and the left and right frontoparietal network (FPN).

(2) For DWI, we compared Fractional Anisotropy (FA), which indicates the main direction of diffusion of water molecules. By using ExploreDTI and FSL, FA-maps were compared between survivors and controls within the WM. Analyses were multiple-voxel and Bonferroni-corrected. Clusters larger than 30 voxels were retained.

Results: First, lower functional connectivity was found in survivors between the DMN and the left inferior parietal lobule (IPL), which is located close to the DMN and within the FPN ($p<0.05$, clustersize: 147 voxels). Second, we observed higher FA in controls compared to sur-

vivors in central WM regions, including the right splenium of the corpus callosum, the anterior and posterior internal capsule, and the cingulum ($p<0.05$, clustersize: 30-101 voxels).

Conclusion: This neuroimaging study shows lower functional connectivity in attention-related networks and reduced structural connectivity in central WM regions for survivors of childhood solid tumors. Future research is necessary to identify the relationship with cognitive functioning, and specific biomarkers.

PD-059 | Longitudinal Follow-Up in Female Childhood Cancer Survivors: No Signs of Accelerated Ovarian Function Loss

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Background/Objectives: Female Childhood Cancer Survivors (CCS) have an increased risk of gonadal impairment. It is conceivable that, in addition to this gonadal impairment, AMH shows a more rapid decline in female CCS than in healthy females. We assessed if the long-term decline of ovarian function, measured using anti-Müllerian hormone (AMH) serum concentrations, is accelerated over time in female CCS.

Design/Methods: A retrospective single-center cohort study was performed in Rotterdam, The Netherlands, between 2004-2014. Paired serum AMH levels of 192 adult female CCS were assessed, at least five years after cessation of treatment and at a second visit at least 2 years after the first measurement. AMH levels were compared to the age-based p50 of AMH.

Results: At the first visit, median AMH levels were $-0.59 \mu\text{g/L}$ below the age-based p50 of AMH (range: $-4.07 - 17.05$). At the second visit with a median of 3.2 years later (range: 2.1 - 6.0 years), the median AMH levels were still below the age-based p50 of AMH (median: $-0.22 \mu\text{g/L}$, range: $-3.75 - 20.50$). Analysis showed that in women with a sustained ovarian function (AMH $> 1.0 \mu\text{g/L}$), the decline in AMH in CCS was not different from the decline seen in the normal population (difference in decline per year: $-0.07 \mu\text{g/L}$ (range: $-2.86 - 4.92$), $p=0.08$). Neither was one of the treatment modalities of childhood cancer correlated with a significant acceleration of decline in AMH per year.

Conclusion: Our study shows that after initial impairment due to childhood cancer treatment, the further decline in ovarian function, as measured in AMH, is not accelerated in CCS. This finding may help physicians to counsel female CCS about their expected reproductive lifespan.

PD-060 | Late Outcomes of Adult Survivors of Childhood Acute Myeloid Leukemia (AML): The St. Jude Lifetime (SJLIFE) Cohort

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Background/Objectives: AML therapy is intensive and may include hematopoietic stem cell transplantation (HSCT) and radiotherapy (RT). Comprehensive clinical assessments of long-term outcomes in this population are lacking. Our aim was to estimate the prevalence and severity of chronic health conditions and neurocognitive deficits among adult survivors of childhood AML.

Design/Methods: AML survivors treated at St. Jude Children's Research Hospital, who survived >10 years and were >18 years of age, returned for a clinical evaluation. Clinical outcomes were graded using a modified Common Terminology Criteria for Adverse Events (grade 1 [mild] to grade 4 [life-threatening]). Neurocognitive function, measured using standardized tests, was graded using age-adjusted z-scores, with mild impairment between -1 to -2 and moderate/severe impairment <-2 z-scores.

Results: Survivors of AML ($n=114$, 54% female, 44% received HSCT, 45% RT) were evaluated at a median age of 30 years (range: 19-51) and a median of 19.3 years (range: 10.7-37.6) from diagnosis. At least one Grade 1-4 condition was identified in 94% (most prevalent were hypertension 61.4%, obesity 59.6%, hypertriglyceridemia 43.9%); 18.4% had a Grade 3-4 condition. Moderately/severely impaired short-term memory was identified in 12.8% (95% CI 6.3-19.2%), cognitive flexibility in 19.2% (95% CI 11.7-26.8%), and sustained attention in 14.2% (95% CI 7.5-20.8%), each significantly more prevalent than national norms (2.3%, $p<0.0001$). No significant difference was found between HSCT and non-HSCT survivors (Grade 1-4: RR=0.97 95% CI 0.88-1.1; Grade 3-4: RR=1.7 95% CI 0.78-3.7). Those exposed to RT were more likely to have a grade 1-4 or grade 3-4 condition (RR=1.1 95% CI 1.03-1.2; RR=2.5 95% CI 1.1-5.7, respectively) than unexposed survivors. Neurocognitive deficits did not differ by HSCT group. Irradiated survivors were more likely to have moderately/severely impaired cognitive flexibility and sustained attention than non-irradiated ($p<0.05$) survivors.

Conclusion: Prospective systematic clinical evaluation identified significant chronic conditions and neurocognitive deficits among adult survivors of childhood AML.

PD-061 | Relationships among Hypertension Susceptibility Loci, Hypertension, and Late Anthracycline-Related Cardiotoxicity in Long-Term Childhood Cancer Survivors

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Background/Objectives: Hypertension has been shown to increase risk of anthracycline-induced cardiotoxicity. We hypothesized that genetic susceptibility loci for hypertension may serve as early predictors of the development of late cardiotoxicity in long-term childhood cancer survivors previously treated with anthracyclines.

Design/Methods: In a cohort of long-term childhood cancer survivors (N=108) who received anthracyclines and were subsequently screened for cardiac function via echocardiographs following Children's Oncology Group guidelines, we reviewed all blood pressure measurements and categorized patients as not hypertensive (<120/80), pre-hypertensive (125-139/<90), and hypertensive (systolic \geq 140 or diastolic $>$ 90). Cardiotoxicity was defined in survivors with two subsequent echocardiograms demonstrating reduced cardiac function (ejection fraction \leq 45) and/or prescribed cardiac medications. We determined the association between 12 polymorphisms previously implicated as hypertension-susceptibility loci in the general population and the development of hypertension, as well as risk of cardiotoxicity.

Results: Clinical hypertension was a significant risk factor for cardiotoxicity (OR: 2.58, 95% CI: 1.18-5.66, $p=0.018$). *PLCE1*:rs9327264 hypertension susceptibility variant was associated with an increased risk of developing hypertension or pre-hypertension (OR: 3.48, 95% CI: 1.01-11.92, $p=0.047$). Paradoxically, this allele was associated with a protective effect on cardiotoxicity risk (OR: 0.37, 95% CI: 0.18-0.76, $p=0.0066$).

Conclusion: Our findings confirm hypertension as a risk factor for late cardiotoxicity and demonstrate that pre-hypertension may also be a risk factor. Of the 12 hypertension-susceptibility loci investigated, one variant, *PLCE1*:rs9327264, was associated with increased hypertension risk and decreased cardiotoxicity risk. The opposite effects of *PLCE1*:rs9327264 on hypertension and cardiotoxicity warrants further investigation to understand the potential basis for these associations. The lack of association between the other established variants with hypertension in this survivor cohort suggests that etiology of hypertension may be different than that in the general population. Together, our findings highlight a complex relationship between genetic variation, hypertension, and cardiotoxicity in long-term childhood cancer survivors.

LIVER TUMOURS

PD-062 | Preclinical Drug Testing of Multikinase Inhibitors in Metastatic Hepatoblastoma by Collagen-Gel Droplet Embedded Culture Drug Sensitivity Test

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Background/Objectives: Complete surgical resection is essential for cure of hepatoblastoma. However, effective chemotherapy is also important in the treatment of metastatic and recurrent hepatoblastoma to improve tumour resectability and to prevent further metastases. Because of a rarity of the disease, it is difficult to develop new chemotherapy for patients who failed to respond to the standard treatment. To exploit new therapies using multikinase inhibitors, the preclinical evaluation of sorafenib and sunitinib was performed by the collagen-gel droplet embedded culture drug sensitivity test (CD-DST).

Design/Methods: In 5 patients with recurrent hepatoblastoma, lung or lymph nodes metastatic tumors were surgically resected. The tumour tissues were tested for the sensitivity to sorafenib, sunitinib, and SN-38 by the CD-DST. The tested drug concentrations were decided based on the clinically achievable serum concentrations. Drug exposure time was 24h for SN-38, and 144h for sorafenib or sunitinib. The study was approved by the institutional ethics board and the guardians' informed consent were obtained.

Results: The CD-DST was successfully done in 4 out of 5 tumors. The 50% growth inhibition was achieved by sorafenib in all samples at 0.45 – 2.2 $\mu\text{g/ml}$, and in 3 out of 4 samples by SN-38 at 0.062 – 0.11 $\mu\text{g/ml}$. Sunitinib at the tested range of concentration did not achieve 50% growth inhibition in 2 out of 3 tested samples.

Conclusion: Sorafenib showed good activities in heavily pretreated hepatoblastoma. Our results warrant the future clinical trials using sorafenib for recurrent and refractory hepatoblastoma. The CD-DST is a useful tool for preclinical drug evaluation which is necessary to develop the background of the clinical trials, especially in the rare tumors such as paediatric hepatoblastoma.

PD-063 | Novel PRETEXT / POST-TEXT Based Scoring System Developed to Evaluate Anatomic Response to Chemotherapy in Hepatoblastoma: A Report from the Children's Oncology Group AHEP0731 Study

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Background/Objectives: Chemotherapy response assessment in patients with hepatoblastoma is challenging: AFP falls quickly in often still unresectable tumors; RECIST does not assess

liver vasculature involvement. Ideally, preoperative chemotherapy only necessary for safe surgical resection would be given; however, objectively measuring this is limited. Additionally, response detection is important for identification of potentially active new agents on phase I/II studies. Finally, for future phase III studies, identification of good/poor responders may help in stratification of surgical timing and/or chemotherapy regimen.

Design/Methods: Patients with non-metastatic, unresectable hepatoblastoma enrolled on AHEP0731 were analyzed by AFP, RECIST and PRETEXT/POSTTEXT (Pre/Post-treatment Extent of disease) central review at various treatment timepoints. We experimented retrospectively with a novel PRETEXT/POSTTEXT scoring method assigning points for PRETEXT group (I, II, III, IV), IVC/hepatic venous involvement (V), bilateral/bifurcation portal involvement (P), multifocality (F), contiguous-extrahepatic (E) and caudate lobe involvement (C).

Results: Preliminary data was available for 82 of 105 patients. POSTTEXT score decreased by a mean of 36% in 70 patients after 2 cycles. Seventy-eight% of these responders had further decrease following 4 cycles (overall median decrease 38%). After two cycles, fourteen/18 patients without response by RECIST showed response by POSTTEXT score, and 9/12 patients with $<$ 90% AFP decline showed POSTTEXT score response. Of 8 patients with intravascular tumour thrombus, one cleared on preoperative chemotherapy. Of 66 patients with vascular compression/encasement, forty-seven (71%) improved to simple vessel contact or less. POSTTEXT score decrease did not differ for patients with/without an event.

Conclusion: POSTTEXT score decline is worth exploring as a measure of response to chemotherapy in patients with unresectable hepatoblastoma. As our data become more complete, we hope to statistically model various potential scoring systems aiming to develop a tool taking into account not only tumour size decrease, but also clearance of anatomic involvement of contiguous vital structures that may preclude surgical resectability.

PD-064 | Congenital Abnormalities and Genetic Background Associated with Paediatric Malignant Liver Tumour in the Japanese Study Group for Paediatric Liver Tumour

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Background/Objectives: The risk of developing hepatoblastoma is high among very low birth weight infants (VLBW) and patients with genetic syndromes including Beckwith-Wiedemann syndrome (BWS) or familial adenomatous polyposis (FAP). We investigated possible congenital or genetic related factors for paediatric malignant liver tumour in a nationwide study by the Japanese Study Group for Paediatric Liver Tumour (JPLT).

Design/Methods: A total of 435 children with malignant liver tumors were registered to the JPLT database from February 1999 to December 2013. The institutional physicians documented the presence or absence and the types of associated anomaly or congenital abnormality as well as family history on a case report form. We collected the data and retrospectively analyzed the incidence and types of congenital or genetic factors associated with malignant liver tumors.

Results: Sixty-nine patients (15.9%) were documented to have either any congenital abnormality, family history of any cancer or genetic syndromes, or maternal hepatitis virus carrier. Of those, eight patients (1.8%) were VLBW. Five patients (1.1%) had family history of FAP, and 15 patients (3.4%) were associated with known genetic syndromes: BWS (8), trisomy 18 (2), Sotos syndrome (2), Li-Fraumeni syndrome (1), Niemann-Pick disease (1), and Down syndrome (1). Ten patients (2.3%) were documented to have family history of various types of cancer including hepatocellular carcinoma in 4. Twenty-four patients (5.5%) without known genetic disease had congenital abnormalities as follows: congenital heart disease (6), renal hypoplasia or aplasia (4), renal tubular acidosis (1), absence of portal vein (2), infantile hepatitis (1), Hirschsprung disease (1), esophageal atresia (1), intestinal malrotation (1), precocious puberty (2), skeletal system disorder (1), hemangioma (1), and incontinentia pigmenti (1).

Conclusion: Children with malignant liver tumors are associated with genetic disorders or congenital abnormalities other than known genetic syndromes. Accumulation of such data may uncover novel conditions at risk for developing malignant liver tumors.

PD-065 | Feasibility of Irinotecan Monotherapy as Adjuvant Chemotherapy for Hepatoblastoma after Liver Transplantation

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Background/Objectives: Liver transplantation (LT) is a preferred treatment option for unresectable hepatoblastoma (HB), however, the efficacy of chemotherapy after LT has been controversial. We have treated post LT patients with irinotecan alone, which has been reported in its effectiveness for recurrent HB with little toxicity. The purpose of this study is to evaluate the feasibility of irinotecan monotherapy for post LT patients.

Design/Methods: We retrospectively reviewed 6 children who received chemotherapy with irinotecan after LT for HB to assess feasibility of this post-operative treatment. All 6 patients

received 3 cycles of therapy; irinotecan 20 mg/m² (2) per day from day 1 to 5, 8 to 12, every 21 days.

Results: Median age of the patients was 26 months (range: 7–44 months) at LT. Median follow-up period since LT was 14.5 months (range: 4–35 months). None had extrahepatic infiltration and metastasis at diagnosis. As Pretreatment Extent of Disease System (PRETEXT), one was III, and 5 were IV. All patients received LT from family living donors with tacrolimus and low-dose steroids as immunosuppressants after 3 to 6 courses of cisplatin and anthracycline-based chemotherapy. In the postoperative pathological findings, there was no patient showed tumour infiltration at surgical margin. Postoperative chemotherapy was started on median 35 days (range: 22–39 days) after LT. During chemotherapy, 2 patients had grade 4 neutropenia, and 1 patient had grade 4 thrombocytopenia. As with non-hematological toxicity, grade 2 or 3 viral reactivation were observed in all 6 cases; cytomegalovirus (n=4) and Epstein-Barr virus (n=2). These viral reactivation subsided after the accomplishment of chemotherapy. No patients experienced grade 4 hepatobiliary and renal disorders. All 6 patients survived without relapse or graft failure during observational period.

Conclusion: As adjuvant chemotherapy for post LT for HB, irinotecan monotherapy might be a feasible therapy. Further prospective study should be warranted.

PD-066 | Review of Histopathology of Hepatoblastoma Resected after Neoadjuvant Chemotherapy: An Institutional Experience of 95 Patients

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Background/Objectives: Histologic types are incorporated in the risk stratification of hepatoblastoma. Pure fetal epithelial variant is of favourable histologic type while small cell variant is associated with aggressive behaviour. However, the relevance of histologic subtypes is applicable in chemo-naïve setting. We studied histopathology of tumours from 95 patients which were resected after neo-adjuvant chemotherapy and attempted to correlate with outcome.

Design/Methods: 95 patients with hepatoblastoma treated at our institution were included for study over 11 years duration. Clinical information was obtained from electronic medical records. Histopathology of all cases was reviewed by two observers. Percentage of residual tumour, histologic subtype of residual tumour and status of resection margins were correlated with survival.

Results: Age range of patients was 3 months to 15 years. Male:female ratio was 2.3:1. All patients received neo-adjuvant chemotherapy. Only 47 patients had pre-operative biopsy/FNAC. Of 95 patients, only one had complete pathological response. Pure fetal epithelial morphology was seen in 37 tumours, mitotically active fetal morphology in 3, embryonal histology in 24, while rest 31 showed mixed epithelial and mesenchymal histology. Focal small cell histology was seen in only two tumours. Nine patients had cut margin involved by the tumour. Six patients died of disease, 8 patients are alive with disease while 63 patients are free of disease. None of the histologic parameters were found to be prognostically significant.

Conclusion: Although histologic classification of hepatoblastoma is being refined, its applicability is reserved for patients who have not been treated with neoadjuvant chemotherapy. Study of series of 95 patients with hepatoblastoma at our centre underlines the fact that most of the patients in our set up cannot undergo upfront surgery, thus precluding prognostic assessment using histologic subtypes. Secondly, none of the parameters namely histologic subtype, percentage necrosis and status of resection margins showed statistical significance towards prognosis.

PD-067 | Tumour Rupture in Hepatoblastoma: A High Risk Factor?

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Background/Objectives: Hepatoblastoma rupture is a high-risk criterion in SIOPEL-3/4 protocols. The outcome of these children has not been described so far.

Design/Methods: A central radiological review performed in 150 French patients between 01/2000 and 12/2014 reported radiological signs of tumour rupture defined as sub-capsular hematoma ± peritoneal effusion in 26 patients. Nineteen patients with available clinical, radiological and histological data were included in the present analysis.

Results: Median age was 3 years. PRETEXT group was I-II in 6 patients, III in 6 and IV in 7; 4 had lung metastases. Two patients had no sign of rupture before biopsy and presented a hepatic rupture (sub-capsular hematoma and peritoneal effusion) between 1 and 10 days after a surgical biopsy. Six patients had a sub-capsular hematoma only before biopsy; three of them experienced a hepatic rupture between 6 and 13 days after biopsy (needle guided in 1, needle guided and surgical in 1, unknown in 1). Eleven patients suffered from hepatic rupture before biopsy.

All patients except three were treated with high-risk regimens. Liver surgery was performed in 17/19 patients (3 transplantations). Thirteen patients (68%) achieved complete remission. With a median follow-up of 5.5 years, 6 progressions (1 peritoneal), 3 relapses (2 peritoneal) and 6 disease-related deaths occurred. The 4 patients with lung metastases suffered from pulmonary progressive disease, without peritoneal event. Among the 9 patients without lung metastases but with other risk factors (PRETEXT-IV, age > 8 years), 2 peritoneal events occurred. Among the 6 patients without other risk factor than tumour rupture 1 peritoneal event occurred. Concerning the 3 patients with sub-capsular hematoma only, no peritoneal event occurred. The 3y-EFS and OS were 52.6% (95%CI=32-73) and 68.4% (95%CI=46-85), respectively.

Conclusion: Tumour rupture portends a poor prognosis with a risk of peritoneal progression/relapse. Liver biopsy should be very cautious in patients with sub-capsular hematoma.

LYMPHOMAS

PD-068 | Clinical Trial and Survival in African Burkitt Lymphoma: Experience in a Population of Nigerians

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Background/Objectives: To determine the predictors of survival of patients with endemic Burkitt lymphoma (eBL) treated under a sponsored multicentre international study using cyclophosphamide, oncovin and methotrexate (COM)

Design/Methods: All previously untreated patients with eBL that consented were enrolled into the study between 2004 and 2013. A complete history was taken and physical examination done on all patients. Sites and organs involved with BL were identified and documented appropriately. Staging of the disease was as described by Magrath et al. All patients were treated with COM regimen with intrathecal methotrexate and cytarabine. Data management of patients was overseen by a trained data manager who also did home visits to ensure clinic compliance and follow-up. Data analysis was done using Statistical Package for Social Sciences Version 21 software. The overall survival (OS) and relapse free survival (RFS) were computed using the Kaplan-Meier method. Values of 'p' less than 0.05 were accepted as statistically significant.

Results: Of the 109 patients enrolled, the OS at one, two and five years were 65%, 62% and 56% respectively while the RFS at one, two and five years were 59%, 56% and 53% respectively. Median OS and RFS are not yet reached. On log-rank statistical test, receiving at least four cycles of chemotherapy was associated with significantly better OS (p = 0.049). On multivariable Cox regression analysis, receiving at least four cycles of chemotherapy (p = 0.004, OR = 2.577, 95% CI = 1.364 - 4.868) and jaw involvement (p = 0.007, OR = 2.665, 95% CI = 1.314 - 5.403) remained strong independent predictors of OS. None of these variables was a predictor of RFS.

Conclusion: COM is an effective regimen in treating endemic Burkitt lymphoma and receiving at least four cycles of this regimen is a good predictor of overall survival.

PD-069 | Prognostic Significance of "B" Symptoms in Paediatric T-Lymphoblastic Lymphoma: An Analysis of 46 Patients Treated with BFM-90 LL Protocol

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Background/Objectives: "B" symptoms are routinely not taken into account for staging in paediatric patients with non-hodgkin lymphoma and data are limited assessing its prognostic significance.

Design/Methods: This is a single institutional review of patients upto 18 years of age with diagnosis of T-lymphoblastic lymphoma (T-LL) treated with uniform chemotherapy protocol (BFM-90 LL) between June'03-Jan'15. "B" symptoms were defined as - unexplained weight loss of more than 10% of the body weight in 6 months prior to presentation, unexplained fever with temperature > 38 °C, and night sweats.

Results: Forty six patients of T-LL were treated with median age 13 years (range: 1-18); male: female ratio- 32:14 and median symptom duration of 53 days (range: 12-365). "B" symptoms were present in 26 (57%) patients (fever in 51%, weight loss and night sweat in 9% each). Hypoalbuminemia (≤ 3.5 g/dl) was associated with presence of "B" symptoms (p=0.03), whereas high white blood cell count ($> 11,000$ /ml) had slightly higher association with "B" symptom (p=0.09). After median follow-up of 30.2 months (range: 1.1-97.9) 5 year event-free-survival (EFS) and overall survival (OS) was 65.8±7.2% and 79.1±6.2%, respectively. Absence of "B" symptoms predicted superior EFS (5 year value-89.4±7.1% vs 50±9.8%, p=0.03) in univariate analysis whereas hemoglobin > 10 g/dl showed a trend towards superior EFS (4 year value- 73.8±7.5% vs 37.5 ±16.1%, p=0.065), but no factor predicted OS. On multivariate analysis, absence of "B" symptoms independently predicted superior EFS (p=0.04).

Conclusion: Long term outcome was reasonable in our patients with T-LL treated with uniform chemotherapy protocol. Presence of "B" symptoms was associated with hypoalbuminemia and was the only independent predictor of inferior EFS.

PD-070 | Relapsed Refractory Paediatric Hodgkin Lymphoma (rrHL) - Single Centre Retrospective Study Over 16 Years

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Background/Objectives: Pediatric Hodgkin lymphoma (HL) is a highly curable disease, with estimated 5 year survival rates exceeding 95%.

Because of the small number of patients that fail primary therapy, no uniform prognostic factors and second-line treatment strategy exist for this patient population with relapsed/refractory HL (rrHL).

Our objective was to evaluate the prognostic factors and outcome of patients diagnosed with rrHL at our center.

Design/Methods: We completed a cross-sectional retrospective study of all children diagnosed with rHL over 16 years. We evaluated the characteristics of the patients at initial presentation and at relapse, salvage regimens used, response, overall survival (OS) rates, and incidence of progression.

Results: From 1996 to 2012, 30 patients (median age 14 years) with refractory ($n = 8$) or first relapse ($n = 22$) rHL were diagnosed out of a total of 310 patients registered with Hodgkin lymphoma. Median time from end of initial treatment completion to relapse was 4.5 months (1–96). Salvage therapy consisted of chemotherapy with or without radiation and stem cell rescue. Twenty-six patients received high dose chemotherapy - autologous stem cell transplantation (HDCT-ASCT). Consolidative radiotherapy (cRT) was given in 13 cases.

With a median follow-up of 46 months (3–169), significant prognostic factors were time to progression/relapse ($P=0.005$), bulky nodal disease ($P=0.02$) and response to salvage chemotherapy ($P=0.001$). Overall survival (OS) for the entire cohort was 47.7%. OS in patients with refractory disease (relapse < 3 months) and early relapse (relapse 3–12 months) were 12.5+23.4% and 55.9 + 26.2% respectively. All patients with late relapse (> 12 months) were salvaged.

Conclusion: In our study, salvage rates for rHL cases diagnosed less than 12 months from first treatment completion remain poor. Prospective cohort studies with the use of novel agents in combination with HDCT-ASCT/cRT are required to define the optimal treatment for this patient subgroup.

PD-071 | Screening of Renal Dysfunction among Burkitt Lymphoma Survivors by Novel Markers

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Background/Objectives: Burkitt lymphoma (BL) represents the most common pathological type of non-Hodgkin lymphoma in our region. Recently, high success rates have been achieved in BL treatment. Little is known about long-term renal dysfunction in this vulnerable group. In the present study, we tried to detect early chronic kidney diseases (CKD) among BL survivors by using novel screening modalities.

Design/Methods: We investigated 53 children (aged 10 ± 2.8 years, 34 boys) who successfully treated for Burkitt lymphoma, based on LMB96 protocol, as "patient group" and 30 children as control. All eligible participants were subjected to history taking, physical assessment, and routine laboratory investigations including urine analysis, kidney function test. Estimated glomerular filtration rates using New Schwartz formula (GFR_{CKD}) were calculated and chronic kidney disease prevalence was diagnosed accordingly. Also, serum Cystatin-C (Cys-C) and Neutrophil-Gelatinase-associated Lipocalin (NGAL) were determined as novel markers aiming at early and accurate detection of subclinical CKD in BL survivors.

Results: After 18.3 ± 5.2 months of BL cytotoxic therapy completion, almost one third of BL survivors showed evidence of subclinical CKD when estimated GFR_{CKD} (26.3%), serum Cystatin-C (32%) and serum Neutrophil-Gelatinase-associated Lipocalin (28%) were used for kidney function monitoring. This prevalence was 4–6 folds higher than that detected by routine serum creatinine screening (5.5%). Significant persistent albuminuria was diagnosed at 4/53 (7.53%) of BL survivors and asymptomatic hypertension were reported in 1/53 (1.9%) of them compared to none of the controls. Positive correlation could be displayed between serum Cys-C and serum NGAL. Conversely, negative correlations between both of them and estimated GFR_{CKD} were documented.

Conclusion: Novel modalities such New Schwartz formula (GFR_{CKD}) estimation, serum Cys-C and serum NGAL assessment should be incorporated in the routine follow-up screening for CKD among BL survivors for accurate diagnosis of such detrimental morbidity.

PD-072 | Risk Factors for Predicting Survival in Paediatric Advanced Hodgkin Lymphoma Treated with ABVD: A Multicenter Study of 186 Patients

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Background/Objectives: Clinical stage alone is used for risk stratification in treatment of paediatric advanced Hodgkin lymphoma (HL) with hybrid and aggressive chemotherapy regimens. Identifying other risk factors predicting survival is important to avoid over-treatment of majority, and escalate therapy only in high risk patients.

Design/Methods: We collected data from 3 tertiary cancer centers on 186 patients with advanced stage (IIB-IV) consecutively treated with ABVD chemotherapy. Radiotherapy was given to patients with bulky disease. Freedom from treatment failure (FFTF) and overall survival (OS) were end points. Based on risk factors identified in multivariate analysis, a risk score was formulated for predicting FFTF and OS.

Results: With median follow-up period of 57.9 months (Range: 1–151 months), 5-yr FFTF and OS for entire cohort was 84.8% (95% CI-78.6–89.3%) and 95.3% (95% CI- 90.78–97.6%) respectively. We identified stage 4 [HR-3.58(1.25,9.97); $p=0.017$], high total leukocyte count ($>15000/mm^3$) [HR-2.91(1.04,8.18); $p=0.042$] and lymphopenia (lymphocyte count $\leq 8\%$) [HR-5.06(1.67,15.33); $p=0.004$] predictive of inferior FFTF. Patients with none of these risk factors had significantly better 5-yr FFTF (92.3%) as compared to those with one risk factor (74.01%; $p=0.016$) and two risk factors (33.33%; $p=0.001$). Stage 4 disease [HR-8.6(1.07, 69.95); $p=0.043$] and lymphopenia [11.2(1.32, 95.12); $p=0.027$] were predictive of inferior OS. Based on these risk factors, OS for patients with no risk factors (98.8%) was significantly better than patients with 1 risk factor (87.3%; $p=0.015$) and 2 risk factors (50%; $p=0.006$).

Conclusion: Lymphopenia and high total leukocyte count are additional risk factors apart from stage 4 disease to predict inferior FFTF. Stage 4 disease and lymphopenia predict inferior OS. Only patients with presence of these high risk factors may require aggressive or hybrid regimens. Aggressive therapy can be avoided in majority of advanced paediatric HL patients and these may be managed with a relatively less toxic ABVD regimen with excellent outcome.

PD-073 | Lactate Dehydrogenase (LDH) and Clinical Stage in Endemic Burkitt Lymphoma: A Model for Risk-Stratification in Sub-Saharan Africa

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Background/Objectives: Survival rates for endemic Burkitt lymphoma (eBL) vary, ranging from 30–60% in sub-Saharan Africa. Conversely, cure rates for sporadic Burkitt lymphoma in high-income countries approach 90%, where children are effectively risk stratified using clinical stage and lactate dehydrogenase (LDH) level at time of diagnosis. Such standardized risk-stratification approaches for eBL in sub-Saharan Africa are lacking.

Design/Methods: We analyzed data from a prospective cohort of children ≤ 18 years with pathologically confirmed eBL between 2013–2015 in Lilongwe, Malawi. Elevated LDH was defined as $>2x$ the upper limit of normal. St. Jude stage was assigned based on physical exam, abdominal ultrasound, chest x-ray, and CSF cytology. The chemotherapy regimen was a modified CHOP protocol (cyclophosphamide, doxorubicin, vincristine, prednisone) given over 6 cycles.

Results: Among 73 children with eBL, median age was 9.2 years with 25 (34%) females. Stage I/II presentation occurred in 12 patients (16%), while advanced stage III and IV disease occurred in 36 (49%) and 25 (34%) respectively. There were 66 patients with baseline LDH assessment. Of these, 24 (36%) had elevated LDH and 55 (83%) presented with stage III/IV disease. Of 24 patients with elevated LDH, 23 (96%) had stage III/IV disease. All stage III patients with elevated LDH had palpable abdominal masses. None of the 7 patients with abdominal involvement identified only by ultrasound had elevated LDH. The 12-month overall survival (OS) for the cohort was 40% (95% CI 28–52%). Twelve-month OS for patients with elevated LDH was 27% (95% CI 11–45%) compared to those without elevated levels 57% (95% CI 38–72%, $p=0.012$).

Conclusion: Among children with eBL in Lilongwe, elevated LDH at presentation was associated with stage III/IV disease, palpable abdominal mass, and worse survival. Routine use of LDH with clinical stage could allow for more effective risk-stratification to guide therapy and improve survival.

PD-074 | Is PET Based Treatment of Hodgkin Disease in Children Cost Effective in Developing Country; Experience from a Tertiary Care Center from Karachi

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Background/Objectives: PET is an established imaging modality to assess response and provide treatment guideline for Hodgkin Disease in children. Its use is limited in Pakistan because of expense. The objective of this study is to assess cost effectiveness of PET based treatment of Hodgkin disease.

Design/Methods: Retrospective review and prospective follow up of children treated with PET based protocol from September 13 to July 15. Three treatment groups (TG I, II and III) assigned based on staging. PET done at diagnosis and after 3 cycles. If complete remission no radiation. In TGI treatment was stopped, in TGII and III further 2 and 4 cycles given. Those with obvious activity on PET received radiotherapy. Outcome is analysed to assess efficacy and cost effectiveness of this approach.

Results: We had 78 untreated patients enrolled. Age ranged (3–16 years) median 8 years. Male to female ratio 4.5:1. Nodular sclerosis was most common subtype (42/78) followed by mixed cellularity (32/78). In TG I 22/23 had CR after 3 cycles and only one patient needed radiation. Survival to date is 100%. In TG II 15/16 had good response. One child with poor response needed radiation and relapsed but alive. The overall survival is 100%. In TG III 6/39 had no CR and needed extended chemo, radiation was not offered due to extensive disease. Overall survival in this group is 84%. 4 children expired due to toxicity and death before chemotherapy. The overall survival of whole group is 92% with a median follow up of 2 years.

Conclusion: With the PET based approach not only money is saved with reduced number of chemo cycles and less radiation but also late side effects are minimised with improved quality of life. Overall survival is excellent but longer follow up is needed to validate this finding.

MYELOID LEUKEMIAS, MYELOYDYSPLASTIC AND MYELOPROLIFERATIVE SYNDROMES

PD-075 | Increased Survival for Children with Acute Myeloid Leukaemia Results from Improved Post-Relapse Treatment

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Background/Objectives: The treatment for paediatric acute myeloid leukaemia (AML) has not changed significantly over the past 3 decades, yet outcomes have improved with cure rates increasing from 30% to over 50% of all newly diagnosed children over this period. This improvement in survival has been attributed to both treatment intensification and improved supportive care over the decades, although the precise impact of each remains unknown.

Design/Methods: We retrospectively analysed a unique cohort of 276 patients with *de novo* AML diagnosed in childhood, all treated with the same chemotherapy protocol over a 25-year period from 1986–2012. All patients were followed up until 1st January 2015 or death, whichever was sooner.

Results: The contemporary cohort (2000–12), compared to historical cohorts (1986–99) had significantly improved overall survival (OS, 75% vs. 50%, HR 2.17, 95% CI 1.15–2.93), lower disease related mortality (38% vs. 19%, $p = 0.02$) and were significantly more likely to receive an allogeneic transplant after relapse (SCT, 73% vs. 12%, $p < 0.0001$). Allogeneic transplant post relapse was associated with a significantly improved survival across the entire cohort (OS 50% for allogeneic SCT vs. 12% for autologous or none, $p < 0.0001$). There was no significant difference between the contemporary and historical cohorts in treatment related mortality (13% vs. 7%, $p = 0.42$) or relapse rates after induction (50% in older cohort vs. 40% in recent era, $p = 0.25$), suggesting consistency of induction treatment efficacy and toxicity across the two periods.

Conclusion: Our data suggests improved survival in paediatric AML in the modern era has predominantly resulted from changes in treatment post relapse, including increased use of allogeneic SCT. These results also indicate that increased use of unrelated donors for stem cell transplants in CR2 can lead to improved outcomes for children with AML in the modern era.

PD-076 | Outcomes of Acute Myeloid Leukemia in Children with Down Syndrome Treated with Low-Dose Cytarabine and 6-Thioguanine

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Background/Objectives: Children with Down syndrome (DS) have up-to 20 fold increased risk of acute leukaemia. In the young children with DS, acute myeloid leukaemia (AML) is commonly found and have better outcome when using less intensive chemotherapy. The aim of this study is to evaluate a less intensive chemotherapeutic protocol for children with AML and Down syndrome (AML-DS).

Design/Methods: Retrospectively, infants and children with DS who was diagnosed as AML at our institute between June 1997 and March 2016 were included. All patients were treated with chemotherapy consisted of cytarabine (100 mg/m²/day) and 6-Thioguanine (100 mg/m²/day) for 7 days during induction and for 5 days during maintenance phase. The maintenance phase was repeated every 4 weeks for the total of 20 cycles. Prophylaxis with intrathecal cytarabine was administrated.

Results: There are 15 patients (9 males and 6 females) diagnosed with AML-DS. The median age at diagnosis was 18 months (range 1–47 months). Twelve of them (80%) were acute megakaryoblastic leukaemia (M7) and the rest were acute erythroblastic leukaemia (M6). Six patients were previously diagnosed with myelodysplastic syndrome (MDS) by the average time to develop AML was 3.4 months (range 1–8 months). One patient was excluded due to parental refusal. Thirteen of the 14 treated children achieved complete remission (CR) and only one patient never remitted. The 5-year event-free survival rate was 73.33% (95% CI, 29.69–84.52) and 5-year overall survival was 73.33% (95% CI, 29.69–84.52) with the median time to follow up of 42 months. During the maintenance chemotherapy, two of them (14.28%) had bone marrow relapses and unable to achieve second remission. Four patients died, 3 of them died due to uncontrolled disease and one died due to infection.

Conclusion: This non-intensive protocol is effective for AML-DS and has better treatment outcome compared to non-DS children who received more intensive protocol.

PD-077 | Fungal Infections in Paediatric Acute Myeloid Leukemia: A Report on 188 Patients at King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia

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Background/Objectives: Fungal Infections represent a growing problem in paediatric leukaemia. A fungal colonization is sometimes followed by a subsequent fungal infection, resulting in prolonged hospitalization and delay in chemotherapy. In various studies, the incidence of Invasive Fungal Infections is reported to be from 5–13% with a peak of up to 24% in paediatric AML patients.

Design/Methods: We performed a retrospective study where 52 AML patients with fungal infections were compared with 136 AML patients without fungal infections. All patients were between 0–14 years of age and attended our institute between 2005 to 2015.

Results: Median age at diagnosis was 6.63 years with ranges (min: 0.56–max: 13.65) & 5.36 years (min: 0.11 – max: 13.84) for infected and non-infected groups respectively. There were 27 (52%) males in infected and 77 (57%) males in others. Amongst the infected group, 33 patients (63.4%) had proven fungal infections with 26 culture and 7 pathology positive while the remaining 19 (36.5%) had presumptive evidence based on radiology. There were 16,(48.4%) *Candida Albicans*, 6, (18%) *Aspergillus Flavus*, 4, (12%) *Candida Tropicalis*, 2 (6%) *Candida dubliniensis*, and one (3%) *Candida krusei*, *Epidermophyton floccosum*, *Rhizopus*, *Trichosporon asahii* and *Fungal Osteonecrosis* each. Fungal infection sites were represented predominantly by Lungs 6, (18%), Oral Cavity 4, (12%) and Blood 4,(12%) respectively. There were 21(40%) deaths in the infected group in which fungal infections contributed for 7(33.3%) deaths, with a five year overall survival of 55.6%. Our non-infected group had 56, (41%) deaths, with a five year overall survival of 50.3%. 18, (34.6%) patients relapsed in the infected group compare to 53(38.9%) in the non-infected group.

Conclusion: Our results showed early detection and treatment of fungal infections has a major impact on the overall survival of AML patients with fungal infections.

PD-078 | Germline Variants in MLL3 in Infantile Leukemia Skew Myeloid Hematopoietic Differentiation

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Background/Objectives: Infant leukaemia (IL) is a rare disease that arises *in utero* and has a mortality rate of >50%. The disease is marked by >75% of cases with a rearrangement in *MLL*, but these rearrangements typically fail to result in short latency leukaemia in model systems when expressed at physiologic levels. Curiously, whole genome sequencing has shown that IL has the lowest mutation rate of any sequencing cancer at 1.3 non-synonymous mutations per genome. We have shown that patients with IL have a significant enrichment of non-synonymous germline variants. Specifically, 100% of AML patients and 70% of ALL patients ($N \sim 100$) have bi-allelic non-synonymous variants in *MLL3*, which has been shown to be a tumour suppressor gene for AML in myelodysplastic syndrome.

Design/Methods: We investigated the impact of *MLL3* knockdown by shRNA on hematopoietic differentiation in human umbilical cord blood (UCB) and CRISPR-mediated homozygous knockout of *MLL3* in human iPSC cells as well as mouse models with homozygous frameshift mutations in the 5' end of *MLL3*.

Results: We find that in IL, germline, bi-allelic non-synonymous *MLL3* variation must co-occur with either *MLL*-rearrangements or additional germline variation in *MLL1* or *MLL2*. Functionally, 5' frameshift mutations in *MLL3* in mice yields a significant increase in HSCs at the expense of more committed progenitors. In human UCB and iPSC, *in vitro* knockdown or knockout of *MLL3* leads to expansion of multipotent myeloid progenitors with a corresponding decrease in erythroid progenitors.

Conclusion: Infant leukaemia has exceptionally few acquired mutations, but has a very distinct signature of germline variation in mechanisms regulating hematopoietic development. Our results suggest that *MLL3* may help to balance myeloid and erythroid progenitor development. Without *MLL3*, myeloid differentiation predominates in what may be a pre-leukemic state. Additional work will profile transcriptomes and epigenetics to determine the mechanisms of myeloid skewing and transformation.

PD-079 | Comprehensive Genetic Studies in Paediatric Myelodysplastic Syndromes

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Background/Objectives: Myelodysplastic syndromes (MDS), a group of heterogeneous stem-cell bone marrow disorders, constitute nearly 3–7% of all hematopoietic neoplastic disorders in children. Characterized by an ineffective hematopoiesis in one of the three myeloid lineage cells, MDS is primarily seen in adults; paediatric MDS is rare and is usually associated with poor prognosis. Due to the rarity of the disease and lack in consensus for classification and clinical diagnosis, there is a paucity of comprehensive genetic studies in paediatric MDS.

Design/Methods: We examined the cytogenetic and FISH data in 205 consecutive specimens from paediatric cases with MDS that were referred to the Human Genetics Laboratory at the University of Nebraska Medical Center. To determine submicroscopic genomic changes that could not be detected by cytogenetics or FISH, we performed single nucleotide polymorphism (SNP) microarray studies utilizing CytoScan[®] HD array (Affymetrix) in 20 cases with additional available bone marrow specimens.

Results: Abnormal cytogenetic and/or FISH findings were noted in 55 (55/205; 27%) specimens and 43 of these contained MDS-associated alterations: monosomy 7/del(7q) observed in 35%; trisomy 8 in 18%; del(20q) in 18%; monosomy 5/del(5q) in 9%; and abnormality of 11q23 in 4% of the 43 specimens. Microarray detected additional genetic alterations in 50% (10/20) of the cases with partial or complete gain/loss of MDS-associated genes and/or genes involved in hematopoiesis, cell cycle proliferation/regulation, or apoptosis. Gain of *PRDM16*, *EXT2*, *MYH11*, *CBFA2T3*; gain/loss of *IRF4*; and loss of *KIF14*, *ALK*, *PIMI1*, *RUNX2*, *IKZF1*, *CHEK2* were noted. Gain of *PRDM16* an MDS-associated gene located within chromosome region 1p36, was observed in 5/10 cases with abnormal microarray findings.

Conclusion: Our results helped identify novel and distinct genetic changes that can be useful in categorizing paediatric MDS and emphasized the need for comprehensive genetic studies, including microarray, for improved therapeutic approaches in paediatric MDS.

PD-080 | Arsenic Trioxide and All-Trans-Retinoic Acid Exert Synergistic Cytotoxicity Selectively Against FLT3-ITD Leukemia Cells Via Co-Inhibiting FLT3 Signaling Pathways

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Background/Objectives: FLT3-ITD mutations occur in approximately 30% of acute myeloid leukaemia (AML) and are independently predictive of adverse outcomes. Currently available FLT3 inhibitors have *in vitro* but limited clinical activity in FLT3-ITD AML because of acquired resistance during treatment. Arsenic trioxide (ATO) combined with all-trans-retinoic acid (ATRA) has greatly improved the prognosis of FLT3-ITD acute promyelocytic leukaemia, and ATO or ATRA respectively has been reported to enhance the apoptosis of FLT3-ITD AML cells induced by the FLT3 inhibitors, providing a rationale to investigate the role of ATO/ATRA in FLT3-ITD AML.

Design/Methods: Twelve human leukaemia cell lines including those with FLT3-ITD mutations (MV4;11/MOLM-13) were treated with ATO and ATRA, and the growth inhibition,

apoptosis and cell cycle arrest of the cells were measured by CCK-8 assay, western blot and flow cytometry respectively. FLT3 signaling pathways affected by ATO/ATRA were investigated including using RNA sequencing, PCR validation, gene silencing technique and western blot.

Results: ATO/ATRA combination exerted synergistic cytotoxicity only selectively against FLT3-ITD AML cell lines (MV4;11/MOLM-13) of the 12 cell lines tested via co-repressing FLT3. The signaling pathways in the FLT3-ITD cells affected by ATO/ATRA include FLT3/STAT5/MYC, FLT3/STAT5/E2F1, FLT3/ERK/ATF5/cyclin D_{1/3} and FLT3/AKT/ATF5/cyclin D_{1/3}. Moreover, ATF5 was first identified as an oncogene in FLT3-ITD AML cells.

Conclusion: Our study indicates that ATO/ATRA combination exerts synergistic anti-leukemic effects via co-inhibiting FLT3 signaling pathways, which may provide a novel therapeutic approach for refractory FLT3-ITD AML.

NEUROBLASTOMA

PD-082 | Activation of Mitochondria Mediated Cell Death through Targeting VDAC1 with MIR-324-5p in Neuroblastoma

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Background/Objectives: miRNAs are post-transcriptional regulators of gene expression. Their dysregulation is associated with clinico-pathological parameters in neuroblastoma. Thirty-seven miRNAs were significantly over- or under-expressed in MYCN amplified tumours in comparison with MYCN diploid tumours. In the present study, we hypothesized that miR-324-5p can activate cell death pathways in neuroblastoma.

Design/Methods: We carried out Kaplan-Meier analysis to validate clinical significance of miR-324-5p in a cohort of 364 neuroblastoma tumours. Biological function of miR-324-5p was assessed in MTT and BrdU assays using neuroblastoma cell lines NB1691, SKNAS and Kelly. Expression of VDAC1 was examined with RT-qPCR and Western blot.

Results: The low expression of miR-324-5p is significantly associated with poor prognosis (raw $p=1.4E06$; $p=4.5E04$, Bonferroni correction). Ectopic over expression of miR-324-5p in neuroblastoma cell lines significantly inhibited cell viability and proliferation ($p=0.016$, Anova) and inversely correlated with the expression of the Voltage-Dependent Anion Channel 1 (VDAC1) on mRNA and protein levels. Luciferase assay confirmed the direct targeting VDAC1 3'UTR with miR-324-5p. Both siVDAC1 and miRNA-324-5p transfections reduced VDAC1 mRNA levels in comparison with scramble control to 25% ($p=0.011$, t-test) and 44% ($p=0.0098$, t-test), respectively. VDAC1 protein levels decreased in a similar manner. Down regulation of VDAC1 causes significant reduction in mitochondria genes: MT-CYB ($p<0.001$) and MT-ND4L ($p<0.001$).

Conclusion: miR-324-5p suppresses cell viability and proliferation in neuroblastoma cells through direct targeting of VDAC1 - the primary protein in the outer mitochondrial membrane. VDAC1 down regulation causes reduction of mitochondria genes leading to cell death. Our findings mark miR-324-5p as a negative regulator of VDAC1.

PD-083 | Circulating Tumour DNA for Disease Monitoring in Neuroblastoma

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Background/Objectives: Circulating tumour DNA (ctDNA) has been used for disease monitoring in several types of cancer. Therefore, the aim of our study was to investigate whether ctDNA can be used for treatment response monitoring in neuroblastoma.

Design/Methods: 121 plasma samples from 50 patients were analyzed for the detection of hypermethylated RASSF1A DNA. DNA was isolated and total cell free-DNA (cfDNA) was determined by qPCR for albumin and the amount of ctDNA was determined by qPCR for methylated RASSF1A after bisulfite conversion. Detection of ctDNA was compared with clinic-biological patient characteristics, such as BM and PB MRD (qPCR), MIBG scans and urinary catecholamines.

Results: In 13/20 diagnostic samples ctDNA was detected. In all 7 diagnostic samples from patients with localized disease no ctDNA was detected. During induction chemotherapy (stage 4 patients only) in 13/42 samples ctDNA was detected (30%). At relapse in 8 out of 14 samples ctDNA was detected (57%). The amount of cfDNA was significantly higher in neuroblastoma patient at time of diagnosis and relapse than in healthy controls and stage 4 patients had the highest amount of cfDNA. There was a significant correlation between ctDNA and PB or BM MRD, when tumour levels were high or no tumour was detected. Discrepancies were observed in 20 samples and were studied in detail. The discrepancies were mainly observed in samples during treatment when tumour burden was lower.

Conclusion: Hypermethylated RASSF1A can be used as marker for monitoring of ctDNA in neuroblastoma patients and highly correlates with the disease status at diagnosis. Our data indicate that there is no correlation when tumour load is lower because during treatment in several samples discrepancies were observed. It is likely that ctDNA can originate from both

primary tumour as metastases and may be of special interest for disease monitoring in patients relapsing in other organs than the BM.

PD-084 | Harnessing Cross Reactivity of Cytomegalovirus Reactive Gamma Delta T Cells in Paediatric Neuroblastoma

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Background/Objectives: Neuroblastoma is the commonest cancer in infants. Survival in high risk groups is low at 40-50%. Newer treatments are needed to improve survival and morbidity. Cytomegalovirus (CMV) is a common viral infection which increases gamma delta ($\gamma\delta$) T cells. We investigated the use of CMV reactive $\gamma\delta$ T cells as a potential new immunotherapy.

Design/Methods: Peripheral blood mononuclear cells from 30 paediatric haemato-oncology patients with/without CMV infection were analysed by flow cytometry. $\gamma\delta$ T cells were expanded, then co-cultured with CMV infected fibroblasts or neuroblastoma cells. Interferon gamma secretion was measured by ELISA, cytotoxicity by MTT assay and blocking assays identified receptors involved. $\gamma\delta$ T cell receptors (TCR) were determined by sequencing.

Results: Paediatric haemato-oncology patients with acute CMV had higher proportions of V δ 1 and non-V δ 1/V δ 2. There was a statistical difference between the frequencies of V δ 1 and V δ 2 ($p=0.0035$) and non-V δ 1/V δ 2 and V δ 2 ($p=0.0013$). V δ 1 frequency was higher in CMV infected patients than negative patients but V δ 2 frequency was lower ($p=0.0312$, $p=0.0314$ respectively). $\gamma\delta$ T cells were expanded to significant numbers for adoptive transfer. $\gamma\delta$ T cells from patients with acute CMV infection had statistically significantly higher interferon gamma release in co-cultures with CMV infected fibroblasts and showed cytolytic activity against CMV infected fibroblasts and neuroblastoma cells which was mediated by the $\gamma\delta$ TCR and NKG2D receptor. Sequencing showed the dominant chains in CMV infected patients were V δ 1 and V γ 2. V δ 1 CDR3 sequences had minimal diversity but the gamma chain had wide variations.

Conclusion: Acute CMV infection in paediatric haemato-oncology patients leads to an increase in V δ 1 $\gamma\delta$ subtype of $\gamma\delta$ T cells. They can be expanded for adoptive transfer. They recognise and kill CMV infected targets and neuroblastoma cells via the $\gamma\delta$ TCR and NKG2D receptor. CMV reactive $\gamma\delta$ T cells are therefore a potential form of immunotherapy for neuroblastoma.

PD-085 | The PPM1D-Encoded Wip1-Phosphatase is a Candidate Oncogene on 17q Contributing to Neuroblastoma Development and Providing a Novel Therapeutic Target

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Background/Objectives: In neuroblastoma 17q-gain is the most powerful genetic predictor of adverse clinical outcome. 17q+ correlates with poor survival in our population-based material where we found aberrations of chromosome 17 in 85% of primary neuroblastomas, specifically, gain of PPM1D/Wip1 at 17q23 was present in all these tumours. Wip1 is a serine/threonine phosphatase encoded by PPM1D, described as a gatekeeper in the Mdm2-p53 regulatory loop involved in genetic stability, inflammation and a potential oncogene contributing to carcinogenesis.

Design/Methods: Comparative genomic hybridization (CGH), immunostaining, mRNA arrays, qPCR, exome- and RNA-sequencing was used to examine PPM1D/Wip1 in neuroblastoma. Genetical and pharmacological inhibition was used to analyse the function of Wip1 in preclinical neuroblastoma models.

Results: CGH-array analysis detected PPM1D/Wip1 extra copies in all tumours and cell lines containing 17q-gain. Expression arrays and immunostaining showed high expression of Wip1 in neuroblastoma corresponding to poor survival. RNA-sequencing confirmed PPM1D-gain and revealed truncated isoforms with oncogenic potential. Exome-sequencing detected a mutation leading to constitutive PPM1D/Wip1 activation in an aggressive metastatic neuroblastoma belonging to an infant girl. Wip1 knockdown experiments showed significant decrease of cell viability, proliferation and colony formation as well as substantial increase of DNA-damage response in neuroblastoma cells. Tumour xenograft development was significantly delayed showing median tumour development (0.10 mL) to be more than doubled (median 15 days, vs. 33 days, $p<0.001$) after Wip1 downregulation compared to scrambled controls. A novel Wip1 inhibitor was highly potent in cytotoxic/cytostatic effect in neuroblastoma cell lines (median IC50 0.8 nM). Furthermore, this Wip1 inhibitor significantly inhibited growth of established human neuroblastomas in nude mice after 12 days of treatment ($p<0.01$). Tumour volumes were reduced 56% compared with untreated controls.

Conclusion: The p53-regulating PPM1D/Wip1 phosphatase is oncogenic in neuroblastoma development and activated due to 17q-chromosomal gain, alternative RNA-isoforms and/or specific DNA-mutation. PPM1D/Wip1 provides a novel druggable therapeutic target in high-risk neuroblastoma.

PD-086 | Targeting the Benign to Kill the Malignant : Inhibition of Inflammatory Progression of Neuroblastoma by Targeting mPGES-1 in Cancer Associated Fibroblasts in the Tumour Microenvironment

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Background/Objectives: High-risk neuroblastoma often show treatment resistance or relapse despite intensive multimodal therapy. We recently described (PNAS 2015) the common neuroblastoma promoting microenvironment with infiltrating cancer associated fibroblasts (CAFs) expressing the mPGES-1 enzyme, essential for prostaglandin E₂ (PGE₂) synthesis. PGE₂ regulates tumour inflammation and immune suppression, angiogenesis, genetic instability, tumour progression and therapy resistance. We now investigated the impact of novel therapy targeting the COX/mPGES-1/PGE₂ pathway.

Design/Methods: Human neuroblastomas were investigated for immunosuppressive microenvironment and expression of the COX/mPGES-1/PGE₂/EP-receptor pathway. High-risk *in vivo* models, human 11q-deleted xenografts and transgenic MYCN-driven tumors, were treated with a novel specific mPGES-1 inhibitor. Inflammatory lipid mediators were analyzed by LC-MS/MS. Tumour tissues were analyzed by immunohistochemistry, immunofluorescence and FACS.

Results: Tumour microenvironment in human high-risk neuroblastomas and both 11q-deleted xenografts and MYCN-driven transgenic mice displayed mPGES-1 expression in PDGFRb+ cancer associated fibroblasts. The inflammatory regulator STAT3 was active in mPGES-1 expressing CAFs. Expression of the inflammatory COX/mPGES-1/PGE₂/EP-receptor pathway in experimental tumors resembled human high-risk neuroblastomas.

Targeting mPGES-1 with a novel compound reduced PGE₂, induced M1 polarization of macrophages, decreased CAFs and reduced angiogenesis significantly in treated tumors. Tumour development in the xenograft model was delayed ~50% (median 38 vs. 25.5 days) and growth of established xenografts and transgenic tumors was significantly decreased ~50% compared to tumors in untreated animals ($p < 0.05$ - $p < 0.003$). Tumour cell stimulated CAF migration was inhibited by targeting mPGES-1.

Conclusion: Tumour-promoting inflammation and suppression of anti-tumour immunity in neuroblastoma is mediated through PGE₂ and STAT3 expression in CAFs in tumour microenvironment. Early targeting of mPGES-1 may inhibit CAF infiltration and tumour development. This novel tumour treatment modulates tumour-promoting microenvironment and inhibits significantly tumour growth. We conclude that treatment targeting non-malignant cells in neuroblastoma microenvironment may constitute a novel clinical therapeutic approach.

PD-087 | Maintenance DFMO Increases Survival in High Risk Neuroblastoma

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Background/Objectives: High Risk Neuroblastoma (HRNB) remains a challenge, accounting for 15% of all paediatric cancer deaths. While most attain remission, the natural history of HRNB is well documented with approximately half of patients relapsing within 5 years after completion of immunotherapy. This study evaluated the effectiveness of the ODC inhibitor difluoromethylornithine (DFMO) as a maintenance therapy to prevent relapse in HRNB patients after the completion of standard therapy.

Design/Methods: This study was a single agent, multicenter study, enrolling from June 2012 to February 2016. Patients received 27 four-week cycles of oral DFMO at a dose of 750 ± 250 mg/m² twice daily. Event free survival (EFS) and overall survival (OS) were determined on an intention-to-treat basis.

Results: A total of 101 patients received DFMO, 98 were eligible for the intention to treat (ITT) analysis. For all ITT patients, EFS was 89% (± 4%) and OS 98% (± 2%) at 2 years. For the subgroup of patients (n=79) who had been previously enrolled on ANBL0032 prior to starting this study, the 2 year EFS was 92% (± 4%) and OS 98% (± 2%). DFMO was well tolerated, with grade 2-3 transaminitis being the most common toxicity reported in <10% of patients.

Conclusion: DFMO at 750 ± 250 mg/m² BID following completion of standard therapy for HRNB is safe and associated with improved EFS and OS in children with HRNB. DFMO is now currently undergoing further evaluation in a prospective confirmatory study for additional safety and pharmacokinetic analysis.

PD-088 | 5 Year Outcomes after Proton Therapy for Treatment of High-Risk Neuroblastoma (HR-NBL)

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Background/Objectives: Patients with HR-NBL require radiation to the primary tumour site. Proton radiotherapy (PRT) may promote organ sparing, but long-term outcomes have not been studied.

Design/Methods: Sequential patients with HR-NBL received PRT at our institution: 2160 cGy(RBE) was delivered to the primary tumour bed (pre-surgical gross tumour volume, 1 cm expansion to clinical target volume, and 0.5 cm expansion to planning target volume). Residual

disease was boosted to 3600 cGy(RBE). Persistent metastatic sites received 2160 cGy(RBE). 4D CT was utilized for planning. All procedures were IRB approved.

Results: From 9/2010-9/2015, 45 patients with HR-NBL received PRT following multiagent chemotherapy, resection, and high-dose chemotherapy; 10 (22%) also received therapeutic MIBG. Median age was 46m at the time of PRT (10m – 12y); 24 (53%) were boys. Primary tumors were adrenal in 40 (89%); 11 (24%) received boost. Ten metastatic sites in 8 patients were radiated. Double scattered (DS) proton beams were used for 19 (41%) patients, in combination with x-rays for 2 (4%). The remaining 26 (58%) received pencil beam scanning (PBS) which became available in 1/2013. With median follow-up of 26m (6 - 58m) from PRT, 38 (84%) patients are alive, and 36 (80%) disease free. One (2%) experienced abdominal local recurrence; the remaining 8 (18%) experienced relapse at distant, non-radiated sites. No patient has experienced WHO G3/4 long-term toxicity. Intended constraints for organs at risk were achieved for all, including 80% of combined kidneys < 1800 cGy(RBE) and 70% of liver < 20 cGy(RBE). Posterior beams were used for both DS and PBS, although PBS plans required, on average, fewer iterations.

Conclusion: We observe excellent outcomes in patients treated with PRT for HR-NBL over a 5 year period, with 84% of patients alive and 98% free of local recurrence. This safe treatment maximizes normal tissue preservation and is appropriate for this patient population.

NEW DRUGS/EXPERIMENTAL THERAPEUTICS

PD-089 | The Impact of Paediatric Legislative Initiatives on Approval and Paediatric Labeling Information for Cancer Drugs Approved for use in the U.S.

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Background/Objectives: The Pediatric Research Equity Act (PREA) and the Best Pharmaceuticals for Children Act (BPCA) dictate the U.S. regulatory framework for evaluation and marketing approval of drugs for children. PREA mandates the paediatric assessment of new drugs when the clinical indication occurs in both adults and children. BPCA provides a 6-month extension of marketing exclusivity for drugs studied voluntarily under a Written Request (WR) issued by Food and Drug Administration (FDA). Our objective is to review the impact of U.S. legislative initiatives on the approval and labeling of drugs for children with cancer.

Design/Methods: A retrospective review of FDA's Document Archiving, Reporting, Regulatory Tracking System (DARRTS) and of published literature was performed to identify oncology drugs with paediatric labeling information from 2002 to present.

Results: Prior to enactment of paediatric legislation, 16 oncology drugs contained labeling information related to safe and effective use in children. Since 2002, 9 of 10 new drug applications (NDAs) or supplemental NDAs submitted to FDA for paediatric cancer indications have been approved; two of the 3 NDAs for products intended for treatment of paediatric-specific cancers were approved. Since the implementation of BPCA, over 55 WRs for oncology drugs have been issued. 19 products have been granted exclusivity, and more than 25 products continue to be investigated. Three drugs have been approved as a result of the WR mechanism; sixteen additional drugs have had paediatric information added to the label. No drug approvals or substantive labeling changes have resulted from PREA since requirements for paediatric evaluation of most oncology products for adult cancers are waived.

Conclusion: BPCA has resulted in approvals and informative labeling of drugs for paediatric cancer. The paucity of paediatric-specific drug discovery and appropriate preclinical research platforms and legislation mandating evaluation based only on indication pose barriers to new paediatric anticancer drug development.

PD-090 | Clinical Integration and Feasibility of Molecular Analysis and Counseling in Paediatric Solid Tumors

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Background/Objectives: Targeted therapies represent a promising alternative in paediatric oncology when prognosis with conventional therapy is dismal, but need the identification of a specific alteration. The positioning of tumour molecular profiling, allowing broad screening of targets, is yet to be defined in children. We aimed to study the feasibility and clinical outcomes of a sequencing and molecular counseling program for paediatric solid tumors.

Design/Methods: We report a single-center molecular biology board experience of 60 patients under 22 years with a poor prognosis or relapse/refractory solid tumour screened from October 2014 to November 2015. Tumour molecular profiling was performed with gene-panel based next generation sequencing and array comparative genomic hybridization.

Results: Mean age was 12 ± 5.7 years, main tumors were high-grade gliomas (n=14), neuroblastomas (n=8) and rare sarcomas (n=8). For 16 patients (27%), indication was poor prognosis tumour at diagnosis, for the 44 others (73%) it was relapse (n=26) or refractory disease (n=18).

Molecular profiling was feasible for 58 patients (1 necrotic and 1 insufficient tumour sample). Twenty-three patients (38%) had a potentially actionable finding, of which the most frequent (n=6) was homozygous *CDKN2A* deletion. Patients with high-grade gliomas had the higher yield of targetable alteration (57%). Six of the 23 patients (26%) had a subsequent targeted therapy for 16 days to 11 months. The main reasons for not receiving targeted therapy were a too poor general health (n=5), pursuit of conventional therapy (n=6) or a lack of available paediatric trial (n=4).

Conclusion: Pediatric molecular profiling is feasible with around a third of patient who were eligible to receive targeted therapy but only a small part who really did. Analysis at diagnosis may be useful for children with high-grade gliomas. Broader prospective protocols, early analysis of selected patients and larger development of phase I/II trials could improve targeted therapies accessibility to children.

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PD-091 | Results of Recent Phase 1 Trials in Children with Cancer

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Background/Objectives: Little information is available regarding the cumulative results of contemporary Phase 1 trials. This information is important given recent changes in trial design and categories of drugs under investigation. Therefore, this study examines the efficacy and toxicity in phase 1 trials published between January 2010 and 1st March 2016.

Design/Methods: Studies were identified by searching Medline and Embase using 'Phase 1' and 'Paediatric Cancer' as search terms. Additional clinical trials were identified by searching clinical trials registries.

Results: Eighty-seven trials investigating 83 different single drug (n=66) or drug combinations (n=17) were identified. Forty trials included additional treatment, most often chemotherapy (n=30).

Trials investigated chemotherapy (n=32), receptor/signal inhibitors (n=34), immunotherapy (n=12), drugs in two categories (n=2) and 'other' (n=7). Trial designs most used were 3+3 (n=54), 3+3 with expansion cohort (n=8) and rolling six (n=12).

A total of 2,304 participants were enrolled, 2,037 were available for response and 2,043 for toxicity assessment. Overall, 25 deaths were due to toxicity (TD) (1.2%), objective responses (OR) occurred in 252 patients (12.4%) and stable disease (SD) in 454 (22.3%). Chemotherapy is most toxic (TD 2.3%) and most effective (OR 17.2%, SD 28.6%). Receptor/signal inhibitors are least toxic (TD 0.8%) but least effective (OR 9.1%, SD 18.5%). Current efficacy compares favourably with older data (OR 12.4 v 7.9%) but TD is higher (1.1 v 0.7%)¹.

Mean recruitment period was 27.9 months (range 6-84). Rolling six design showed shorter recruitment (23.4 months, range 6-38) and less toxicity (TD 0%). However, these differences largely disappear when investigated drug category is taken into account.

Conclusion: Phase 1 trials in children remain safe and efficacy is improving. From these data, differences in toxicity or enrolment duration based on trial design cannot be inferred.

¹ J Ped Hemat/Onc 1998 20(5):431-438

PD-092 | Supporting Development and Authorization of Anti-Cancer Medicines for Children - Paediatric Legislative Initiatives in the European Union (EU)

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Background/Objectives: In 2007, incentives and obligations were introduced in the EU to increase the availability of medicines for children, to foster high-quality ethical paediatric research and to improve knowledge how to use medicines in children, without delaying medicines for adults. To this effect, the EMA Paediatric Committee (PDCO) agrees paediatric investigation plans (PIPs).

Design/Methods: We present a review of EMA data on development and authorizations of medicines for children with cancer.

Results: Until 2007, fewer than 30 anti-cancer medicines were authorized throughout the EU for children, often with limited product information.

In contrast, from 2008 to 03/2016, 5 new medicines and 5 new indications for already authorized anti-cancer medicines were authorized for children (4 novel mechanisms of action).

In total, 68 oncology PIPs were agreed (more than 30 novel mechanisms); 7 are completed, 7 were discontinued (lack of efficacy), the rest are ongoing. In PIPs, the first non-clinical or clinical study is to be completed no later than 0 (-1 to 3) years (median, interquartile range) after applying for marketing authorization for adults.

EudraCT data show 30 phase-1 trials in PIPs with at least 8 involving one or more paediatric oncology networks. Since 2008, paediatric oncology community projects on 6 medicines were

funded by the EU. Academics as well as pharmaceutical companies have obtained EMA Scientific advice for 28 medicines for children with cancer for free.

Based on its experience and to encourage a discussion of each medicine's mechanism of action of interest for paediatric cancers, the PDCO has revoked oncology class waivers.

Conclusion: Tangible progress is made with increased and earlier access to trials and new medicines for children with cancer. Continuing collaboration with academic and other stakeholders is sought to further enhance the quality and timely conduct of trials and medicine developments.

PD-093 | Next Generation Sequencing of Paediatric Malignancies from High Risk or Relapsed/Refractory Patients

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Background/Objectives: To profile neoplastic tissue from high risk or relapsed/refractory paediatric oncology patients in a single institution.

Design/Methods: Patients with high risk or relapsed/refractory leukaemia or solid tumors were consented to participate in a clinical trial piloting the use of comprehensive genomic profiling (CGP) at our institution. CGP was performed by Foundation Medicine (Cambridge MA) using profiles for hematologic malignancies and sarcomas. Genomic alterations, therapies available to the specific genomic alteration, and variants of unknown significance were reported for each sample. Results were reviewed by combined Medical and Pediatric molecular tumour board.

Results: Twenty four paediatric oncology malignancies with high risk or relapsed/refractory disease were studied. There was 1 lymphoblastic leukaemia sample and 23 solid tumour samples. Genomic alterations were seen in 21 patients. The mean number of genes altered per tumour was 1.9 (median=1; range, 0-8). The most common alterations were *CDKN2A* loss which occurred in 4, *BRAF V600E*, *CCND3* amplification and *TP 53* mutations, occurred in 3, followed by *PIK3CA*, *FOXO1*, *EWSR1*, *PTEN* loss, and *CDK4* amplification, occurred in 2 samples. All of the samples, except for the leukaemia sample, had no FDA approved targeted therapies in the patient's tumour type, but 13 of 21 samples had FDA approved therapies in another tumour type and 18 of 21 samples had potential clinical trials but none approved for paediatric patients.

Conclusion: Although modern treatment of paediatric malignancies result in cure rates approaching 75%, relapsed and refractory tumors are still a significant challenge to cure with survival rates as low as 10-15% at 5 years. Targeted therapy provides a novel interventional strategy for these patients. These data suggest that a significant number of tumors from these patients have genomic alterations that are potentially targetable for clinical benefit.

PD-094 | Pharmacologic Inhibition of SHP2 Suppresses Ras-Driven Cancer Progression

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Background/Objectives: The three human Ras genes (*H-Ras*, *N-Ras*, and *K-Ras*) are the most commonly mutated oncogenes in cancer. They encode highly related 188-189 amino acid proteins that are membrane-bound GTP/GDP-binding proteins, which serve as a 'molecular switch' linking receptor and non-receptor tyrosine kinase activation to downstream cytoplasmic and nuclear signaling events involved in a wide range of biological processes such as cell proliferation, differentiation and apoptosis. Despite its significance in cancer, Ras has remained 'undruggable'. We sought to uncover new mechanistic insight into the regulation of Ras with the supposition that with better understanding we will be able to target Ras for effective cancer therapy.

Design/Methods: In vitro biochemical analysis of Ras GTPase cycle and preclinical testing of identified novel potential target proteins impinging on the activity of Ras.

Results: We had previously shown that phosphorylation of Ras on a conserved tyrosine at position 32 within the switch I region via Src kinase inhibits the binding of effector Raf while promoting the engagement of GTPase activating protein (GAP) and GTP hydrolysis. Here we identify SHP2 as the ubiquitously expressed tyrosine phosphatase that preferentially binds to and dephosphorylates Ras to increase its association to Raf and activate downstream proliferative Ras/ERK/MAPK signaling. In comparison to normal astrocytes, SHP2 activity is elevated in astrocytes isolated from glioblastoma multiforme (GBM)-prone H-Ras(12V) knock-in mice as well as in glioma cell lines and patient-derived GBM specimens exhibiting hyperactive Ras. Pharmacologic inhibition of SHP2 activity attenuates cell proliferation, soft-agar colony formation and orthotopic GBM growth in NOD/SCID mice and decelerates the progression of low-grade astrocytoma to GBM in spontaneous transgenic glioma mouse model.

Conclusion: These results identify SHP2 as a direct activator of Ras and a potential therapeutic target for cancers driven by a previously 'undruggable' oncogenic or hyperactive Ras.

PD-095 | Novel Constructs for Specific Tumour Targeting in Cellular Immunotherapy

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Background/Objectives: Chimeric antigen receptors (CARs) link MHC-unrestricted antigen specificity with T-cell signaling, facilitating potent and regulatable antigen-specific cancer recognition and killing. Clinical trials of CAR gene modified T-cells show unprecedented clinical responses, with the major limitation of on-target off-tumour toxicity due to expression of most cancer antigens on some normal tissues. δ 2+ gamma-delta ($\gamma\delta$ T) cells engage danger

associated molecular patterns in an MHC independent manner and are therefore amenable to more subtle manipulation using CARs.

Design/Methods: We have devised "Co-stimulation-only" CARs (CSO CARs) targeting GD2 and expressed them in $\gamma\delta$ T cells, using alpha-beta T ($\alpha\beta$ T) cells expressing the same construct and non-transduced cells as controls. In ^{51}Cr cytotoxicity assays, target cells including $\gamma\delta$ TCR-engaging GD2+ neuroblastoma cells and GD2+ CT-26, which do not engage the $\gamma\delta$ TCR were used. An identical construct targeting CD33 was also generated, and the cytotoxicity assessments repeated using AML cell lines and healthy monocytes as targets. Toxicity of $\gamma\delta$ T cells expressing anti-CD33 CARs against myeloid progenitors was assessed using co-culture followed by colony formation assay. The mechanism of cell activation was demonstrated using latex beads loaded with antibodies engaging either the $\gamma\delta$ TCR, the CAR or both, followed by flow cytometric analysis of cytokine production and cell exhaustion.

Results: Our novel CSO-CAR design expressed in $\gamma\delta$ T instead of $\alpha\beta$ T cells leads to enhanced killing of solid and haematological tumour cell lines without significant on-target off-tumour toxicity. $\gamma\delta$ T cells expressing these constructs require stimulus of both the $\gamma\delta$ TCR and the CAR in order to mount a full activatory response. CSO-CAR transduced $\gamma\delta$ T cells also showed a less exhausted phenotype than those expressing classical second generation CARs.

Conclusion: $\gamma\delta$ T cells expressing CSO-CARs offer an opportunity to overcome on-target off tumour toxicity. This has the potential to make immunotherapy safer and to broaden the available repertoire of targets.

NURSES

PD-096 | Development of a Haematology/Oncology Telephone Triage Toolkit for Children and Young People for Use in All Principal Treatment Centres in the UK

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Background/Objectives: Members of The Children's and Young People Cancer Nurses Group of the Royal College of Nursing and the Children's Cancer and Leukaemia Group developed a risk assessment tool kit to support the telephone triage of children and young people who contact hospital advice lines. The group recognised that: -there was a lack of relevant guidelines and training to support members of the clinical team who were undertaking telephone assessment of paediatric oncology/haematology patients advice and support provided relied upon the experience and knowledge of the professional answering the call some local models of good practice existed but there were no consistent validated tools in use documentation and record keeping differed from trust to trust.

Design/Methods: The group adapted an adult triage tool kit which consists of an evidence based assessment tool with a RAG rated scoring system and a colour coded log sheet incorporating an assessment checklist. There is also a booklet containing a user guide and competency framework. The adapted tool was subject to a pilot and positive evaluation in 5 Principal Treatment Centres (PTCs) and 2 Paediatric Oncology Shared Care Units.

Results: This process has shown that the group has developed triage guidelines that: Improve patient safety and care by ensuring a robust assessment Assessments are of a consistent quality and use an evidence-based assessment tool Provide management and advice appropriate to the patient's level of risk. Patients who require urgent assessment are identified and appropriate action is taken, but also identifies and reassures those patients who are at lower risk and may safely be managed by the primary care team or a planned clinical review so avoiding unnecessary attendance

Guidelines for triage training and competency assessment support process

Improve record keeping.

Conclusion: This is the first validated telephone triage toolkit that will be used across PTCs in the UK and has already improved nurse confidence.

PD-097 | The Value of Nurse Practitioners in the Involvement and Ongoing Follow Up with Early Phase Clinical Trials in Paediatric Oncology Patients

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Background/Objectives: Early Phase clinical trials require clinician expertise, keen attention to detail, and collaboration among interprofessional teams. Continuity of clinicians for patient assessment and management ensures accurate reporting of toxicity and improved support and education to families living with uncertainty. Developing clinical expertise in complex early phase trials supports adherence to protocols, ethical and Health Authority regulations and guidelines.

Nurse Practitioner's (NP's) practice independently and have advance training in health assessment, physical examination, diagnostics and therapeutic management.

Design/Methods: In 2014, the early phase clinical trials team was challenged with reorganizing the model of care within the program. This reorganization recognized the opportunity to 1. Significantly increase the number of open early phase trials and 2. Become the lead referral center for early phase trials in Canada. Program investments included increased pharmacy support, increased clinical research assistants, and the addition of three NP's. The vision of the NP's within this new model was to provide consistency not only for patients and families but also within the program as identified resources with expertise of early phase trials.

Results: Over the last two years SickKids has increased recruitment of early phase study patients by 40%. In addition the majority of these patients are staying on trial for months

to years. The addition of NP's has improved communication with accurate and timely toxicity assessment, documentation, management, and strict adherence to protocol requirements. The NP's have provided leadership in interprofessional education, and developing relationships with hospital partners.

Conclusion: The involvement of NP's within the early phase trials program at SickKids has improved consistency of patient care and enhanced interprofessional communication of patients enrolled on early phase clinical trials. The NP's support adherence to protocol regulations and guidelines, provide interprofessional education, assist with audits and are identified as early phase trial resource experts within the program.

PD-098 | A Study to Explore Use of Complementary and Alternative Medicine (CAM) among Children with Cancer in Tertiary Care Cancer Hospital

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Background/Objectives: Cancer patients are always looking for new hope, and many have turned to non-traditional means. The use of Complementary and Alternative Medicine (CAM) is increasing in paediatric age groups. We aimed to investigate the number of children receiving CAM, with the objectives of identifying the number of children receiving CAM, as reported by their caregivers, and the pattern of use of CAM among children with cancer.

Design/Methods: The research design adopted for this study is a non-experimental survey. Non-probability, convenient sampling technique was used to gather the sample of 100 care givers of children with cancer at Tata Memorial Hospital, Parel. The investigator conducted face to face interviews using a semi-structured questionnaire. Data gathered was entered into the SPSS software and was analyzed with the use of descriptive statistics.

Results: The analysis of data revealed that of the 313 care givers of paediatric oncology patients approached, 100 (32%) care givers had used or were using CAM for their children. The most prevalent therapies used were ayurveda (35%), homeopathy (34%) and herbal therapy (25%). Majority (77%) care givers consulted a CAM practitioner. The prevalent reasons for the use were for the overall improvement of the child's health, and to relieve symptoms. Eighty-one percent did not disclose their use of CAM to the treating doctor. No statistical association was found between CAM use and demographic variables.

Conclusion: The findings suggest that a considerable portion of paediatric cancer patients use CAM therapies, of which many continue to use the therapy without their physician's knowledge. This insinuates the need for open lines of communication between the clinicians and the families. Healthcare providers must remain attentive to the potential implications of CAM usage in order to proactively counsel patients.

PD-099 | Benchmarks for Transition: Informing and Supporting Change

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Background/Objectives: Transitional care for survivors of childhood cancer has been defined as, 'an active, planned, coordinated, comprehensive, multidisciplinary process to enable childhood and adolescent cancer survivors to effectively and harmoniously transfer from child-centred to adult-oriented healthcare systems' (Mulder, 2016). Despite the numerous policy and guidance documents available, it is clear from current evidence that many young people have poor experiences of transition (Fegran, 2014). Benchmarks offer a guide/standards that services can measure themselves against to see how they are doing and where they can improve (Aldiss, 2015). The benchmarks for transition (see www.transitionstudy.co.uk) offer a new direction to inform and support changes in service delivery where previous policy and guidance has failed.

Design/Methods: The benchmarks were developed with experts leading on transition, young people with long-term conditions, parents and professionals. Dissemination of the benchmarks began with their launch at a conference in December 2014. In 2015, four sites piloted the benchmarks: meetings were attended by approximately 130 professionals, from specialties spanning child and adult health services. Teams discussed indicators of best practice for each benchmark factor and recorded the evidence they would use to demonstrate achievement: feedback was collated from each site.

Results: The benchmarks provided a useful focus for more formal and shared discussions between child and adult teams, allowed teams to consider what is currently in place within their service and what they would like to achieve in the future. They helped teams to see some processes are informal/not well documented and needed formalising.

Conclusion: The benchmarks are relevant across services for young people with long-term conditions, including cancer survivors. Working with sites to pilot the benchmarks has demonstrated their usefulness in facilitating dialogue within teams about improving transition and in sharing good practice. Local champions and support from Royal Colleges has enabled active dissemination and early uptake of the benchmarks.

PD-100 | Fertility Preservation Counseling: Utilizing Advance Practice Registered Nurses to Improve the Patient's Access to Care

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Background/Objectives: Increased survival rates for childhood cancer has raised awareness regarding the long-term consequences of treatment, including the potential for infertility. Research confirms patients and parents are concerned about infertility from time of

diagnosis to survivorship. Fertility preservation counseling is not routinely provided to paediatric, adolescent, and young adult patients and their parents prior to receiving treatment. The utilization of an Advanced Practice Registered Nurse (APRN) to educate and counsel patients and families is an effective method of offering patients and families' information to make decisions regarding fertility preservation. The APRN is qualified to implement fertility preservation counseling, coordinate care between reproductive specialists and the oncology team, and consent patients for research studies. Here we report our data on the number of patients receiving counseling regarding risk of infertility, as well as the number of patients undergoing standard or experimental preservation techniques.

Design/Methods: We reviewed our data on fertility preservation consults and the number of patients undergoing fertility preservation at Ann & Robert H. Lurie Children's Hospital of Chicago from January 2010 to December 2015.

Results: The number of referrals for fertility preservation consults, for both male and female patients, has increased annually from a total of 13 consults in 2010 to 64 consults in 2015. Counseling is provided by the APRN prior to oncologic treatment initiation. The majority of patients undergoing fertility preservation are adolescent and young adult males pursuing sperm banking, but there is also an increase in the number of families interested in experimental fertility preservation options such as testicular tissue cryopreservation and ovarian tissue cryopreservation.

Conclusion: The APRN possesses the expertise and skills needed to counsel patients and parents on fertility preservation options, coordinate complex medical care between multiple services, and consent patients for research studies.

PD-101 | Quality of Life and its Related Factors among Children and Adolescents with Cancer

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Background/Objectives: Quality of life (QoL) increasingly is being assessed in paediatric patients with cancer. However, little is known regarding QoL predictors during and after treatment for children and adolescents with cancer. The aims of this study were to examine the relationships and covariates among QoL, distress behaviors, and fatigue, and to identify QoL predictors in children and adolescents with cancer.

Design/Methods: A cross-sectional descriptive study involving 154 participants treated at two medical centers between 2012 and 2014 was conducted. All participants were diagnosed with cancer, ranged in age from 7 to 18 years, and had no developmental delay or mental illness. Three instruments including the Pediatric Quality of Life Inventory, Distress Behaviors Scale, and Multidimensional Fatigue Scale, were administered. Spearman's correlation coefficient was used to determine relationships among variables. QoL predictors were examined by multiple regression analysis.

Results: School functioning was the lowest-rated QoL indicator among participants. QoL was significantly and negatively correlated with fatigue and distress behaviors. QoL decreased in proportion to age at diagnosis but increased with time since diagnosis. Sex, treatment status, and age at assessment were not significantly related to QoL. General fatigue, relationship distress, time since diagnosis, and family structure were significant predictors of QoL, accounting for 63% of the total variance.

Conclusion: Cancer diagnosis and treatment in children impair school functioning. General fatigue, relationship distress, time since diagnosis, and family structure were predictors of QoL in children and adolescents with cancer.

PD-102 | Prevalence and Outcome of Febrile Neutropenia in Paediatric Cancer Patients at Korle Bu Teaching Hospital, Accra, Ghana

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Background/Objectives: Febrile Neutropenia is a life threatening complication in children undergoing chemotherapy. Due to challenges in access to effective supportive care, febrile neutropenia may result in serious morbidity and mortality in resource poor settings such as Ghana. The aim of this study was to ascertain the prevalence and outcome of febrile neutropenia at the Paediatric Oncology Unit of the Korle-Bu Teaching Hospital, Ghana, a low-middle income country.

Design/Methods: In this retrospective study undertaken between January to December 2015, patients who had fever (38.0°C and above) and neutropenia (ANC < 1000/mm³) during or after chemotherapy and who were admitted to the Paediatric Oncology Unit, Korle Bu Hospital, were included.

Results: Twenty-one episodes of febrile neutropenia occurred during the study period which formed fourteen percent of total admissions into the paediatric oncology unit in 2015. The highest numbers of episodes with regard to cancer type were seen in patients with Nephroblastoma followed closely by Acute Lymphoblastic Leukaemia. Eighty percent of the patients presented within the first twenty four hours of onset of fever and a little over half of them developed febrile Neutropenia within one week after completion of a cycle of chemotherapy. No organisms were isolated from blood and urine cultures. In all episodes, patients responded well to empirical treatment with intravenous Ceftriaxone and Gentamycin with majority of patients having fever resolution within three days. Patients recovered without any complications.

Conclusion: The outcome of febrile neutropenia in our setting is good because there has been strict adherence to protocol in starting appropriate antibiotics immediately upon diagnosing febrile neutropenia. This may have contributed to the negative growth, as cultures are usually taken after starting antibiotics, due to lack of funds by most parents to pay for blood cultures on presentation.

PD-103 | Efficacy and Safety of Aprepitant in the Prevention of Chemotherapy-Induced Nausea and Vomiting: A Meta Analysis

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Background/Objectives: Oral aprepitant, a neurokinin-1 receptor antagonist, is recently recommended in combination with other antiemetic agents for the prevention of nausea and vomiting associated with moderately or highly emetogenic chemotherapy in adults by MASCC/ESMO, ONS, and ASCO. But its efficacy and safety in paediatric patients are unknown. Data about use of aprepitant in children is limited.

To synthesize the available clinical evidences on the efficacy and safety of aprepitant for the prevention of chemotherapy-induced nausea and vomiting (CINV) in paediatric patients receiving moderately or highly emetogenic chemotherapy.

Design/Methods: A meta-analysis was performed using trials identified through Pubmed (1966 to March 2016), Embase (1980 to March 2016), Cochrane Library (up to 2015), CNKI (in Chinese, 1980 to March 2016), CBM (in Chinese, 1980 to March 2016), and Wanfang database (in Chinese, 1980 to March 2016). Data on acute and delayed CINV were collected. All randomized controlled studies and clinical controlled studies comparing aprepitant to routine qualified antiemetics (ondansetron +/-dexamethasone) were critically appraised and analyzed.

Results: Of 529 citations screened, 4 studies with 493 paediatric patients were included in the meta-analysis. Aprepitant was superior to routine qualified antiemetics (ondansetron +/-dexamethasone) for complete protection from acute CINV [OR=2.48, 95%CI (1.48, 3.20), P<0.0001], delayed CINV [OR=3.90, 95%CI (2.58, 5.88), P<0.0001], and overall CINV [OR=2.85, 95%CI (1.80, 4.53), P<0.0001]. The drug-related adverse effect was similar in both groups in incidence of febrile neutropenia [OR=1.01, 95%CI (0.60, 1.67), P=0.98].

Conclusion: Aprepitant is clearly effective in protecting paediatric patients with cancer from CINV both in the acute and delayed phases, without increasing the possible adverse effect.

PD-104 | Educating Families of Children with Cancer: Insights of a Delphi Panel of Experts

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Background/Objectives: Patient/family education is a core responsibility of paediatric oncology nurses. A paucity of research exists in regard to the essential content for education of families of newly diagnosed children with cancer. The purpose of this study was to use Delphi methodology to gain consensus from paediatric oncology experts in identifying essential content for parent/caregiver education at the time of a paediatric cancer diagnosis.

Design/Methods: This Delphi study employed three questionnaire rounds to gain expert consensus. The purpose of Round 1 of the Delphi study was to generate the essential content to be reviewed in subsequent rounds. One hundred participants completed Round 1 and consisted of paediatric oncology professionals and patient advocates. This initial round yielded 494 responses and iterative analysis of this data identified 20 topics of importance for inclusion in initial discharge education for all newly diagnosed paediatric oncology patients. For Delphi Rounds 2 and 3, a sample of 60 experienced paediatric oncology clinicians was selected to comprise the Expert Panel.

Results: There was clear consensus among the expert panel regarding the importance of educating newly diagnosed families about the child's diagnosis and treatment plan, as well as fever management. One hundred percent of participants indicated that they considered fever, whom/how to call and when/why to call the treatment team as mandatory. Over 90% of participants agreed that managing medications, care of the child at home, central line care, follow-up appointments, and side effects of treatment should be included.

Conclusion: Results of this study provide multidisciplinary consensus regarding key content essential for newly diagnosed paediatric oncology patients and their family members. Delphi methodology is an extremely useful tool to gain consensus from a multidisciplinary panel of experts as exemplified in this study and can be used to identify essential educational topics with other diagnoses.

PD-105 | Nutrient Deficiencies in Children with Cancer from Sao Paulo, Brazil

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Background/Objectives: Despite advances in paediatric oncology, malnutrition is still a major concern among these patients all over the world. Both over and undernutrition are determinants of chemotherapy tolerance, treatment compliance, relapse and survival. Studies have shown that children undergoing chemotherapy have considerably lower oral energy and nutrient intakes than age-based recommendations, which can impact on toxicity and increase susceptibility to infections, among other complications. To discriminate possible nutrient deficiencies is essential in order to plan an appropriate intervention. The objective of this research is to evaluate the diet of paediatric patients with cancer and identify common nutritional deficiencies.

Design/Methods: This was a prospective cross-sectional observational study. Trained dietitians collected 24-hour dietary recalls (R24) of children and adolescents on cancer treatment

from the outpatient clinic of a tertiary hospital in Sao Paulo, Brazil. The R24 were sent to St. Jude Children's Research Hospital in Memphis, USA, and evaluated using the software Nutritionist Pro[®]. Dietary intake was then compared with the recommended dietary references for macro and micronutrients for age and gender.

Results: Thirty (n=30) patients were evaluated (mean age: 9.4±5.2), 40% female. When the nutritional intake was compared to recommendations, 80% (95%CI 64.8-95.2) of patients reached 75% or greater of their energy goals and 83% (95%CI 69.2-97.5) reached 100% or greater of recommended protein. Only 20% (95%CI 4.8-35.2), 57% (95%CI 37.9-75.5) and 60% (95%CI 41.4-78.6) of patients met the guidelines for vitamin D, vitamin A and vitamin K, respectively, while over 75% (22 of 30 patients) met recommendations for vitamins E, C and B12, iron, dietary fiber, thiamin, zinc, niacin and folate.

Conclusion: The majority of outpatients have good energy and protein intake, as well as most micronutrients, whilst poor intake of vitamins D, A and K. These findings provide important information to targeted dietary interventions, preferably using local foods usually consumed by Brazilian children.

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PD-106 | Measuring Determinants for the Use of An Innovative Tool to Monitor and Discuss Electronic Patient-Reported Outcomes in Paediatric Oncology Practice

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Background/Objectives: The KLIK method (Dutch acronym for 'Quality of Life in Clinical Practice') is an online tool to monitor and discuss electronic patient-reported outcomes (ePROs) during outpatient consultations, which has proven to enhance patient-physician communication, detection of psychosocial problems and satisfaction with care. However, making the successful transfer from research to clinical practice remains a challenge. The aim of this study was to identify what innovation, user and organization determinants impede or enhance the use of the KLIK method in paediatric oncology practice during treatment for paediatric cancer.

Design/Methods: The Measurement Instrument for Determinants of Innovations (MIDI) was completed by 29 healthcare professionals (HCPs-response 90%) who used the KLIK method as part of standard care during outpatient consultations at 1, 3 and 6 months post childhood cancer diagnosis. This validated questionnaire contained 28 questions on implementation determinants regarding the innovation, the user and the organization. Items were assessed on a 5-point scale (completely disagree-completely agree). Impeding determinants were identified when ≥ 20% of HCPs completely disagreed and enhancing determinants were identified when ≥ 80% of HCPs completely agreed.

Results: Impeding determinants regarding the use of the KLIK method were mainly related to the organization (turmoil in organization-82%, time-21%, formal ratification-25%, regular feedback-21%, staff turnover-32%) and less frequently to users (social support-25%, descriptive norm-25%, motivation to comply-39%) or the innovation (compatibility-21%).

Enhancing determinants were: simplicity (86%), positive outcome expectations (82%), normative beliefs (96%), motivation to comply (100%), sufficient knowledge (86%), and content awareness (86%).

Conclusion: When implementing ePROs in outpatient paediatric oncology practice, HCPs report determinants that influence successful ePRO integration. To improve implementation and outcomes, tailored organizational (e.g. formal ratification by management, time) and specific local (e.g. individualized assessments) strategies should be developed to achieve optimal ePRO discussion.

PD-107 | Education, Employment and Marriage in Survivors of Teenage and Young Adult Cancer

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Background/Objectives: Teenage and young adult (TYA) cancer patients are faced with cancer during a challenging period of psycho-social development. We aimed to i) determine differences in social outcomes between TYA cancer survivors and healthy controls, and ii) identify risk factors for adverse social outcomes.

Design/Methods: We sent a questionnaire to TYA cancer survivors (diagnosed between 16-25 years; ≥5 years after diagnosis) registered in the Cancer Registry Zurich and Zug in Switzerland. Information on controls was obtained from the Swiss Health Survey 2012. We assessed educational achievement, employment status, marital status and life partnership (survivors only), and compared these outcomes between survivors and controls. We used logistic regression to determine socio-demographic and cancer-related risk factors for adverse social outcomes.

Results: We included 160 TYA cancer survivors and 999 controls. More survivors than controls had a low educational achievement (more survivors had basic education only and fewer had tertiary education). We found no significant differences for employment (p=0.515) and marital status (p=0.357). We found no cancer-related risk factors for basic education only. After adjusting for socio-demographic variables, cancer-related risk factors for unemployment were: younger age at diagnosis (OR=6.83, CI:1.63-28.65), and self-reported late effects (OR=3.38, CI:0.97-11.79); for not being married: radiotherapy (OR=3.42, CI:1.24-9.48); younger age at diagnosis (OR=2.12, CI:1.00-4.50); and for not having a life partner: younger age at diagnosis (OR=2.19, CI:0.94-5.10).

Conclusion: In TYA cancer survivors employment and marital status were comparable to healthy controls. However, our findings indicated that cancer during adolescence and young adulthood negatively interferes with long-term educational achievement. Age-appropriate support strategies targeting TYA cancer survivors' educational progress may improve long-term educational achievement.

PD-108 | Finding A Way to Support Children and Young People in Shared Treatment Decision-Making in Paediatric Oncology: The Spirit Framework

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Background/Objectives: Shared decision making (SDM) is a process in which children, parents, and healthcare professionals share information, express treatment preferences, and agree to the decision made. Although significant conceptual work has taken place to delineate the concepts underpinning SDM, much of this work is based on research with adults. Furthermore this work cannot be easily extrapolated to children because of: concerns about children's competence to participate, parents' desire to protect children from distressing information, burden of decision-making, and child's position in the triadic relationship. Hence this paper will outline and discuss the SPIRIT framework which has been developed to support children and young people (CYP) participation in shared treatment decision-making.

Design/Methods: A secondary analysis was conducted of qualitative datasets from three completed studies on shared decision-making with children and young people (aged 7-16 years) in Ireland. Study one explored CYP with cancer preferences for decision-making, study 2 explored decision-making with CYP with acute and chronic illnesses, and study 3 explored decision-making with CYP with mental health issues. The data from the three studies had been previously analysed using the constant comparative method and managed with NVivo. The datasets were re-examined to draw out the concepts central to decision-making and to establish commonalities and differences.

Results: The antecedents included demographics, experience, information provision, family background, salience, beliefs. The influencing factors on decision-making included trust, relationships, nature of the illness, and utilities (usefulness and achieving one's goals). The concepts central to the decision-making process were trust, control, and cooperation. The actions to promote decision-making included information-sharing, eliciting preferences, offering choices, negotiating and flexibility.

Conclusion: This framework requires further development and refinement through longitudinal studies on decision-making. In the meantime it may serve as a useful framework to assist healthcare professionals in promoting and facilitating children and young peoples' participation in shared decision-making in a cancer unit.

PD-109 | When Parents Refuse Potentially Curative Treatment for their Child's Cancer - Does Legal Intervention Improve Outcome?

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Background/Objectives: Several recent high profile cases of parental refusal of treatment for potentially curative childhood cancers prompted us to study outcomes of these children. Whilst it might be assumed that recourse to the courts will result in treatment, no studies report such outcomes or the potential pitfalls. Using a large data set, we aim to provide a resource to guide the medico-legal profession facing this rare but ever-increasing situation.

Design/Methods: An extensive Internet search for publicised cases of parental refusal of treatment for childhood cancer was performed to identify cases in the media, medical and legal domains. Additional cases were sought from paediatric oncologists in Europe, Canada, Australia and New Zealand. Any case in which the diagnosis, initial prognosis, action taken and outcome could be identified was included.

Results: Fifty-one cases of parental refusal with known outcomes were identified between 1975 and 2015. Mean age was 9.3 years. Diagnoses included haematological malignancies, solid and brain tumours. Forty (78.4%) cases were taken to court. Eleven (27.5%) did not receive custodial/treatment orders with death resulting in 8 (72.7%) cases. Twenty-nine (72.5%) court orders were given but this did not guarantee treatment. Only 13 (44.8%) patients, all of whom achieved remission, were compliant with therapy. The remainder died during the legal process, were non-compliant or absconded. Eleven (21.6%) cases not taken to court resulted in universally fatal outcomes. Thirty-three percent of all patients absconded at some point during the process.

Conclusion: Each case of parental refusal is complex and unique. Although rare, paediatric oncologists must be aware of not only the ethical principles and laws, but also the potential pitfalls of judicial involvement. Legal recourse is highly effective if followed by compliance, but one must pre-empt the high risk of absconding. Conversely, taking no action is fatal. These results will inform future medico-legal care of such patients.

PD-110 | Non-Graduation after Comprehensive School, and Early Retirement but not Unemployment are Prominent in Childhood Cancer Survivors - A Finnish Registry-Based Study

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Background/Objectives: The aim of this study was to explore the educational and vocational attainments of childhood cancer survivors in comparison to matched population controls.

Design/Methods: Cancer survivors born from 1960 to 1992, aged below 16 at cancer diagnosis, and alive in the beginning of the year of their 18th birthday ($n=3,243$) were identified from Finnish Cancer Registry, and age, sex and living place matched controls from the Population Register Centre ($n=16,215$). Data on educational achievements, yearly income, employment status, and retirement were retrieved from Statistics Finland.

Results: The proportion of those with no education after comprehensive school was higher for all the diagnostic groups: brain tumour (BT) (33.5% vs 23.0%), solid tumour (ST) (25.0% vs 21.4%), and leukaemia/non-Hodgkin lymphoma (NHL) (29.2% vs 23.1%) in survivors than controls. Odds ratios for unemployment were not significantly elevated, but survivors of BT were 14.8 (95% CI 10.4-21.0), ST 2.2 (95% CI 1.5-3.0), and leukaemia/NHL 4.0 (95% CI 2.8-5.8) times more often retired than their controls. Irradiation significantly increased the odds for being retired only in after BT. Survivors of BT had lower income level than controls ($p<0.001$), and irradiation ($p<0.001$) but not gender ($p=0.43$) was associated with this. Survivors of ST had a lower income level ($p=0.03$) than their controls. Among them, females ($p<0.001$), those treated most recently ($p=0.002$), and those with no irradiation ($p=0.02$) had lower income than the others. Similarly, survivors of leukaemia/NHL had lower income than their controls ($p<0.001$), and this was pronounced in females ($p<0.001$).

Conclusion: All survivors had higher frequencies than controls of not graduating from any further education than comprehensive school. Cancer survivors had no increased risk for unemployment, but risk for early retirement was significantly increased in each three survivor group. Also the level of yearly income was significantly lower for all survivor groups.

PD-111 | Onco-Hematological Painful Procedures in Sedoanalgesia: Psychosocial Risk and Intensity of Treatment

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Background/Objectives: The present study applied the Pediatric Psychosocial Preventative Health Model (Kazak et al., 2006) which describes the illness as an interaction between biological, psychological and social factors. In accordance with this multidimensional concept, particular attention is given to the intensity of treatment (Kazak et al., 2012) an index defined by type of disease, diagnosis (risk level or stage) and treatment modalities (surgery, chemo, radiation, transplant).

Therefore the present study aims to assess the psychosocial risk degree associated with specific levels of intensity of treatment and the psychological health conditions in paediatric patients with cancer and their parents during the onco-hematological painful procedures under sedoanalgesia.

Design/Methods: The study carried out on ninety-six paediatric patients recruited by age, disease type, treatment and used a questionnaire consisted of: behavioral and contextual indicators *ad hoc* related to three moments of the procedure (pre, during and post-procedure) measuring patient/parent anxiety and setting conditions; ITR 2.0 (Intensity of Treatment Rating Scale, Kazak, 2012) and PAT (Psychological Assessment Tool, Kazak et al., 2006).

The statistical analyses carried out (using SPSS-20 software) were: Pearson correlations and Logistic regressions.

Results: Data shows significant interaction effects between specific levels of intensity of treatment and degree of psychosocial risk in predicting pre-post procedural anxiety. Moreover the influence of setting procedural conditions (i.e. waiting, fasting, parent' presence/absence) on psychological distress and significant associations between levels of intensity of treatment, degree of psychosocial risk and specific pharmacological plan (premedication) for better managing pre/post-procedural distress were found.

Conclusion: Findings proposed a multi-disciplinary intervention to support patients and parents taking into account intensity of treatment and psychosocial risk as relevant index to prevent and manage the anxiety related to painful procedures.

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PD-112 | Genetic Testing for Childhood Cancer Survivors' Risk of Late Effects: Consumer Understanding, Acceptance and Willingness-To-Pay

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Background/Objectives: Most childhood cancer survivors are currently given generalized information about their risk of developing late effects from their cancer and its treatment. However, many late effects are associated with specific genetic mutations. Identifying at-risk survivors and providing genetically tailored follow-up advice could therefore be of clinical benefit. Genetic testing to determine childhood cancer survivors' risk of developing late effects is therefore likely to be offered to young survivors of the future.

Objectives: To explore the extent to which childhood cancer survivors (CCS) and parents understand and accept genetic testing for late effects and its implications.

Design/Methods: Stage 1 involved a pilot study ($N=24$), which informed the development of the Stage 2 interview schedule. In Stage 2, 20 CCS (55% female; mean age 26.0 (18-39), $SD=0.80$) and 20 parents of CCS (55% male; mean age of child survivor 14.2 (10-19), $SD=0.79$) completed a semi-structured interview (response rate 40%). Interviews were transcribed verbatim and analysed using NVivo 10.0 software.

Results: Most participants (95%) reported that they would be willing to undergo genetic testing to determine their risk of late effects, and over two-thirds reported that it would be acceptable to pay <AUD5000 for the service. The majority reported that it would be acceptable if results were returned up to six months post-testing, and if it were offered after treatment or when the survivor reached adulthood. Participants were asked to rate how fourteen potential benefits/concerns would influence their decision-making. Ratios indicated a positive decisional balance amongst survivors ($M=0.5$, $SD=0.38$) and parents ($M=0.5$, $SD=0.39$), with both groups leaning towards testing.

Conclusion: Though clinical efficacy is yet to be clearly demonstrated, survivors and parents describe positive interest in genetic testing for risk of late effects. Perceived benefits outweighed negatives, and the majority of participants would be willing to pay, and wait, for testing.

PD-113 | The Transition Off Treatment for Paediatric Cancer: The Role of Neurocognitive Difficulties in Patient Health-Related Quality of Life, Patient and Parent Distress and Family Functioning

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Background/Objectives: Treatment-related physical, neurocognitive and psychosocial complications contribute to challenges with "normalization" of family life following cancer treatment. Limited research on the period between active treatment and survivorship indicates a mixed picture in terms of patient health-related quality of life (HRQL), and scant studies have examined family functioning. Based on social ecological models of adaptation in childhood cancer, this study examined treatment-related correlates of patient, parent and family functioning during the transition off treatment.

Design/Methods: Parents ($N=86$) and patients ($N=32$; ages 8 and older) completed validated surveys online within 3-months of the end of cancer treatment. Surveys assessed parent proxy and patient self-report of patient HRQL and neurocognitive functioning, parent and patient distress, and parent report of family functioning in the context of cancer treatment.

Results: Patients were primarily male (62%), White (81%), 15.88 months since diagnosis and had an average treatment intensity of 2.59 (scale=1-4). Cancer diagnoses were solid (38.9%), leukaemia/lymphoma (37.8%), and brain tumour (23.3%). Parents were primarily female (86%) and White (73%). Lower parent-reported patient neurocognitive functioning was significantly associated with time since diagnosis, parent proxy report and patient self-report of lower HRQL, parent distress, and parent report of poorer family functioning (r range = -.36 to -.62). Lower patient-reported neurocognitive functioning was significantly associated with parent proxy and patient self-report of lower HRQL and patient and parent distress (r range = -.35 to -.66). Intensity of treatment and patient cancer diagnosis were not identified as correlates. Regression analyses confirmed neurocognitive functioning as an independent predictor.

Conclusion: Across reporters, neurocognitive difficulties were associated with lower patient HRQL, increased patient and parent distress, and poorer family functioning during the critical transition off treatment. Findings suggest the importance of early and regular screening for neurocognitive difficulties after treatment along with anticipatory guidance for families.

PD-114 | Screening for Psychosocial Distress in Paediatric Cancer Patients and their Families: A Comparison of Screening Tools

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Background/Objectives: To establish a 'paediatric minimum data set' capable of screening for distress in paediatric cancer patients and their families across the cancer continuum (diagnosis, treatment, and survivorship).

Design/Methods: Families were recruited from a paediatric oncology program at different stages of the cancer trajectory. At least one parent from each family completed a standardized self-report measure (BSI) and parent-proxy measure (BASC-2) of psychosocial functioning, as well as three distress tools: Distress Thermometer (DT; self and proxy-report); Psychosocial Assessment Tool (PAT2.0; self-report); and Pediatric Quality of Life Inventory (PedsQL; proxy-report), and a satisfaction questionnaire. Patients between 8-18 years of age completed self-report measures of the same distress tools.

Results: Ninety-five patients (58 male) across the cancer trajectory (new diagnosis, $n = 20$; active treatment, $n = 22$; long-term survivor, $n = 53$) participated in the study. The mean age of participants was 11.47. Screening tools were comparable with respect to their performance on content validity, psychometrics, and satisfaction. The DT took the least amount of time to complete, while the PedsQL offered the most robust data, with respect to content validity and psychometrics.

Conclusion: Each of the three distress tools displayed strong content validity, satisfactory psychometric properties, and acceptable participant satisfaction. Future research will demonstrate how screening for distress can be easily and successfully implemented as part of routine standard care for paediatric cancer patients.

PD-115 | Challenges to Psychosocial Screening in Paediatric Oncology as Perceived by Health Care Providers

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Background/Objectives: There is some evidence that psychosocial screening is not widely practiced in paediatric oncology in western countries but little is known regarding the challenges in conducting psychosocial screening in this setting. We investigated health care professionals' (HCPs, oncologists, nurses, social workers) perspectives regarding psychosocial screening, follow-up and services in paediatric oncology. This presentation is focused on the challenges for conducting psychosocial screening.

Design/Methods: Twenty-six HCPs (11 oncologists, 4 female; 8 female nurses; and 7 female social workers) who worked in a large North American paediatric oncology center participated in a semi-structured interview. Interviews were transcribed verbatim and content analyzed to derive emerging themes.

Results: The following major themes emerged: *Inadequate funding and resources* available to conduct psychosocial screening; *lack of institutional policy and support for psychosocial screening* as part of standard care¹; *lack of psychosocial standard*²; *limited psychosocial screening tools available*; *limited training* in psychosocial screening; *HCPs' beliefs about families* - fear of being judged, stigmatized, cultural values regarding personal and family problems, difficulties communicating in English; *HCPs' beliefs about themselves* - cultural beliefs about sharing family information, fear that psychosocial screening tools will replace clinical personal contact; use of standard tools was unnecessary; fear of sharing psychosocial information with other team members.

Conclusion: These findings emphasize the importance of examining the challenges HCPs perceive regarding psychosocial screening, (the institutional, systemic and personal beliefs regarding families and themselves), to address them and improve psychosocial outcomes for children who are treated for cancer and their families². Addressing these challenges would facilitate the translation of research to the clinical setting.

¹ Since this study was conducted, efforts to improve psychosocial services in this institution have begun and research on the impact of conducting early psychosocial screening is ongoing.

² Psychosocial standards for psychosocial services in paediatric oncology were published at the end of 2015, after this research was completed.

PD-116 | Gender Bias Impacts Cancer Registration and Treatment Abandonment in Children with Cancer: Time Trends Over Three Decades from India

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Background/Objectives: Gender Bias (against the female child) is highly prevalent in India in social, educational and healthcare spheres. We sought to find its impact on childhood cancer registration as well as treatment abandonment, its trends in last three decades, and impact of targeted interventions to support girls.

Design/Methods: Cancer case numbers and age-standardised incidence rates for all paediatric cancers registered from 1985-2015 were retrieved from hospital based registry at Tata Memorial Hospital, Mumbai. Cancer 2case sex ratios (male : female) and age-standardised cancer rate sex ratios were calculated for all cancers and compared with published data from other hospital based registries from India. Treatment refusal and abandonment (TRA) data was retrieved from a prospective treatment database maintained on a web-based data entry software (IndiaPod) from 2010-2015.

Results: A total of 27307 children were registered of which 18496 were boys and 8811 were girls with an overall M:F ratio of 2.1:1, which is significantly higher than ratio of 1.2:1 in high-income countries. The analysis of M:F ratio for every 5 year period since 1985 to 2015 showed a marginal decrease from 2.2:1 in 1985 to 2.08:1 in 2015. This M:F ratio was similar in Northern India(2.1:1) but lower in Eastern(1.36:1) and Southern India(1.5:1). The disease specific M:F ratio was highest in Lymphomas (HL, 5.1:1; NHL, 4.3:1) and lowest in germ cell tumours(0.8:1). Analysis of TRA incidence showed that 540(6%)children abandoned therapy from 2010-2015. The incidence of TRA in girls was significantly higher at 8.5% compared to boys at 4.5%. The TRA incidence in girls decreased from 11% in 2010 to 4.5% in 2015 with targeted social support initiatives for girls.

Conclusion: Persistent gender bias leads to underregistration with regional variations and increased abandonment of girls in India. Targeted social support initiatives can reduce the rate of abandonment in this population.

PD-117 | Psychosocial Follow-Up in Paediatric Oncology

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Background/Objectives: Childhood cancer survivors often suffer psychosocial late effects from their cancer diagnosis and need psychosocial support. Importance of psychosocial follow-up has been recognized and to ensure adequate care of survivors, it has been recommended to consider survivors' needs when drawing up models of psychosocial follow-up.

Design/Methods: The present study aimed at evaluating needs regarding psychosocial follow-up in Austria and drawing up a model proposition. Via semi-structured interviews 11 survivors and 11 psychosocial experts in the field of paediatric oncology were asked about their needs regarding psychosocial support, prevailing inhibitions regarding utilization of psychosocial support services and structural obstacles regarding the realization of psychosocial follow-up.

Results: Eighty-two percent of survivors stated that they had experienced need for psychosocial support following their cancer treatment, however only 18.2 percent stated to have received psychosocial support from their treatment centre. Sixty-four percent of survivors reported poor education about possible late effects as well as the need for better health education. The majority (90 percent) of psychosocial experts stated a need for action regarding available psychosocial follow-up services. Another 70 percent reported that survivors needed better health education. Regarding structural obstacles in the way of providing optimal support for survivors, 80 percent of psychosocial experts stated the need for additional financial resources as well as better networking between treatment centres in order to create joint guidelines for psychosocial follow-up.

Conclusion: Results suggest that existing psychosocial follow-up services cannot cover prevailing needs. Survivors lack psychosocial support services, knowledge of available support services and cancer-related information. To ensure optimal psychosocial follow-up, financial and personell resources are needed as well as guidelines for psychosocial follow-up, research and networking between treatment centres. Psychosocial follow-up models should focus on staying in touch with survivors and educating them about possible late effects. Concrete measures are proposed.

PROS

PD-118 | Improved Target Coverage While Simultaneous-Integrated-Sparing of Kidney and Liver by VMAT in Children Undergoing Whole-Abdomen Irradiation for Wilms Tumour

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Background/Objectives: Whole-abdomen irradiation is applied in children with Wilms tumors and gross intra-abdominal contamination by pre-operative or intra-operative rupture or in case of diffuse intra-peritoneal spread. The feasibility of maximum dose-reduction to the kidney and the liver, without concession to the target coverage (V95%) by a volumetric arc therapy technique (VMAT) was the purpose of this study.

Design/Methods: Dose-calculation using the Monaco 5.1 treatment planning system (Elekta Ltd., Crawley, UK) was performed in ten patients undergoing whole-abdomen irradiation. Dose-prescription was 15.0Gy for the intermediate-risk group (n=5), and 19.5Gy for the high-risk group (n=5), both in daily fractions of 1.5Gy. 4D-CT information was used for intra-fraction organ motion.

Full-arc 10MV VMAT-plans were compared to a conventional 10MV APPA-technique with shielding of the remaining kidney. Treatment plans were generated aiming to obtain target coverage of at least 95% (V95% ≥95%) while sparing the kidney (mean dose ≤12Gy) and the liver by ALARA (As Low As Reasonably Achievable). Dose-volume statistics of the target and organs at risk were used to evaluate the two planning techniques.

Results: Mean target coverage (V95%) was 95% versus 75% for VMAT compared to APPA, respectively. Conformity (CI 95%) was superior for VMAT compared to APPA (0.84 vs. 0.47). With VMAT+simultaneous-integrated-sparing (VMAT+SIS), mean dose reductions around 40% and 15% of the prescribed dose are observed for the remaining kidney and liver, respectively. This leads to an absolute mean dose reduction to the kidney of 3.5Gy and 2.5Gy for the liver, compared to APPA. Additional dose-reduction is observed with VMAT for breast tissue, heart and hip region.

Conclusion: VMAT+SIS offers superior target coverage and a considerable dose-reduction to the organs at risk. Therefore VMAT+SIS is a valuable strategy to be considered as standard of care for Wilms tumors and indication for whole-abdomen irradiation.

PD-119 | Result of Large International Medical Physics Survey on Paediatric Radiation Therapy

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Background/Objectives: The Paediatric Radiation Oncology Society coordinates a large international network of medical physicists with an interest in radiation therapy (RT) of children. The network has 95 members from 64 different institutions in 32 countries. A survey was done to compare RT treatment practice and techniques.

Design/Methods: The survey was drafted and then reviewed by a subgroup of 7 network members, who suggested changes and new questions. The survey totaling 39 questions was sent out to the entire network. Forty responses from 25 countries were submitted, with only one response per institution. Each question was answered by at least 20 respondents, with a median of 29 responses per question.

Results: On average, centers treated 2,000 patients per year with RT. Excluding three children-only hospitals the centers treated an average of 60 children per year. Available hardware ranged from telecobalt units to linacs, Gamma Knife, TomoTherapy, CyberKnife, and proton therapy. Half of centers without proton therapy would refer paediatric patients to protons elsewhere. Only 17% of the centers used brachytherapy for children. Most centers had advanced IGRT capabilities available, but the use of these varied greatly. Advanced treatment techniques like IMRT and VMAT were widely used for children, despite earlier warnings from radiobiologists of possible increased risk of secondary malignancies from modulated techniques.

Conclusion: Paediatric malignancies are a challenge due to their rarity and histological variety. An individual center will only treat a relative small number of patients with RT, and collaboration between centers is essential. This survey provides new information about treatment practice across a very large number of centers and countries. It can form a base for further collaboration, and it demonstrates that international networks have a large potential as a source of information and knowledge exchange between centers.

PD-120 | Needs Assessment for a Paediatric Proton Therapy Program in Canada

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Background/Objectives: Proton therapy enables normal tissue sparing for curative-intent treatment of children with cancer who require radiation therapy. In the USA and elsewhere, proton therapy is being rapidly adopted, and many new proton centres are being established. Without a proton centre in Canada, children and their families must travel abroad for treatment at high cost and has raised the question whether a Canadian proton therapy facility is needed.

Design/Methods: Canadian paediatric oncology centres were surveyed to assess current and future clinical practices. Needs were modeled by screening the Alberta Cancer Registry, ascertaining the number of children eligible for proton RT and comparing to the number who actually received this therapy.

Results: Most centres (63%) referred children abroad for proton therapy each year. Between 2008 and 2013, inclusive, 49 children (a mean of 4.9 children per centre) were referred to the United States for proton therapy. It is estimated referrals will increase to 36 cases per annum across Canada. Most respondents (75%) believe proton therapy will reduce late effects in all or some cases compared to photon therapy. The registry search revealed 37,170 patients irradiated of which 379 children (1.0%) were potentially eligible for proton therapy, accounting for 15.9% of the 2378 new cases of childhood cancer diagnosed in Alberta over the interval.

Conclusion: A strong perceived need for paediatric proton therapy in Canada was identified. Proton therapy utilization (actual number of cases referred out of country) was far lower than modeled needs, suggesting relative clinical need for at least one proton centre in Canada. Referrals are anticipated to increase in following years, with annual estimated cost of approximately \$60 million that is spent outside of Canada that could be invested in infrastructure and jobs within the Canadian health care economy. These issues are worthy of further national discussion and planning.

PD-121 | Metastatic Rhabdomyosarcoma: Does Radiation Therapy to Metastases Affect Clinical Outcomes?

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Background/Objectives: Therapy for metastatic rhabdomyosarcoma (RMS) includes chemotherapy with radiation therapy at metastatic sites. While the efficacy of radiation therapy in patients with localized RMS is well described, there are limited data demonstrating the efficacy of radiation therapy at metastatic sites.

Design/Methods: We conducted a retrospective study of 16 consecutive patients with metastatic RMS at presentation treated at our medical center between January 1, 2000 and July 31, 2012. We calculated control rates using Kaplan-Meier analysis of metastatic sites both treated with radiation therapy and metastatic sites not treated. All metastatic sites were pooled between patients for analysis.

Results: We found tumour recurrence in 4 of 28 treated non-pulmonary metastatic sites resulting in a 24-month control rate of 77% (95% CI: 49%, 91%). We found tumour recurrence in 6 of 47 untreated non-pulmonary metastatic sites resulting in 24-month and 36-month control rates of 74% (95% CI: 55%, 86%) and 46% (95% CI: 25%, 66%) respectively. We found tumour recurrence in 1 of 3 pulmonary metastatic sites treated with whole lung irradiation resulting in a 36-month pulmonary local control rate of 50% (95% CI: 6%, 91%).

Conclusion: We found the control rate for treated distant non-pulmonary metastases to be lower than previous series. The control rates for treated and untreated metastatic sites were similar but may be confounded by intention to treat. Randomized studies are required to demonstrate the true efficacy of radiation therapy at metastatic sites and influence on disease course.

PD-122 | Managing Dose to Non-Target Tissues Using A DVH Registry for IMRT-CSI Planning During A Change in Practice

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Background/Objectives: Craniospinal irradiation (CSI) is a complex treatment used in patients with malignancies at risk of leptomeningeal dissemination. An intensity-modulated radiation therapy technique for CSI (IMRT-CSI) delivered on a Tomotherapy unit had been used at our centre from 2008 until 2015. In June 2015, our centre moved to a new facility where Tomotherapy was no longer available. A new IMRT-CSI treatment technique for the Varian TrueBeam linac was developed. During and after development of our new technique, dose constraints to organs at risk (OAR) were guided by use of a dose-volume histogram (DVH)

registry. Our DVH registry allows us to compare new the DVHs of new treatment plans with the aggregate of previously-treated plans.

Design/Methods: The DVH registry consists of a backend database and frontend web pages that are served via a web-server internal to the clinic. Approved plans are added to the registry via a filter that standardizes the names of the OARs. Planners may also graphically compare DVH data for a new treatment plan with existing aggregate data without submitting the new data to the registry.

We used the registry to extract median dose constraints from two cohorts of IMRT-CSI patients treated using Tomotherapy: (1) CSI dose 36 Gy in 20 fractions and (2) CSI dose 23.4 Gy in 13 fractions and we used these to guide development of our new technique.

Results: Using the DVH registry we demonstrated that our new IMRT-CSI treatment technique spares OARs as well or better than our previous Tomotherapy technique.

Conclusion: For some organs, such as the eyes, lungs and the bowels we are able to demonstrate improvements that, if confirmed as the cohort of patients treated with our new technique increases, may provide reduced OAR toxicity. We are presently adding to our patient cohort and linking toxicity measures to the DVH dataset.

PD-123 | Robustness of Craniospinal Treatment Plans with Superior-Inferior Deviations in Isocenter Separation

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Background/Objectives: While photon treatment remains the standard for craniospinal irradiation (CSI), studies have shown the superiority of proton therapy for normal tissue sparing. We investigate daily deviations in the separations between CSI isocenters and the robustness of photon and proton plans with regard to superior-inferior deviations in isocenter separation.

Design/Methods: The daily deviation in isocenter separation was studied for 14 CSI patients. All patients were positioned using daily kV imaging and the couch coordinates were recorded to determine the separation between the brain, upper and lower thoracic isocenters. The planning target volume expansion was calculated using the van Herk formula. Differences in dose to the spinal cord and spine target were determined for 5 patients assuming a weighted distribution of shifts in superior-inferior isocenter separation between the brain and upper thoracic isocenters. The proton plans used 4 sequential junction shifts while the photon plans included up to 6 intrafractional shifts. Both used posterior beams for the spine.

Results: The average deviation in isocenter separation was -0.2 ± 0.3 cm in the superior-inferior, 0.0 ± 0.4 cm in the right-left, and 0.0 ± 0.1 cm in the anterior-posterior direction, with an average rotation of $0.0^\circ \pm 0.8^\circ$. The PTV expansion was calculated to be 0.85 cm. The proton plans showed greater dose uniformity with an average difference between minimum and maximum doses within the spine target of 4.7 Gy for the proton plans and 8.4 Gy for the photon plans. Robustness analysis including superior-inferior deviations led to an average increase in the maximum spinal cord dose of 0.6 Gy for the proton plans and 3.6 Gy for the photon plans.

Conclusion: A generous PTV expansion should be considered in CSI planning, even with daily imaging. Proton plans provide a more homogeneous dose and deviations from the nominal plans are also much smaller compared with photon plans.

PD-124 | Cyberknife in Paediatric Posterior Fossa Ependymoma

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Background/Objectives: Limited data are available regarding the use and benefit of cyberknife in paediatric ependymoma. We are presenting our Cyberknife experience in treating paediatric posterior fossa ependymoma.

Design/Methods: Eleven posterior fossa ependymoma (age less than 16 years) were treated using cyberknife between 2010 and 2014. Data of pathology, extent of surgery, radiotherapy plans parameters, disease control status at time of analysis and side effects were retrospectively reviewed the dose to the nearby critical structures. Long-term follow-up is needed to determine the long-term efficacy and associated toxicities.

Results: Eight patients who had subtotal resection received cyberknife treatment boost following Rapidarc conventional fractionation plan to a total dose of 59.4 Gy (1.8 Gy per fraction). Spinal cord was excluded from target volume after 54 Gy. Boost dose using cyberknife ranged from 5.4 to 9 Gy in 3- 5 fractions. Three patients received 20 Gy in 5 fractions in the context of palliative radiotherapy /re-irradiation using cyberknife. Dose was prescribed to 70- 81% isodose line. The average gross tumour volume was 8.7 cc. All patients tolerated treatment well with no Grade III toxicity reported. After a median follow up period of 21 months, the 3 years local progression free-survival was 53% in patients treated with radical intent to a total dose of 59.4 Gy. Two of the three patients received re-irradiation were alive at the time of analysis 23 and 61 months from treatment time. The third patient died 15 months after treatment with local disease progression.

Conclusion: Using cyberknife, we were able to escalate the dose to residual/recurrent posterior fossa ependymoma without exceeding the brain stem/spinal cord constraints. Treatment was well tolerated. Rapidarc and cyberknife composite plans can potentially reduce the long-term toxicities associated with radiation therapy by reducing the amount of irradiated normal brain parenchyma and by limiting.

PD-125 | Peripheral and Low Doses Measurement for Three Stereotactic Radiotherapy Techniques

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Background/Objectives: The main aim of this work is to compare the peripheral and low doses absorbed during stereotactic treatment of a brain lesion delivered using three stereotactic techniques; Arcs, noncoplanar fixed conformal fields (3DCRT) and intensity modulation (IMRT).

Design/Methods: Treatment plans (ARCs, IMRT, 3DCRT) were created for the paediatric anthropomorphic phantom for different target sizes. Peripheral doses (PD) for the three stereotactic different techniques were calculated and measured at various distance in cranio-caudal direction from the isocenter of the PTV. Measurements were performed with thermoluminescent detectors (TLD) inserted at various depths inside the paediatric phantom. Three TLDs were placed at distances (5, 10, 15, 20, 25, 30, 35, and 40) from the isocenter of PTV in the cranio-caudal direction, at roughly the locations of the thyroid, the brain stem, the optic nerves, the lungs, the ovaries, and the testes. The calculated peripheral doses of the three different Stereotactic Techniques for different PTVs sizes (5.8, 11.3, 14 CC) as the most common PTVs volumes in stereotactic treatment created for a child phantom.

Results: The IMRT technique has the highest values of PDs at distance close to the PTV the next is Arcs technique followed by 3DCRT technique which has the lowest values. At distance 10 up to 40 cm the PDs values converted to be the Arcs has the highest values followed by 3DCRT and the IMRT.

Conclusion: Knowledge of the PDs is important and of clinical interest. It is worth noting that patients often receive stereotactic treatment for non-malignant lesions and thus have relatively long potential lifetimes. Physician must be able to estimate the dose out of field and the resultant risk to patients.

PD-126 | Development of a Four-Dimensional Computed Tomography (4DCT) Imaging Sequence for Paediatric Radiotherapy Planning

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Background/Objectives: Individual motion assessment is potentially important for optimising dose delivery, when using intensity-modulated radiotherapy (RT) for paediatric tumour sites affected by respiratory-related motion. 4DCT is the current gold standard for lung and upper abdominal motion assessment in adults but is not routinely used for children. We have undertaken to devise and implement a paediatric specific 4DCT protocol for upper abdominal tumours.

Design/Methods: Following routine planning spiral CT scan of the abdomen (120kVp, 16x1.5mm collimation, 0.938 pitch and tube current modulation enabled), a slow spiral 4DCT scan (120kVp, 16x1.5mm collimation, a pitch adjusted to the patient's breathing period and tube current modulation enabled) was acquired. X-ray projection data tagged with the respiratory signal captured by lower thoracic bellows. Images reconstructed in 10 phases; labelled 0-90%. Phase 0%: end-inspiration, 50%: end-exhalation.

Results: Six patients undergoing abdominal RT were eligible for 4DCT. Five patients were scanned: median age 4.1 years (range 1.9- 4.7 years), including four patients with neuroblastoma, one with Wilms tumour. Three required general anaesthesia. One with an undetectable respiratory trace did not proceed to 4DCT. Spiral 4DCT was acquired with median pitch value 0.15. Median dose-length product 583mGycm (range 390 to 1181mGycm), compared to 217mGycm (range 130 to 279mGycm) for spiral CT scan. Median value of ratio in pre-scribed mAs between scans was 3.2 meaning spiral 4DCT scan was acquired at three times the dose of the spiral CT scan. Motion information from 4DCT was used to create individualised ICRU 62-appropriate internal target volumes.

Conclusion: Using a paediatric-specific 4DCT scanning protocol minimises additional radiation exposure and its potential benefits arguably justify the increased dose. A proportion of paediatric patients may exist where only minimal motion is present. Further studies are required to fully determine the benefits of 4DCT for children and the interpatient intrafraction variability in respiratory motion.

PD-127 | Radiotherapy Quality Management System for Conducting Nationwide Clinical Trials: An Instrument Established by the Japan Children's Cancer Group

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Background/Objectives: Japan Children's Cancer Group (JCCG) was launched in December 2014 as a unification of nationwide cross-sectional paediatric oncological clinical trial groups, including disease-specific trial groups in Japan. Radiotherapy quality management (RQM) has been required in disease-specific oncology trial groups. Implementation of the RQM system, which can be utilized for various paediatric cancers, is one of the major advantages of the unified trial groups, JCCG. This study aimed to investigate the establishment of the RQM system and its applicability.

Design/Methods: The JCCG RQM system is a Web-based clinical image capturing and reviewing system. It was developed as a tool for radiotherapy standardization and quality assurance. We established three objectives for the RQM system. First is to conduct consultations to

indicate radiotherapy based on the clinical images. Second is to collect radiotherapy planning data. Finally, third is to review treatments for quality assurance.

Results: The clinical image capturing and reviewing tool was introduced in July 2015. Through this system, radiotherapy committee of JCCG define the indication of a case after reviewing images and the consensus report of the diagnostic imaging committee of JCCG. The implementation of the viewer for RQM allowed the simultaneous review of images by four paediatric radiation oncologists from different institutions. Additional tools for handling treatment planning data to attain the remaining objectives have been implemented.

Conclusion: The radiotherapy quality management system is expected to facilitate standardization and quality assurance of radiotherapy delivered in clinical trials. The development and practical evaluation of the system is currently undertaken by JCCG.

PD-128 | Impact of Radiation Fraction Dose on Hearing Impairment: Retrospective Analysis of 19 Medulloblastoma Patients Treated with Conventionally-Fractionated or Hyperfractionated Radiotherapy

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Background/Objectives: This study compares high frequency hearing loss (HFHL) in medulloblastoma patients receiving conventionally-fractionated (CRT) and hyperfractionated radiotherapy (HRT).

Design/Methods: Between 2008 and 2015, 19 children with medulloblastoma, mean age 5.5 years (range 15 months - 17.5 years), were treated sequentially with radiotherapy and cisplatin-based chemotherapy (HIT 2000 protocol). Radiotherapy was administered using helical tomotherapy to the craniospinal axes (CSA), boost to the posterior cranial fossa (PCF) and, where necessary, to the primary tumour site. 12 patients received 35.2Gy (1.6Gy x 5 per week) CRT to the CSA and 55Gy (1.8Gy x 5) to the PCF. 7 patients received HRT (1Gy x 2 daily x 5) of 40Gy (CSA), 60Gy (PCF) and 68Gy (primary tumour site). Post-radiotherapy HFHL was determined by audiometry and classified according to the "Muenster classification".

Results: The average cochlear dose (Dmean) for CRT was 45.4Gy (right) and 44.9Gy (left), and 56Gy (right) and 55.1Gy (left) for HRT (for both ears $P > .05$). Bilateral HFHL was observed in all patients. Mean duration before initial detection of hearing impairment was 3.5 (SD±3.4) months (CRT) and 2 (SD±0.6) months (HRT) ($P = .028$). In the CRT group, grade 2 HFHL (worst threshold >20 dB HL at ≥4 kHz) was found in 8 patients (66%) and grade 3 (>20 dB HL at <4 kHz) was found in 4 patients (34%). Hearing losses of grades 2 and 3 were found in 3 (43%) and 4 (57%) patients respectively after HRT. No linear correlation between severity of HFHL and number of cis-platin cycles was observed.

Conclusion: These results demonstrate the impact of radiation fraction dose on the severity of HFHL in medulloblastoma patients. More severe HFHL was found following HRT than CRT. Further investigations to establish an optimal radiation treatment modality are necessary because of the rarity of medulloblastoma.

PD-129 | Quality of Life and Patient Reported Outcomes in Teenagers and Young Adults Receiving Palliative Radiotherapy

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Background/Objectives: Radiotherapy is firmly established as palliative therapy for children and teenagers with cancer, with variable evidence for symptom relief and control of disease burden. The measurement of health related quality of life (HRQoL) and patient report outcomes (PROs) is becoming increasingly important for demonstrating treatment benefit, as evidence of both clinical and economic efficacy. In this study, we conducted a search of the literature to determine what tools have been used to measure HRQoL and PRO in this population, and what themes can be identified from published data.

Design/Methods: The NHS Evidence portal was used to conduct a literature search of Medline, PsychINFO, CINAHL and EMBASE, with search terms matched to the MESH/encyclopaedia of each database where relevant. Predetermined inclusion and exclusion criteria were used, and data extracted from included articles using tools relevant to study type.

Results: 32 articles were identified. Several tools for the assessment of HRQoL in this population were identified, with varying degrees of appropriate validation. Teenagers report numerous sources of distress in receiving palliative radiotherapy, including fatigue, impact on daily living and seeing friends and site specific morbidities.

Conclusion: Teenagers represent a unique cohort patients when receiving both curative and palliative treatments, with unique problems and difficulties of which clinical and nursing team and individuals must remain vigilant too. Decisions around palliative radiotherapy must include the patients and the consideration of how treatment will impact on daily activities as well as symptoms and the end-of-life period. Further work is needed to validate HRQoL and PRO measures in this population.

RARE TUMOURS

PD-130 | Chloroquine Sensitizes Nasopharyngeal Carcinoma Cells but not Nasoepithelial Cells to Irradiation by Blocking Autophagy

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Background/Objectives: Treatment of nasopharyngeal carcinoma requires the application of high dosages of radiation, leading to severe long-term complications in the majority of patients. Sensitizing tumour cells to radiation could be a means to increase the therapeutic window of radiation. Nasopharyngeal carcinoma cells display alterations in autophagy and blockade of autophagy has been shown to sensitize them against chemotherapy.

Design/Methods: We investigated the effect of chloroquine, a known inhibitor of autophagy, on sensitization against radiation-induced apoptosis in a panel of five nasopharyngeal carcinoma cell lines and a SV40-transformed nasopharyngeal cell line. Autophagy was measured by immunoblot of autophagy-related proteins, immunofluorescence of autophagosomic microvesicles and electron microscopy. Autophagy was blocked by siRNA against autophagy-related proteins 3 and 6 (ATG3 and ATG6).

Results: Chloroquine sensitized four out of five nasopharyngeal cancer cell lines towards radiation-induced apoptosis. The sensitizing effect was based on the blockade of autophagy as inhibition of ATG3 and ATG6 by specific siRNA could substitute for the effect of chloroquine. No sensitization was seen in nasopharyngeal cells.

Conclusion: Chloroquine sensitizes nasopharyngeal carcinoma cells but not nasopharyngeal cells towards radiation-induced apoptosis by blocking autophagy. Chloroquine therefore could be a candidate to increase the therapeutic window of radiotherapy in patients with nasopharyngeal cancer. Further studies in a mouse-xenograft model are warranted.

PD-131 | Breast Cancer in Very Young

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Background/Objectives: Breast cancer in women aged less than 25 years (defined as very young breast cancer, VYBC) is rare and accounts for 0.25% of all breast cancer in the West. There is no data available on VYBC from developing country. The aim of this study was to analyze the clinical, pathological, prognostic factors and outcome in this group.

Design/Methods: This analysis was performed in 31 patients aged 25 years or less who were registered at All India Institute of Medical Sciences (AIIMS), New Delhi, India over an 11 year period between 2004 and 2014.

Results: The median age was 22 years (range 18-25). Positive family history (siblings and parents) was elicited in 5 patients and 3 patients have pregnancy associated breast cancer. The TNM stage distribution was: Stage I was 0, stage II - 3 stage III - 18 and stage IV - 10 patients. The median clinical tumour size was 6 cm. Modified radical mastectomy was the most common surgical procedure and performed in 19 non-metastatic patients (90%). All patients had histology of Invasive ductal carcinoma. Seventy percent of tumors were high grade and 90% had pathological node positive disease. Estrogen, Progesterone and human epidermal growth factor receptor 2 (HER2)/neu positivity were 25%, 25% and 35% respectively. Triple negative breast cancer constituted 40% of patients. With a median follow-up of 36 months, 3 years relapse free survival (non metastatic disease) and overall survival was 30% and 50% respectively.

Conclusion: Very young women constituted 1% of all breast cancer cases. Advanced disease at presentation, triple negative status (40%), HER2/neu positivity (35%) and high histologic grade (70%) results poor outcome. Breast cancer in this group have more aggressive biological behavior and need early diagnosis with prompt treatment.

PD-132 | Could We Adapt Radiotherapy Dosages to Tumour Response after Chemotherapy in Young Patients with Undifferentiated Nasopharyngeal Carcinoma?

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Background/Objectives: French paediatric rare tumors group (*Fracture*) advice for patients with nasopharyngeal carcinoma (NPC) to adapt RT dosages to initial chemotherapy response: "reduced doses" (59.4/54/45Gy) in case of VGPR/CR/PR>50-90% and "standard doses" (66.6/66.6/45Gy) if response<50% or progressive disease (OR/PD), respectively on residual tumour/initial tumour volume/non-invaded cervical area. Concomitant radiotherapy/chemotherapy (RT/CT) was optional and specifically recommended in case of poor response. RT/CT association leads to frequent mucosal toxicity needing temporary interruption of the RT schedule. Questions are to answer if the RT interruption impacts survivals and if RT dosages could be safely adapted in area of conformational RT.

Design/Methods: We retrospective analyzed 95 patients, < 25years, with non-metastatic NPC treated in France from 1999 to 2015. RT was "optimal" if radiation treatment duration was unraised without interruption; "non-optimal" if duration >15% or/and interrupted.

Results: Median age was 15 years (range: 7-23). Initial CT was delivered for 90 patients and 29 had maintenance therapy mainly with β -interferon. Cisplatin-based-CT was mainly used (98%). Responses were: VGPR/CR 35%; PR 52% and OR/PD 13%. Median radiation dose to primary was 65Gy (range, 45-74Gy) and 60Gy (range, 45-72Gy) to cervical lymph nodes. Concomitant RT/CT was used in 59%, "optimal" for 61% and "non-optimal" for 39% (mucositis responsible for most interruptions). After a median follow-up of 4.5 years [range: 3.6-5.5 years], only 3 loco-regional relapses, 11 had metastatic occurred. The 3-year disease

free survival was 86% [77-92%]. RT interruption did not impact survivals ("optimal" vs. "non-optimal"; HR=0.6 [0.2-2.0], $P=0.42$). With multivariate model, the only significant prognostic factor is the delay to diagnosis ± 5 months (HR=1.2 [1.01-1.35], $P=0.02$).

Conclusion: RT dosage adaptation to CT does not jeopardize survivals in paediatric NPC. Local control is nowadays excellent and encourage to diminish RT dosage according to initial CT response, in order to reduce long term effects. Prognosis is not influenced by RT interruption.

PD-133 | Treatment of Unresectable Lymphangiomas with Sirolimus

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Background/Objectives: Lymphatic malformations (LM), traditionally called lymphangiomas, are localized areas of abnormal development of the lymphatic system that occur most commonly in the head and neck region. The only and definitive treatment modality is surgical removal. During the history various attempts to manage unresectable LM were used with varying degrees of success (interferon, intralesional bleomycin, propranolol, sildenafil or OK432-picibanil). Some sporadic reports appeared within last few years that sirolimus (immunosuppressive agent) is able to decrease production of VEGF (vasculoendothelial growth factor) and in this way to stop the LM progression and decrease the LM volume.

Design/Methods: Since 2015 we have started the administration of sirolimus in 18 children with unresectable LM on various areas of the body: neck - 8, neck + mediastinum - 3, shoulder - 2, lower extremity - 2, lung and bones - 2, abdomen - 1. The daily dose was 1.6mg/m². The plasma level was checked weekly during first month of therapy and then monthly and were maintained between 10 to 15 ng/ml. Radiological investigation were performed in three month interval.

Results: The response was detected within months, only lung effusion and increased intestinal lung density disappeared within weeks. One child with large LM on shoulder completely resolved after 4 months therapy, 2 children with neck LM were able to undergo resection of shrank tumour, a child with abdominal LM and huge ascites depending on diuretics for dyspnea improved well with no present demands of diuretics, no dyspnea and reduction of ascitic volume. Only one child with neck LM had progression after 5 weeks of therapy. Majority of children reported better quality of life and improved feasibility of physical activity. Some of children are still on the treatment.

Conclusion: Sirolimus seems to be a promising agent in management of unresectable LM, preferably the microcystic forms.

PD-134 | Using CRISPR/Cas9 to Explore the Kinome in Malignant Rhabdoid Tumors – A Tool to Identify New Potential Therapeutic Targets

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Background/Objectives: Malignant Rhabdoid Tumors (MRT) are universally lethal embryonal tumors that occur mainly in early childhood. The CRISPR-Cas9 system for genome editing is a powerful tool to identify genes involved in vital biological processes. We hypothesized that a systematic functional screening of the human Kinome will reveal molecules that are essential for tumour survival, growth and migration which can function as therapeutic targets for MRT.

Design/Methods: We have screened 160 kinases in an MRT cell line (MON - Dr. Delattre, Institut Curie, Paris) using Lentiviral-CRISPR particles which contain up to 4 gRNAs per gene (Thermo Fisher Scientific). We first used a lenti-vector to permanently express Cas9 in the cells then infected these cells with the Lentiviral-CRISPR particles and two controls (positive: gRNA for HPRT, negative: scrambled gRNA). After proper transduction and selection, genotypes were evaluated using Genomic Cleavage Detection (GCD) assays and next generation sequencing. Phenotypes were evaluated, by cell proliferation (MTT, Ki-67, PH3), viability (Trypan Blue) and migration (wound healing) assays.

Results: The proportion of positive GFP-expressing cells indicated high transduction efficiencies (95%). GCD demonstrated successful gene editing levels in the positive control and in randomly selected kinases. *In vitro* studies allowed very precise monitoring of proliferation of each of the 160 mutated cell lines. Although the majority of mutated cells did not present changes in phenotypes, mutations in 8 kinases (5%), including the proto-oncogene *BRAF* resulted in impairment of proliferation.

Conclusion: With the help of CRISPR/Cas9 genome editing technology, we identified a set of kinases with the potential to serve as therapeutic targets for MRT.

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RENAL TUMOURS

PD-135 | Is Biopsy a Risk Factor for Wilms Tumour (WT) Relapse? Data from AIEOP (Associazione Italiana Ematologia Oncologia Paediatrica) 2003 Protocol

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Background/Objectives: Other groups have reported on their experience concerning the controversial implications of biopsying WT. We performed a similar analysis on cases registered in AIEOP-TW-2003.

Design/Methods: Patients with unilateral WT treated either with immediate nephrectomy (n=258) or pre-operative chemotherapy (n=185) were eligible (10, missing information). The local responsible physicians chose the initial treatment, basing on the risk of unsafe a/o incomplete surgery. Protocol guidelines strongly supported biopsy if pre-operative chemotherapy was selected. Only open biopsy required treatment as stage III. Risk factors for relapse were analyzed by Cox proportional hazard methods. "Local" relapse was defined as relapse within the abdomen, except for liver metastases and metachronous tumors.

Results: 453 patients (median age 3 years; diffuse anaplasia, 41; male, 132; stage I, 123; stage II, 160; stage III, 101; stage IV, 69) formed the denominator of the analysis. Biopsy was performed in 150 cases (72% core needle technique \geq 18 G, 20% 14-16 G, 8% open). Five-year relapse-free survival (RFS) and OS for the group as a whole were 84.5% (95% CI 81.1-88.1) and 92.4% (89.8-95.1). On univariate analysis for RFS, age (unit increase, Hazard Ratio, HR=1.007; age class < or > 24 months, HR=1.80), anaplasia (HR=2.56), stage IV (HR=2.74), pre-operative chemotherapy (HR=1.66) and biopsy (HR=1.82, 1.12-2.97, p=0.01) were associated with an increased risk of relapse (tumour rupture, lack of lymph node sampling were not). 5-year RFS for patients receiving biopsy was 77.5% (70.7-85.0) (30 relapses/150) comparing with 87.5% (83.7-91.5) (39/297) for patients not receiving biopsy. When analysis was narrowed to "local" relapse, biopsy was not associated with an increased risk (p=0.13). On multivariable analysis only anaplasia remained significant for RFS (Harrel c-index 0.62, apparent; 0.58, bias-corrected).

Conclusion: This analysis supports a lack of association between biopsy and the risk of local relapse.

PD-136 | Study of the Circulant Tumoral DNA for the Molecular Diagnosis of Paediatric Renal Tumors
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Background/Objectives: Circulating tumour DNA (ctDNA) is a potential tool for the molecular diagnosis of cancer. It represents a fraction of cell-free DNA (cfDNA) depending on the pathology, tumour load, tumour spread or necrosis. According to the SIOF strategy, in several countries paediatric renal tumors (RT) are initially considered as nephroblastomas, with post-nephrectomy histological confirmation. However, other histological diagnoses may occur. Genetic abnormalities of paediatric RT are heterogeneous and non-recurrent. Our aim is to validate the feasibility of tumour genetic characterization based on ctDNA from plasma samples in children with RT.

Design/Methods: In this retrospective, monocentric, feasibility study, paediatric patients with RT and available plasma sample at diagnosis were included. Extraction of cfDNA was performed with QIAmp[®] Kit and ctDNA quality was confirmed by capillary electrophoresis. To search for heterogeneous non-recurrent tumour-cell specific alterations, a technique of whole-exome sequencing (WES) in ctDNA recently developed in our laboratory was performed to enable copy-number profiling and mutation calling. WES libraries of ctDNA were prepared with NimbleGen SeqCapEZ[®] Kit. Genetic alterations identified in ctDNA will be compared to those found in tumoral and constitutional DNA.

Results: 20 patients (8 males, 12 females) were identified; median age at diagnosis was 2.1 years (0.1-7.4). Secondary histologic diagnosis confirmed 17 nephroblastoma cases, 2 clear-cell sarcomas and 1 clear-cell carcinoma. Capillary electrophoresis confirmed the presence of cfDNA in all samples. Median concentration was 125.22 ng/mL (22.12 - 2286). WES is ongoing to determine the fraction of ctDNA in these cfDNA samples and to identify somatic genetic alterations.

Conclusion: The study of ctDNA is a promising noninvasive method for the molecular diagnosis/monitoring of tumors still under development. The identification of specific tumoral genetic alterations in ctDNA could be a useful tool to specify the diagnosis of the different RT subtypes, enabling to guide the upfront management and potentially introduce tumour monitoring during treatment.

PD-137 | Outcome of Renal Tumors Registered to the Japan Wilms Tumour Study-2 (JWITS-2): A Report from the Japan Children's Cancer Group (JCCG)
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Background/Objectives: This study aimed to review the outcome of unilateral paediatric renal tumors registered to the Japan Wilms Tumour Study-2 (JWITS-2).

Design/Methods: A total of 671 patients were enrolled in the JWITS-1 (from 1996 to 2005) and -2 (from 2006 to 2014). The therapeutic regimens were similar to those of NWTs-5. Relapse-free survival (RFS) and overall survival (OS) were analyzed for each histological group.

Results: The diagnosis were confirmed by the central pathological system in 553 and follow-up data were available in 400 patients. The 5-year RFS and OS of nephroblastoma were 90% (95% CI: 85-94%) and 97% (95% CI: 92-99%) in JWITS-2 (n=178), as compared to 77% (95% CI: 69-83%; p=0.0003) and 91% (95% CI: 85-95%; p=0.054) in JWITS-1 (n=142). The 5-year RFS of JWITS-2 registered nephroblastoma according to the clinical stages were 96% (95% CI: 84-99%) for stage I, 93% (95% CI: 83-97%) for stage II, 91% (95% CI: 77-96%) for stage III, and 66% (95% CI: 38-84%) for stage IV, respectively. The 5-year RFS and OS of CCSK were 82.4% (95% CI: 63-92%) and 91% (95% CI: 69-98%) in JWITS-2 (n=31), as compared to 69% (95% CI: 40-86%; p=0.3) and 81% (95% CI: 52-94%; p=0.4) in JWITS-1 (n=16). The 5-year RFS and OS of RTK were 19% (95% CI: 5-40%) and 25% (95% CI: 8-47%) in JWITS-2 (n=16), as compared to 24% (95% CI: 7-45%; p=0.9) and 24% (95% CI: 7-45%; p=0.8) in JWITS-1 (n=17).

Conclusion: The long-term RFS and OS of nephroblastoma and CCSK are improving in the JWITS-2 trial; however, the outcome of RTK remains to be unsatisfactory.

PD-138 | Outcomes of Patients with Wilms Tumour and Brain Metastases Enrolled on National Wilms Tumour Studies 1-5: A Report from the Children's Oncology Group

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Background/Objectives: The occurrence of brain metastases in patients with Wilms tumour (WT) is very rare. The optimal management of these patients is not known.

Design/Methods: We retrospectively reviewed the clinical characteristics and treatment outcomes of patients with WT and brain metastases who were enrolled on the National Wilms Tumour Studies (NWTs) 1-5. Patients with non-Wilms renal tumors were excluded.

Results: No patient had brain metastases at initial diagnosis. Relapse involving the brain was documented in 47 of 9424 patients (0.5%). Of the 45 patients with adequate data, 26 (58%) patients were male. Thirty-eight (84%) patients were initially diagnosed with favorable histology WT. In 30 patients (67%) the appearance of intracranial disease was preceded by relapse at another site. Ten patients did not receive any disease directed therapy. Surgical resection was attempted in 15 (33%) patients; gross total resection was achieved in 11 patients. Twenty-nine patients received brain irradiation with a median dose of 3000 cGy (range 1080 - 4000 cGy). Twenty-seven patients received chemotherapy. The five-year overall survival from the time of intracranial relapse was 28.7% (95% CI: 14.4 - 43.1%). Nine patients (all favorable histology WT) were alive with a median follow-up from brain relapse of 140 months (range 35 - 381 months). All nine survivors received radiation therapy, eight received chemotherapy, and four underwent surgery (two gross total resection, two partial resection). Two of 31 patients in NWTs 1-4 were alive at last follow-up compared to seven of 14 patients in NWTs 5. The overall survival after brain metastases of the NWTs-5 patients was significantly higher than the overall survival of the NWTs 1-4 patients (p-value=0.029, log rank test).

Conclusion: Patients with WT recurrence involving the brain may have durable survival, particularly those treated in recent years. Multimodality therapy including radiation and chemotherapy should be considered for these patients.

PD-139 | Treatment of Stage IV Favorable Histology Wilms Tumour with Extra-Pulmonary Metastases: A Report from Children's Oncology Group Study AREN0533

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Background/Objectives: Most patients with stage IV Favorable Histology Wilms Tumour (FHWT) have pulmonary metastases. Patients with extra-pulmonary metastases (EPM) constitute a smaller cohort whose outcome has not been extensively examined. Studies conducted by the International Society of Pediatric Oncology indicate that patients with EPM have inferior outcomes compared to patients with pulmonary metastases. This has not been replicated in the National Wilms Tumour Studies (NWTs). The AREN0533 study sought to determine whether augmentation of therapy with Regimen M (vincristine/dactinomycin/doxorubicin alternating with cyclophosphamide/etoposide) would improve outcome for these patients.

Design/Methods: Patients were enrolled on AREN0533 between February 2007 and February 2013 after undergoing risk assignment on the AREN03B2 Renal Tumour Biology and Classification study. Patients with EPM (with or without pulmonary metastases) were designated "Higher Risk" and treated with Regimen M and radiation therapy (RT) to all metastatic sites: EPM received RT doses dependent on age and site; pulmonary metastases (if present) received 1200 cGy.

Results: Of 391 patients enrolled on AREN0533, 44 patients with stage IV FHWT had EPM. EPM sites were liver (n=35), bone (n=4), other (n=7). Thirty six of 44 patients had pulmonary metastases in combination with EPM. All 44 patients were treated with Regimen M plus RT to all metastatic sites, resulting in a 4 year event-free survival (EFS) of 81.69% and overall survival (OS) of 90.91%. By comparison, on NWTs-5 38 patients with stage IV FHWT and EPM were treated with Regimen DD-4A (vincristine/dactinomycin/doxorubicin) plus RT to metastatic sites, resulting in a 4 yr EFS of 78.95% and OS of 86.84%. The differences in EFS (p=0.6908) or OS (p=0.8612) were not statistically significant.

Conclusion: Regimen M therapy did not improve outcomes for patients with stage IV FHWT with EPM. Other therapeutic strategies should be considered for future studies.

PD-140 | Trisomy 12 Occurs before Alteration of IGF2 Expression and Predicts Favorable Outcome in Patients with Wilms Tumors

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Background/Objectives: Wilms tumour (WT) is an embryonal tumour with genetic and epigenetic heterogeneity, which may occur through developmental abnormality in nephrogenesis. The aim of study is to find molecular markers to predict outcomes in patients with WT.

Design/Methods: We analyzed SNP array CGH patterns, mutations of *WT1*, *CTNNB1*, *DROSHA*, and *DICER1*, and the methylation status of *H19*-DMR in 154 patients with WTs, enrolled in the JWITS-1 and JWITS-2 protocols. Relapse-free survival (RFS) and overall survival (OS) were estimated for each group classified by genetic and epigenetic abnormalities.

Results: 56 tumors showed *WT1* abnormalities (*WT1* tumors); uniparental disomy (UPD) of 11p and *CTNNB1* mutation were frequent, but other genetic abnormalities were scarce. 17 tumors except one with *CTNNB1* mutation showed no other genetic and epigenetic abnormalities (silent tumors). The other 81 tumors without *WT1* abnormality had some genetic and epigenetic abnormalities, and were classified by the *IGF2* status; loss of imprinting (LOI) 29 tumors, retention of imprinting (ROI) 19, UPD 25, and others 8. Deletion and mutation of miRNA processing genes were more frequent in LOI than no LOI tumors (P=0.038). RFS and OS were favorable for patients with *WT1* or silent tumors. Among other 81 patients, 11q and 16q deletions in tumors were associated with poor outcomes (RFS and OS; P=0.004 and 0.012 for 11q-; P=0.032 and 0.054 for 16q-). 41 patients with +12 in tumors had better RFS and OS (P=0.028 and 0.093) than 40 without; +12 was equally distributed in LOI, ROI, and UPD tumors. Among 9 tumors whose mRNA expression levels were examined, 3 with +12 showed higher expression levels of *CCND2* and *CDK4* on chromosome 12 than 6 without.

Conclusion: The present study indicated *WT1* and silent tumors as distinct subtypes, and identified that +12 occurred before *IGF2* alterations in *WT1*-wild-type tumors and predicted a good outcome.

PD-141 | Expression of the Fusion Transcript YWHAE-NUTM2 in a Model of Clear Cell Sarcoma of Kidney (CCSK)

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Background/Objectives: Clear Cell Sarcoma of Kidney (CCSK), the second commonest paediatric renal malignancy, is aggressive, therapy-resistant, and has poor clinical outcomes. The oncogenic mechanisms and tumour biology underpinning CCSK remain poorly understood and effective therapies are lacking. Previously, we characterized the balanced t(10;17)(q22;p13) chromosomal translocation, identified then, the only recurrent genetic aberration in CCSK, demonstrating an in-frame fusion of the *YWHAE* and *NUTM2* genes. The somatic incidence of this fusion was 12% in 50 cases. Certain clinico-pathological features of translocation-positive CCSK tumors suggested that this aberration might be associated with higher stage and grade disease. Here, in order to further clarify the impact of this gene-fusion, we examined whether *YWHAE-NUTM2* expression promotes oncogenesis in a CCSK model.

Design/Methods: We generated stably transfected HEK293, NIH3T3, and BJ-hTERT cell lines containing doxycycline-inducible HA-tagged-*YWHAE-NUTM2*, and demonstrated stable fusion-protein expression over a 100-hours timeline following induction with doxycycline. We then conducted real-time proliferation, migration, and invasion assays with the xCELLigence platform. Furthermore, we determined changes in gene expression following induction of the fusion gene at 24 and 72-hours in HEK293 and BJ-hTERT cells using Affymetrix Human-Gene-ST-Arrays. Differently Expressed Genes (DEGs) with an adjusted p-value <0.05 were selected for further analysis.

Results: *YWHAE-NUTM2*-expressing HEK293 and NIH3T3 cells exhibit significantly greater migration compared to mock-treated controls. Most DEGs in HEK293 and BJ-hTERT cells correlated with biological process such as induction of cell migration, angiogenesis, signal transduction, embryogenesis, and neurogenesis. Furthermore, pathways which are well-established in oncogenesis, including the mitogen-activated protein kinases (MAPK) signaling pathway, were significantly over-represented amongst the DEGs.

Conclusion: These results support the hypothesis that expression of *YWHAE-NUTM2* contributes to oncogenesis, including through increased cell migration. Moreover, the *YWHAE-NUTM2*-associated DEGs identified here constitute intriguing candidates for our ongoing signaling studies and will be included in our efforts to identify novel therapeutic targets.

RETINOBLASTOMA

PD-142 | Ophthalmic Artery Chemosurgery for Intraocular Retinoblastoma: Are three Agents Better than One?

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Background/Objectives: Retinoblastoma (RB) is the most common primary intraocular malignancy of childhood. Ophthalmic Artery Chemosurgery (OAC) is a promising treatment with high globe salvage rates for advanced stage disease. It is unknown whether multi-agent chemotherapy is more effective than single-agent Melphalan.

Design/Methods: We performed a single-institution retrospective chart review following IRB approval. We identified patients with intraocular RB who received single agent melphalan therapy via OAC and matched them to patients who received multi agent chemotherapy via OAC. Matching was based on presence or absence of vitreous seeds and cumulative dose of intra-arterial melphalan. Kaplan Meier curves were constructed for event free survival (EFS) with events defined as enucleation, external beam radiotherapy, or additional chemotherapy. EFS were compared between single agent and multi-agent chemotherapy groups using Cox proportional hazards model with a robust sandwich covariance matrix estimate to account for clustering.

Results: From 2006 to 2015, 292 patients received OAC for intraocular RB. 21 patients received single agent intra-arterial melphalan and were matched with 63 patients who received multi agent intra-arterial chemotherapy. 15/21 (72%) of patients treated with single agent chemotherapy and 42/63 (67%) of patients treated with multiple agents were ICRB group D/E. 18/21 (86%) of patients who received single agent chemotherapy and 42/63 (67%) patients who received multi-agent chemotherapy were naive to treatment. The Kaplan-Meier estimates of EFS at 1 year were 95% (95% CI: 69%-99%) for patients receiving single-agent melphalan and 95% (95%CI: 85%-98%) for patients receiving multi-agent therapy. EFS at 3 years was 91% (95% CI: 80%-96%) for patients receiving single-agent melphalan and 80% (95% CI: 55%-92%) for patients receiving multi-agent therapy. The difference in EFS curves is not significant (p value=0.82).

Conclusion: Melphalan based OAC is highly effective for intraocular RB. The role of additional agents is yet to be determined. Limitations of the study include its retrospective and non-randomized nature.

PD-143 | PDGF-PDGFR Signaling Sustains Angiogenesis in an Autocrine and Paracrine Fashion in Retinoblastoma

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Background/Objectives: Vitreous disease is considered a poor prognostic factor for ocular survival in retinoblastoma (RB) patients. Platelet derived growth factor is highly abundant in the vitreous microenvironment, especially in patients suffering from proliferative retinal disorders. We hypothesize that modulation of PDGF-PDGFR signaling may control vitreous seeds in RB.

Design/Methods: RB cell lines Y79 and Weri-1 represent metastatic and non-metastatic disease (respectively). Cells were cultured with or without PDGF-AB as primary stimulus and evaluated for the expression of angiogenesis-related genes, production of angiogenic factors, and morphological changes by qPCR, Multiplex assays and confocal microscopy. The role of PDGF in RB tumour cell proliferation and angiogenesis was evaluated by administration of imatinib mesylate (IM), a tyrosine kinase inhibitor that affects function of PDGF-R β , and a neutralization antibody against the PDGF-BB isoform. Immunohistochemistry (IHC) for PDGF was performed on retinoblastoma xenografts derived from human samples.

Results: PDGFA and PDGFB isoforms are highly expressed in RB cells by qPCR analysis. The presence of PDGF in the vitreous of human RB xenografts was confirmed by IHC. Western blot, Multiplex and flow cytometry analyses revealed a reduction in the PDGF-AB/BB isoforms ($p=0.04$), FLT-3L ($p=0.02$), and VEGF ($p=0.08$) after concomitant incubation of IM and recombinant human PDGF-AB (rhPDGF-AB), when compared to untreated and rhPDGF-AB stimulation. Cellular migration was significantly impacted in 2D and 3D culture models when RB cells were treated with IM. Additional studies utilizing the neutralizing antibody increased the magnitude of the angiogenic reduction.

Conclusion: PDGF-PDGFR signaling sustain angiogenesis in an autocrine and paracrine fashion. The presence of PDGF in orthotopic xenograft RB models confirms this potential target in humans. These studies are a step in the pursuit of our goal to identify and develop targets of immunotherapy that will control the factors sustaining retinoblastoma tumour cells seeding the vitreous.

PD-144 | Anesthetic Management of Superselective Ophthalmic Arterial Chemotherapy for Retinoblastoma in Children

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Background/Objectives: Superselective ophthalmic artery chemotherapy (SOAC) with melphalan has significantly reduced the need for enucleation in patients with retinoblastoma. Aim: to describe our experience with SOAC in retinoblastoma and to report the serious adverse cardio-respiratory reactions we have observed.

Design/Methods: Between February 2011 and March 2015 in Pediatric Oncology and Haematology Institute 54 eyes in 45 patients were treated. 17 patients with unilateral retinoblastoma and 28 patients with bilateral retinoblastoma were included in the study. 104 cases of catheterization procedures were performed. All patients before procedure received heparin sulfate IV (30 IU/kg-1) and during procedure the same dose of heparin sulfate was administered via arterial micro-catheter.

Results: There were no deaths or major complications. Adverse cardio-respiratory reactions developed during 15 procedures (14%). All reactions occurred during second or subsequent procedures and were characterized by hypoxia, reduced lung compliance followed by a subsequent deterioration in the oxygen saturation (SpO₂) to 70%. Hypotension (BP 54/20 mmHg) and tachycardia (130-150 bpm) were also registered. The microcatheter was withdrawn and ventilation with 100% oxygen was initiated. Adverse events were successfully treated during 10-15 min in all patients by vasopressor support with Phenylephrine (0.05-1 mcg/kg/min) and atropine sulfatis administration. One procedure was interrupted due to prolonged hemodynamic instability. 5 patients required prolonged vasopressor support in early postoperative period. In 3 cases children had an acute ischemic stroke, which was confirmed by MRI.

Conclusion: Adverse cardio-respiratory reactions are commonly observed in SOAC for retinoblastoma. We believe that the adverse clinical signs represent an autonomic reflex response and all patients should be considered at-risk. Reactions occur only during second or subsequent procedures and can be life-threatening. Anesthesiologists must be vigilant for adverse reactions and deal with them quickly and effectively. However, further investigations are needed to improve the understanding of the manifestations, management, and clinical significance of the described oculopulmonary reflex.

PD-145 | Retinoblastoma Treatment: Comparative Results of the Italian RB05-Protocol and New Guidelines at the Italian Referral Center of Siena

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Background/Objectives: Retinoblastoma [RTB] is the most common primary intraocular malignancy of childhood (32 cases/year in Italy). Intra-arterial chemotherapy [IAC] has assumed a major role in its management. We report a comparison of the results of RTB treatment according to the Italian-RB05-Protocol (intravenous chemotherapy [IVC] as first-line conservative strategy) with the results of the new guidelines at our Institution (IAC as first-line conservative therapy except for bilateral or extra-macular low-grade disease). Primary outcomes are rate of globe salvage and long-lasting remission (6 months at least).

Design/Methods: January 2006-November 2008: 107 children (141 eyes) were recruited to the RB05-Protocol, 34 bilateral (31.7%), 73 unilateral (68.3%). September 2013-December

2015: 49 children (62 eyes) were recruited to our new guidelines, 13 bilateral (26.5%) and 36 unilateral (73.5%).

Results: RB05-Protocol results: Sixty-eight/141 eyes (48.3%) were treated with IVC; 60/141 eyes (42.5%) achieved long-lasting remission; 81/141 eyes (57.4%) were enucleated, 73 (51.7%) at diagnosis and 8 (5.6%) after IVC.

New guidelines results: Thirty-six/62 eyes (58%) were treated with IVC, 30 at diagnosis and 6 as second-line therapy. Thirty-four/62 eyes (54.8%) were treated with IAC, 25 at diagnosis and 9 for relapse after IVC. Forty-four/62 eyes (70.9%) achieved long-lasting remission; 17/62 eyes (27.4%) were enucleated, 9 (14.5%) at diagnosis and 8 (12.9%) after conservative strategies (2 IVC, 4 IAC, 2 IVC+IAC).

Conclusion: Long-lasting remission was achieved in 42.5% of eyes treated according to RB05-Protocol and in 70.9% of eyes treated according to our new guidelines. The introduction of IAC reduced the rate of enucleation, especially at diagnosis (14.5% vs 51.7%). The rate of enucleation for treatment failure is 12.9%, according to data published (28%-38% enucleations in 5-year experience by Shields et al. after primary/secondary IAC). An earlier diagnosis and the centralization to a National Referral Center could further increase the rate of globe salvage.

PD-146 | Prevalence of Histopathologic Risk Factors in a Large Prospective Trial of Children with Unilateral Retinoblastoma. A Children's Oncology Group (COG) Study

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Background/Objectives: To define and describe the prevalence of histopathologic risk factors in patients with unilateral retinoblastoma who undergo enucleation.

Design/Methods: All patients who underwent enucleation were eligible for the study. Pathology slides were submitted for central review within 21 days of enucleation. Patients with high-risk features (HRF): posterior uveal invasion grades IIC and D, concurrent optic nerve and choroid involvement and/or post-lamina optic nerve involvement (PLONI) as determined by central review, received 6 cycles of chemotherapy. All patients were followed for extraocular or metastatic recurrences.

Results: Among 312 of 331 patients with central histopathology review, 59 patients had their risk classification changed (17% with no HRF, 25% with HRF had no HRF). 211 did not have any risk factors. Forty-three (13.8%) patients had posterior uveal (choroid) involvement ≥ 3 mm, 33 (10.6%) had the combination of "any degree of concomitant choroid and optic nerve involvement," and 51 (16.3%) had PLONI. These were present in various combinations. Isolated choroidal invasion of ≥ 3 mm occurred in only 7 patients (2.2%) whereas 9.9% of patients had isolated (PLONI). Seventy-eight of 93 patients (84%) had either posterior uveal (choroid ≥ 3 mm), or PLONI, or a combination of both. Twenty-four patients had both choroid involvement ≥ 3 mm and PLONI. Fifteen patients (16%) had concomitant involvement of choroid (<3mm) and optic nerve (pre lamina or lamina) only. Of the 14 patients with anterior chamber seeding only 3 had isolated involvement. 4/5 with scleral invasion had other concomitant risk factors. Ciliary body infiltration (6) and iris infiltration (9) were not isolated findings.

Conclusion: This is the first prospective study with pathologic central review to give a detailed description of histopathologic features in unilateral enucleated eyes which can be used to design future studies.

SOFT TISSUE SARCOMAS

PD-147 | Quality-Of-Life after Childhood Rhabdomyosarcoma Treated with Pencil Beam Scanning Proton Therapy

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Background/Objectives: Radiotherapy can impair the Quality-of-Life (QoL) of children with cancer treated with this modality. Proton therapy (PT) could potentially mitigate this effect and consequentially the QoL of children with rhabdomyosarcoma (RMS) treated with Pencil Beam Scanning (PBS) PT was assessed at the Paul Scherrer Institute.

Design/Methods: QoL data were prospectively collected between January 2005 to December 2014 in RMS patients ($n=34$) aged 5 – 16 (median, 7) years treated with PBS PT. The PedQoL questionnaire is an established, multidimensional instrument that covers 8 domains and is available as proxy-rating version for the parents (PedQoL proxy) and self-rating version for children older than 4 years (PedQoL self). Cross-sectional QoL data from an independent normative group with proxy assessments of healthy children between 5 and 16 years of age provided the comparison data.

Results: All QoL scores of patients were significantly ($p<0.01$) lower when compared to the normative group (Fig.) at the start of PT (E1). Globally the mean QoL scores were 81.02 ± 17.34 and 54.17 ± 30.53 for the normative population and patients, respectively. Two years after PT

(E2), mean scores of patients in all but 3 domains were however either equal or superior to the normative population (Fig.). In two domains (i.e. self-esteem and social functioning family), the observed mean QoL E2 scores were higher in patients when compared to the normative population, although this difference was statistically not significant. The greatest increase of mean scores at (E1) and (E2) was observed for the subjective well-being (E1: 54.17±30.53 vs. E2: 83.33±19.50) and physical functioning (E1: 50.17±15.15 vs. E2: 66.33±7.93) domains.

Conclusion: The QoL was excellent in a majority of children with RMS 2 years after the start of PBS PT. Mean QoL scores of patients were not significantly impaired in all domains when compared to the normative population.

PD-148 | Prognostic Impact of Pathological Classification and Fusion Gene Status in Paediatric Rhabdomyosarcoma from the Japan Rhabdomyosarcoma Study Group (JRSG)

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Background/Objectives: Childhood rhabdomyosarcoma (RMS) is pathologically classified as embryonal (ERMS) and alveolar (ARMS) and the majority of ARMS have PAX3/PAX7-FOXO1 fusion gene. We evaluated prognostic impact of histology and PAX3/7-FOXO1 fusion status by Japan Rhabdomyosarcoma Study (JRSG) cases.

Design/Methods: Patients registered to JRSG study between 2004 and 2013 and whose pathological slides were submitted for central review were analyzed. The pathological slides were reviewed by at least two central pathologists, and tumors were classified according to International Classification of RMS (ICR classification) and immunohistochemistry for Desmin, Myogenin, MyoD1, HMG A2 and AP2 β was also performed. PAX3/7-FOXO1 status was analyzed by RT-PCR for tumors with frozen materials.

Results: Among 218 cases, 99 cases were embryonal histology and 109 cases were alveolar histology. Molecular testing was performed for 151 tumors, and 80 had embryonal histology and 71 had alveolar histology, including 6 mixed embryonal and alveolar tumour. PA3/7-FOXO1 fusions were identified in 77% of alveolar histology tumors. None of the embryonal histology tumour showed PAX3/7-FOXO1 fusion gene expression. Overall survival at 5 years for alveolar histology was significantly worse (58% for alveolar histology vs 75% for embryonal histology), while 5-year overall survival for fusion positive alveolar tumors was more inferior (39% for fusion positive alveolar histology, 82% for fusion negative alveolar histology versus 85% embryonal histology).

Conclusion: While pathological classification was a strong prognostic indicator for childhood rhabdomyosarcoma, fusion status is found to be stronger prognosticator. Fusion negative ARMS had comparable prognosis to ERMS and fusion gene status could be a defining factor for risk grouping of rhabdomyosarcoma in Japanese paediatric age.

PD-149 | Phase 1/2 Study of nab-Paclitaxel in Paediatric Patients with Recurrent/Refractory Solid Tumors: A Collaboration with Innovative Therapies for Children with Cancer (ITCC)

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Background/Objectives: Paclitaxel has demonstrated activity in adult cancers, albeit its use in paediatric patients is limited. nab-Paclitaxel, an ethanol-free albumin-bound paclitaxel, is efficacious in adult cancers. In preclinical models, nab-paclitaxel was effective against various

paediatric cancers, including neuroblastoma, rhabdomyosarcoma, and Ewing sarcoma. This study evaluated nab-paclitaxel in paediatric patients.

Design/Methods: In Phase 1, patients aged ≥ 6 months to <18 years with recurrent/refractory non-central nervous system tumors received nab-paclitaxel on days 1, 8, and 15 of a 28-day cycle (qw 3/4) at 120, 150, 180, 210, 240, or 270 mg/m² in a rolling-6 dose-escalation design.

Results: Sixty-four patients were enrolled (neuroblastoma [n=10], Ewing sarcoma [n=13], rhabdomyosarcoma [n=14], and other [n=27]). Median age was 12 years (range, 2-17); patients were heavily pretreated (prior therapeutic lines: median, 3; range, 1-10). Two dose-limiting toxicities occurred: grade 3 dizziness (120 mg/m²) and grade 4 neutropenia lasting >7 days (270 mg/m²). 270 mg/m² was deemed non-tolerable due to grade ≥ 3 toxicities in \leq cycle 2: neutropenia (n=5/7), skin toxicity (n=2/7), and peripheral neuropathy (n=1/7). 240 mg/m² was considered the recommended phase 2 dose (RP2D); 160% of the weekly dose tested in adults). Of 39 efficacy-evaluable patients, 6 (15%) patients had partial responses: 4 by RECIST (1 Ewing sarcoma, 1 rhabdomyosarcoma, 1 sarcoma [not otherwise specified], and 1 renal tumour), and 2 with neuroblastoma by ¹²³I-metaiodobenzylguanidine; 4 of the responders received nab-paclitaxel at 240 mg/m². Twelve (31%) patients had stable disease (3 lasting ≥ 16 weeks). nab-Paclitaxel pharmacokinetics were dose-proportional across age groups. Paclitaxel clearance and distribution volume increased with increased body surface area.

Conclusion: nab-Paclitaxel was safe and tolerable at doses ≤ 240 mg/m² qw 3/4. The RP2D, 240 mg/m² qw 3/4, demonstrated preliminary clinical activity. Phase 2 is currently accruing patients with recurrent/refractory neuroblastoma, rhabdomyosarcoma, and Ewing sarcoma to evaluate activity and safety at the RP2D.

PD-150 | Preliminary Results of a Phase II Prospective Trial of Proton Therapy for non-Metastatic Paediatric non-Rhabdomyosarcoma Soft Tissue and Bone Sarcoma

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Background/Objectives: This prospective phase II trial investigated rates of acute (AT) and late toxicity (LT), as well as overall (OS) and disease-free survival (DFS), and local (LC) in children with bone or non-rhabdomyosarcoma soft tissue sarcoma (NRSTS) treated with proton radiation therapy.

Design/Methods: Sixty-five paediatric patients with non-metastatic bone or NRSTS were enrolled between 06/2006-08/2015. The CTCv3.0 was used to assess and grade AT and LT. Forty-one (63%) patients had LT data with at least 2 years of follow up. Log-rank testing was performed on Kaplan-Meier curves.

Results: Median age at radiation was 12.3 (1.1-22.1) years; median follow-up was 3.9 years. Histologies included: 34(52%) Ewings, 23(35%) NRSTS, 8 (12%) osteosarcomas or other bone sarcomas. Tumour sites included head and neck (28), spinal/paraspinal (16), pelvic (14), thorax (4) and other (3). Median dose was 55.8 GyRBE (39.6-72) using passively-scattered protons. Surgical resection was total, subtotal, or biopsy only in 10 (15%), 16 (25%), and 27 (42%). 4-year OS, DFS, LC were 81%, 74%, 85%, respectively. There was a non-significant improvement in OS (HR=0.41, 95% CI=0.11-1.5, p=0.17) in the Ewings versus NRSTS cohort. Four-year OS, DFS, LC by histology were 89%, 82%, 89% for Ewings, 69%, 57%, 81% for NRSTS, and 85%, 85%, 85% for osteosarcoma/other. Three second malignancies were diagnosed at a mean of 2.6 years: AML, MDS, and an in-field pleomorphic sarcoma. There were 12 patients with Grade 3/4 non-hematologic AT, and 8 patients with grade 3 LT.

Conclusion: Prospective 4-year OS, DFS, and LC rates after proton multi-modality therapy for localized Ewings, osteosarcoma and NRSTS are reported and consistent with rates of control in photon treated cohorts. Proton radiation appears to represent a safe and effective treatment modality with acceptable acute and late toxicity profiles.

PD-151 | The Impact of Sentinel Lymph Node Evaluation in Paediatric, Adolescent and Young Adult Head and Neck Rhabdomyosarcoma

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Background/Objectives: Regional lymph node disease (N1) has been shown to be an independent prognostic factor in patients with alveolar rhabdomyosarcoma (RMS), and size and PET avidity have been explored as determinants of clinically significant lymph node disease. Here we demonstrate that sentinel lymph node (SLN) evaluation has the potential to reveal unrecognized sites of lymph node metastasis in paediatric and adolescent/young adult (AYA) head and neck RMS patients. Furthermore, we demonstrate the unique spectrum of head and neck lymph drainage and highlight the relevance in systemic and locoregional RMS therapy.

Design/Methods: Seven paediatric and AYA patients (6 mo - 21 yrs) with head and neck RMS prospectively underwent SLN biopsy. After peri-tumoral injection of 125 μ Ci of Tc99m sulfur microcolloid, lymphoscintigraphy and SPECT-CT was used to facilitate anatomic localization of SLNs. Additionally, intraoperative lymphazurin 1% dye was used to aid in SLN identification.

Results: One embryonal, 1 spindle cell, 1 anaplastic, and 4 fusion positive RMS patients underwent successful SLN biopsy without complications. Sites of primary disease included nasal cavity (2), buccal (2), masticator space (1), palate (1), and ethmoid sinus (1). Two to 4 lymph nodes were excised per patient. Lymphoscintigraphy and/or lymphazurin revealed 1 SLN site in 6 patients and 2 SLN sites in 1 patient. Unique SLN locations were identified in 2 patients (contralateral cervical chain). Pathologic evaluation confirmed N1 disease in 4 of 7 patients.

Three patients with positive SLN disease would not have been considered N1 by standard imaging (all nodes less than 1 cm and max SUV below 1.9) and underwent a change in systemic (1 patient) or locoregional (2 patients) therapy as a result.

Conclusion: SLN evaluation in head and neck RMS is safe, identifies nodal metastases not recognized by conventional imaging, and should be considered in head and neck RMS staging evaluations.

PD-152 | The Role of the Mature Lymphocyte Subpopulations of Bone Marrow in Children Sarcomas

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Background/Objectives: The purpose of this study was to analyze clinically significant specificity of composition of mature lymphocyte subsets in bone marrow from children with rhabdomyosarcoma (RMS) and Ewing sarcoma family of tumors (ESFT).

Design/Methods: A total of 49 children aged 1 to 17 years were enrolled in this study. The diagnosis of RMS or ESFT was verified morphologically or immunohistochemically in 34 cases. Malignancy was excluded basing on complex assessment in 15 cases (comparator group). All patients underwent cytological and immunological study of bone marrow.

Results: Immunological studies lymphocyte subpopulation composition of mature bone marrow in children with RMS and ESFT identified a number of characteristics that are different from the composition of bone marrow lymphocytes of children without cancer. We have found that changes were in the innate immune cells: NK-cells, monocytes / macrophages and T-cytotoxic lymphocytes. Differences between levels of these cells in children with RMS from bone marrow lymphocytes ESFT consisted in the predominance TCR $\gamma\delta$ -lymphocytes. When comparing the level of lymphocyte subpopulations studied with adverse prognostic factors at RMS and ESFT. Level of TCR $\gamma\delta$ -lymphocyte in patients with localized stages of the disease in RMS is more than in patients with distant metastases. We have noted the decrease in the level of cytotoxic T-cells with an increase in tumour volume of more than 100 cm³ or length of long bone lesions more than 8 cm in patients at ESFT.

Conclusion: Our study revealed differences subpopulation composition of lymphoid cells in children with RMS and ESFT on the performance in the group of children with no signs of cancer. Subpopulations of lymphocytes in the bone marrow children with RMS and ESFT correlated with prognostic factors.

PD-153 | Germline Mutations in a Population-Based Series of Childhood Rhabdomyosarcoma Cases

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Background/Objectives: Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma in children. Germline mutations in at least 22 genes have been shown to predispose individuals to RMS. Determining a genetic cause of RMS provides information for the parents regarding future reproductive risks, and provides the option of predictive testing in at-risk family members and may direct treatment decisions. We assessed the frequency of variants in 22 genes known to increase risk of childhood RMS in a population-based case series.

Design/Methods: Parallel sequencing of 22 genes known to predispose to childhood RMS was carried out on 64 consecutively ascertained cases from the Manchester Children's Tumour Registry (MCTR), a biobank containing patient samples, phenotype and familial information. DNA was extracted from blood and saliva samples and enriched for the 22 genes associated with RMS using a custom designed Agilent SureSelect capture. Paired-end sequencing was carried out on an Illumina HiSeq 2000. Rare or novel variants were identified by screening against publically available and in-house variant databases. *In silico* predictions were undertaken and variants classified 'clearly' or 'likely to be' pathogenic were confirmed by Sanger sequencing.

Results: 93 rare or novel variants were identified. Following further analysis these were grouped into 5 classes according to likely pathogenicity. 7 variants (from 6 individuals) were classified as clearly pathogenic or likely to be pathogenic. All were identified in genes of the RAS/MAPK pathway -*HRAS*, *SOS1* and *NF1* (five variants). Of these two were predicted frame shifts, one an in-frame deletion and four were missense variants. In 58 cases a 'clearly' or 'likely to be' pathogenic variant was not identified, although sixteen variants of unknown significance were found.

Conclusion: Our results detecting pathogenic variants in 9.4% of cases and putative variants in an additional 25% suggests that further genes associated with RMS remain to be discovered.

SUPPORTIVE CARE/PALLIATIVE CARE

PD-154 | The Risk of Infection-Related Death in Hispanic Paediatric Cancer Patients

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Background/Objectives: Despite recent improvements in childhood cancer outcomes, Hispanic children continue to experience inferior cancer survival rates. A variety of socioeconomic, genetic and biologic factors have been proposed as potential contributors to this disparity. Infection is a known cause of cancer-related mortality; however, little is known about the risk of infection-related death among Hispanic children with cancer. This study explores the impact of Hispanic ethnicity on infection-related mortality.

Design/Methods: We identified 6,198 paediatric cancer patients, diagnosed from 1986-2012, from the Intermountain Healthcare Cancer Registry. Ethnicity was assigned based on Hispanic surname and Utah Population Database records. Death records and causes of death were queried from the Center for Disease Control's National Death Index (NDI). Chi-square analyses and *t*-tests examined demographic variables. Cox proportional hazard models assessed all-cause mortality and infection-related mortality by Hispanic vs. non-Hispanic ethnicity. Intensive Care Unit (ICU) admission rates were modeled using zero-inflated Poisson regression models. Models were adjusted for gender, diagnosis year, age and diagnosis.

Results: Of 6,198 patients, 741 (12%) were Hispanic. Average follow-up time was 9.1 (SD=7.3) years for Hispanics and 11.2 (SD=8.1) years for non-Hispanics. Compared to non-Hispanic patients, Hispanics were younger ($p=0.008$), diagnosed more recently ($p < 0.001$), more urban ($p < 0.001$), and more likely to have leukaemia ($p < 0.001$). NDI matches confirmed death for 1,205 patients (19.4%). Differences in all-cause mortality between Hispanic and non-Hispanic patients did not reach significance (hazard ratio (HR)=1.14, 95% confidence interval (CI): 0.96-1.36). However, Hispanic patients were 67% (HR=1.67, 95% CI: 1.15-2.43) more likely to have an infection-related cause of death. Additionally, Hispanic ethnicity was the only statistically significant predictor of higher rates of ICU admissions (RR 1.32, 95% CI: 1.12-1.56).

Conclusion: Hispanic paediatric cancer patients were more likely to have an infection-related death than non-Hispanics. Infection may be an overlooked contributor to poorer outcomes among Hispanics.

PD-155 | Age, Type of Cancer and Use of Asparaginase are Independently Associated with Requirement of Tissue Plasminogen Activator for Episodes of Central Venous Catheter Dysfunction

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Background/Objectives: Dysfunction (defined as inability to flush and/or draw blood) is a commonly observed central venous catheter (CVC) associated complication. Often, tissue plasminogen activator (tPA) is instilled to reverse episodes of CVC dysfunction. However data on risk factors associated with requirement of use of tPA for CVC dysfunction is unclear. We hypothesized that clinic-demographic and treatment related variables are associated with requirement of use of ≥ 1 dose of tPA for 1 or more episodes of CVC dysfunction in paediatric oncology patients.

Design/Methods: In this population based study, case records of all paediatric oncology patients from the Maritime Provinces managed by the IWK Health Center from January 2000 to December 2015 were reviewed after ethics approval. Clinic-demographic and treatment data were pooled from: (i) paediatric oncology hospital database, (ii) Electronic medical records, (iii) Pharmacy database and (iv) IWK central line database. Patients with ≥ 1 episodes of CVC dysfunction requiring ≥ 1 dose of tPA were identified. Analysis was done using SPSS version 22.

Results: One or more CVCs were required in 741 patients. One or more doses of tPA (mean: 2.3 \pm 2.0) were required by 26% (n=195) of the patients for episodes of CVC dysfunction. On univariate analysis, age>10 years ($p=0.016$), diagnosis (classified as leukaemia, lymphoma, sarcoma, brain tumour and others) ($p=0.001$), and use of asparaginase ($p=0.005$) were significantly associated with use of tPA while gender ($p=0.079$) and blood type ($p=0.376$) were not. On multivariate analysis, age>10 years [$p=0.011$, OR: 1.57 (95% confidence interval) (CI): 1.1-2.2], diagnosis of sarcoma [$p=0.001$, OR: 3.3 (95% CI:2-5.6)] and use of asparaginase [$p=0.001$, OR: 2.1 (95% CI:1.4-3)] were independently associated with a requirement for tPA.

Conclusion: The present study identified independent risk factors associated for use of tPA for CVC dysfunction. After validation, further interventional studies should be considered for high-risk patients to prevent or mitigate CVC dysfunction.

PD-156 | Evaluation of Reading Level and Children's Ability to Complete the Paediatric Patient-Reported Outcome Common Terminology Criteria for Adverse Events (Paediatric PRO-CTCAE)

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Background/Objectives: Traditionally, healthcare staff complete the mandated adverse event (AE) reporting for children enrolled on oncology clinical trials. A new instrument, the Pediatric Patient-Reported Outcome Common Terminology Criteria for Adverse Events (Pediatric

PRO-CTCAE), is in development which will allow children to self-report symptomatic AEs to their providers to inform AE reporting and care. The study purpose was to conduct literacy assessments in conjunction with cognitive interviews in children 7 to 15 years of age to evaluate the child's understanding of the questionnaire in relationship to reading levels.

Design/Methods: At seven sites, children on treatment were invited to complete a written survey regarding specific AEs experienced within the past 7 days. A cognitive interview session then probed understanding of the Pediatric PRO-CTCAE survey content. Lastly, a Wide Range Achievement Test (WRAT) was administered to score individual reading levels.

Results: There were 97 children (53 females, 44 males) who participated in the cognitive interviews and WRAT assessments. Literacy levels ranged from below kindergarten to college level. Cognitive testing revealed good understanding of the Pediatric PRO-CTCAE items in children with a wide range of reading levels. Reading levels by age: 7 years (n=11), ranged from below Kindergarten to 3.7 grade level (median 1.7); 8 years (n=17), ranged 1.2-12.2 grade level (median 5.4); 9 years (n=7), ranged 2.2 - 7.4 (median 4.4); 10-15 years (n=62), ranged 2.3 - college level (median 7.1). Children below a second grade reading level (63% of 7 year olds) commonly required assistance with the questionnaire. Children (ages 9-20) were generally able to independently complete the written questionnaire.

Conclusion: Age is frequently used as an indicator for when children should begin self-reporting. Our findings indicate that age may not accurately predict reading ability. Audio versions of the instrument may be beneficial for those with lower reading levels.

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PD-157 | A Prospective Study of Serum Asparaginase Activity of an Innovator and Six Generic L-Asparaginase Preparations in Children with all in India and its Global Implications

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Background/Objectives: There are more than ten generic L-asparaginase preparations available in India and more than 15 across the globe which are mostly exported from India. Many of generics have same source of active pharmaceutical ingredients and have not undergone rigorous clinical studies. Also, many generic manufacturers do not have the expertise as well access to clinical research infrastructure. Prospective testing of their activity and feedback to manufacturers may confirm and/or improve quality of generics used for children all over the world.

Design/Methods: One innovator E. Coli asparaginase (Leunase, Kyowa Hakko Kirin Co. Ltd., Japan) and six generics (G1-G6) were tested for their quality through measurement of trough asparaginase activity in 72 hours after first intramuscular dose of 10,000unit/m² in children with newly diagnosed acute lymphoblastic leukaemia during induction phase. Asparaginase activity was tested using a validated microplate reader-based method colorimetric assay. All manufacturers were given feedback about results and requested for quality improvement and repeat activity testing of new batch if required.

Results: A total of 92 children underwent prospective testing of activity for 7 preparations. The median serum asparaginase activity of innovator was 475 IU/L. However, the median activity was subtherapeutic (< 100 IU/L) for all generics and varied significantly (32-73 IU/L). Repeat post-feedback testing of fresh batch of G1 in 17 children showed significant improvement with median activity value of 175 IU/L (range 30-2140 IU/L). Overall, 27%(3/11) of innovator and 79%(65/81) of generic treated children did not achieve therapeutic levels.

Conclusion: The asparaginase activity of generic preparations was suboptimal in majority of children. However, quality of some preparations improved after feedback given to the manufacturers. This confirms that generic asparaginase should be tested for quality which may help improve and ensure generic drug quality across the globe.

PD-158 | Serum Angiopoetin Levels are Early Predictors of Mortality in Patients with Febrile Neutropenia

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Background/Objectives: Endothelial barrier breakdown is a hallmark of septic shock, and proteins that physiologically regulate endothelial barrier integrity are emerging as promising biomarkers of septic shock development. Patients with cancer and febrile neutropenia (FN) present a higher risk of sepsis complications, such as septic shock. Nonetheless, these patients are normally excluded or under-represented in sepsis biomarker studies. The aim of our study was to validate the measurement of a panel of microvascular permeability modulators as biomarkers of septic shock development in cancer patients with chemotherapy-associated FN.

Design/Methods: We prospectively evaluated concentrations of Ang-1 and Ang-2 at different time-points (at the beginning of fever and at the 48th hour) during febrile neutropenia, and explored the diagnostic accuracy of these mediators as potential predictors of poor outcome in this clinical setting before the development of sepsis complications such as mortality.

Results: A total of 62 consecutive patients were evaluated in the study in 94 febrile neutropenia episodes. Mortality was seen in 12 FN episodes. Ang-2 concentrations were increased in patients with septic shock both at the beginning of FN and at the 48th hours, whereas an inverse finding was observed for Ang-1, resulting in a higher Ang-2/Ang-1 ratio in patients with septic shock. There were no correlation between C-reactive protein and procalcitonin levels with mortality. After multivariate analysis, the Ang-1, Ang-2 and Ang-2/Ang-1 ratio remained an independent factor for septic shock development and 28-day mortality both at the beginning of fever and 48th hours after fever.

Conclusion: Our data suggest that imbalances in the concentrations of Ang-1 and Ang-2 are independent and early markers of the risk of developing septic shock and of sepsis mortality in febrile neutropenia, and larger studies are warranted to validate their clinical usefulness. Ther-

apeutic strategies that manipulate this Ang-2/Ang-1 imbalance can potentially offer new and promising treatments for sepsis in febrile neutropenia.

ACUTE LYMPHOBLASTIC LEUKAEMIA

P-0001 | Risk Factors Predicting Outcome in Febrile Neutropenia Patients

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Background/Objectives: To analyze the relationship of clinical and laboratory parameters at presentation in febrile neutropenia patients with their ultimate outcome.

Design/Methods: All patients with FN admitted in Haematology/oncology department from 1st September 2015 to 31st 2016 March were enrolled in study. Patients evaluated by complete history, detailed examination and risk stratification done. Laboratory parameters recorded. All these patients were followed for clinical and repeat lab parameters while stay in hospital till their discharge/death.

Descriptive study and spssv16 used in data analysis

Results: Total 95 FN patients enrolled in the study. Most of patients were less than 5 years of age 45% (n43). Males were predominant 68.4% (n65).

ALL was the most common haematological malignancy with FN 80% followed by NHL 11%, Wilms tumour 3.2% and neuroblastoma in 1.8%. High risk disease seen in 67.4% of patients.

Last chemo was given one day ago in 26%, 2 days ago in 16.8%, 4 days before in 14%. Pneumonia was the most common cause of FN identified in 26.3%, 23% URTI, 9.5% had cellulitis. Patient received antibiotics before coming to hospital were 35%. Duration of fever was 24hours before presentation in 46%.

ANC less than 100 was seen in 44%, 101-300 in 21%. Cultures found positive only in 10%. TLC <1.00 in 60%.

Patients discharged were 80%, died 20%. Patients with intravenous access within 30mins of evaluation were discharged more 91%.

Patients with ANC <100 (41) have maximum duration of stay, 15 to 25 days in 6 patients and more than one month in 7.

Most of patients discharged have ANC >300 n30 and TLC count >1.00 in 89%. Those who died have ANC <100 (n12) and TLC <0.6 (14).

Conclusion: There was a significant relation of ANC and TLC with duration of stay and ultimate outcome with p-value of 0.097 and 0.004 respectively. CRP is also related to outcome with p-value of 0.070.

ALL was the most common malignancy and those with High risk disease confers adverse outcome.

P-0002 | Spectrum and Outcome of Paediatric Oncology Patients Admitted in Paediatric Intensive Care Unit of a Resource Limited Country

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Background/Objectives: Every fourth paediatric oncology patient may need admission to paediatric intensive care unit (PICU) due to their disease or treatment related complications. Prompt recognition and management of critically ill oncology patients has added to improved overall survival of this group of patients.

We looked at the frequency, spectrum and outcome of oncology patients admitted to our PICU.

Design/Methods: Retrospective review of medical records of all children (1 month to 16 years) admitted to PICU of our hospital from January 2014 to December 2015 with underlying oncological diagnosis was done. Data was collected on a structured proforma including age, gender, primary diagnosis, reason/indications for PICU admission, treatment/ PICU therapies received, duration of stay and outcome. Descriptive statistics are applied.

Results: Of total 678 admissions in PICU, 59(8.70%) were admitted with underlying oncology diagnosis. Males were 43(72.88%). Mean age was 8.01(SD 4.57) years with 18(30.50%) less than 5 years old. 29(49.15%) were diagnosed during PICU admission (new patients) and 30(50.84%) were already diagnosed oncology patients (old patients). Reasons for admission included tumour lysis syndrome in 25% patients, post operative care in 35%, shock in 12%, respiratory failure in 12% and neurological problems in 12%. Underlying diagnosis included ALL in 34%, AML in 8%, lymphoma in 4%, CNS tumour in 28% and solid tumour in 22%. Mean ICU stay was 3.50(SD 2.45) days. 32(54.23%) required mechanical ventilation. Mortality was 16.94% as compared to overall mortality of 12.97% in PICU during same period.

Conclusion: Postoperative patients and tumour lysis syndrome were main reasons for PICU admission in paediatric oncology patients. Mortality is higher in oncology patients as compared to non-oncology patients in PICU.

P-0003 | Paediatric Malignancy in Sudan: Seven Years Experience in a Large Center

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Background/Objectives: It is estimated that more than 70% of paediatric patient with malignancy in low income countries die before reaching Hospital. Radio Isotope Center in Khartoum (RICK) is the larger of two national centers treating paediatric oncology patients in

Sudan. It provides treatment for more than 75% of paediatric oncology patients in the whole country.

Design/Methods: The aim of this paper is to reflect our experience in 7 years and the challenges we face in a limited resource country. The charts and the medical records data were accessed. All patients who attended the center between April 2004 and December 2011 were reviewed and analyzed.

Results: A total of 1,729 patients was registered in the medical records department computer system. However, 543 charts were either lost or incomplete. Data from the computer system and from the 1186 complete records were analyzed for age, sex and diagnosis. Male patient accounted for 1090 and female patients were 639 with male/female ratio of 1.7. The age range was from 28 days old to 15 years with a mean of 7.1 years. The commonest malignancy was acute lymphoblastic leukaemia 408 (23.6), followed by non Hodgkins lymphoma 276 (16%), acute myeloid leukaemia 185 (10.7), Hodgkins lymphoma 156(9%), Wilms tumour 136(7.8%), retinoblastoma 102 (5.9%), neuroblastoma 66 (3.8%), chronic myeloid leukaemia 51 (2.95), osteosarcoma 30 (1.74). Only the complete records were analyzed to assess the outcome. Five hundred and twenty five patients (44.3%) abandoned treatment, 469 (39.5) were alive, 165 died (13.9%).

Conclusion: Major changes have been introduced to improve the medical records system in the center. Although chemotherapy and basic investigations are available free of charge, there is a high incidence of abandonment. Social and other economic factors should be evaluated.

P-0004 | Association of Prognostic Parameters with Cytogenetic and Molecular Markers at Presentation in Indian Children with High Risk Acute Lymphoblastic Leukemia

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Background/Objectives: Introduction: Acute Lymphoblastic Leukaemia(ALL) is the commonest leukaemia in children. Despite improved treatment regimens and targeted treatment, the mortality and relapse rate are still high in India.

Objective: To determine the association of clinical and hematological prognostic parameters as assessed with treatment response with cytogenetic and molecular markers.

Design/Methods: The association of 18 Indian children with acute lymphoblastic leukaemia with hyper-leukocytosis (total leucocyte count >1,00,000 cells/cmm) was studied with cytogenetic and molecular markers in this observational case series. Chromosomal analysis, Fluorescence in situ hybridization and RT-PCR were done on these patients for known recurrent translocation associated with ALL. IKZF-1 deletions were detected by multiplex ligand probe amplification assay (MLPA) method (IKZF1 P-335, MRC-Holland, Amsterdam, NL) was used to detect IKZF1 deletion and validated with IKZF1 P-202, MRC-Holland, Amsterdam, NL, according to the manufacturer's instructions.

Results: We received eighteen patients of ALL with hyperleukocytosis during the period from Jun 2014 to Oct 2015 at paediatric oncology clinic and Dr BRAIRCH paediatric oncology clinic, AIIMS. Two third (12) of them were B-ALL. Cytogenetic data was available in 14 patients. 41% (5) of patients with B-ALL were BCR-ABL positive. Only five of fourteen patients presented with normal cytogenetics. IKZF-1 deletions were seen in three patients and all were seen in patients with BCR-ABL translocation. Complete gene deletion (exon 2-7) was seen in one patient while del of exon 5-8 and single exon deletions were seen. Eight patients out of eighteen patient with hyperleukocytosis died early due to disease progression. Two out of three patients with IKZF-1 deletions died early during the course of disease.

Conclusion: IKZF-1 deletions are more prevalent in BCR-ABL positive acute lymphoblastic leukaemia as has been noted in previous literature. For establishing the association of IKZF-1 gene deletions with poor prognostic outcome larger sample size will be required.

P-0005 | Non-Catheter Thromboembolic Events in Children with Acute Lymphoblastic Leukemia

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Background/Objectives: Thromboembolic events are serious complications of childhood acute lymphoblastic leukaemia (ALL) therapy, that may result in significant morbidity and occasionally mortality. In these studies, the relationship between thromboembolic events and treatment with steroids and L-asparaginase were reported. The aim of this study is the evaluation of the prothrombotic risk factors in children with ALL under modified BFM protocol.

Design/Methods: Three hundred and seventy children with newly diagnosed ALL were recruited in observational cohort study conducted between 2004 to 2015. Patients with ALL were searched for any accompanying prothrombotic risk factors. All symptomatic thromboembolic events diagnosed were recorded.

Results: Fifteen patients of the overall 380 (3.9%) had thrombosis, of them 80% had venous thrombosis, and 20% had arterial thrombosis. Deep venous thrombosis of the lower extremity was present in six cases. Other nine patients had cerebral thrombosis (three arterial and six venous). All the cerebral thrombosis had developed at the induction phase of the therapy. Prothrombotic risk factors were detected in 8 (53.3%) patients (3 had protein S, 2 had protein C, 3 had homozygous, 1 had heterozygous Factor V Leiden deficiency. One patient had prothrombin 20210A mutation). One of the patients with arterial cerebral thrombosis had died. The rate of death due to thrombosis in children with ALL was found as 0.26%.

Conclusion: Thrombosis in children with ALL is an important complication with high morbidity and mortality. Patients with the prothrombotic risk factors should be followed-up carefully for the possible emergence of cerebral thrombosis and strategies of antithrombotic prophylaxis should be investigated in this setting.

P-0006 | A Portfolio of Phcosocial Interventions for Adolescents and Young Adults with Cancer

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Background/Objectives: Adolescents and young adults (AYAs) with cancer require interventions to increase resilience. The purpose of this study was to improve resilience of the AYAs by portfolio. Hasse's Adolescent Resilience Model was applied as theoretical framework.

Design/Methods: Yin's descriptive case study was used. The data were analyzed using pattern-matching logic. This study was approved by the institutional review board. The physicians identified potential participants from their appointment list. A total of 22 aged 10 to 21 years was outpatient ranged from about 1 month to 7 year. Of these, 19 were newly diagnosed and 3 had experienced relapses. Portfolio was involved by 2 times. The session 1 (T1) was applied at the first visiting time. The purpose was to find the good point and create hope. The session 2 (T2) at the second one was to set and act a goal of the hope. Then, making the effort was asked. Portfolio, Semi-Structured Interview guide, Childhood Trait Resilience Scale (TRS), and Social Network Map were used. The tools were performed face-to-face by an author in a private room and lasted about 60 to 90 minutes in each session.

Results: The meaningful components of the interview, SNM, and Portfolio were identified and transformed into the factors (I am, I have, I can, and I will/do) of TRS (TRS^a). The 3 levels as up, parallel, and down from T1to T2 were found in them. TRS was compared with TRS^a. TRS^a in total and each of levels was more increase than that of TRS.

Conclusion: Portfolio may be used to improve resilience for the AYAs with cancer by built and fulfill a future goal. The authors would like to thank the AYAs for appreciation. This study was founded by KAKENHI.

P-0007 | Thiopurine Methyltransferase Genotyping in Jordanian Paediatric Patients with ALL

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Background/Objectives: 6-mercaptopurine (6-MP) is one of the most widely used medications for childhood ALL. Thiopurine Methyltransferase (TPMT) catalyses the S-methylation of thiopurine drugs including 6MP, 6TG and Azathioprine. TPMT activity exhibits genetic polymorphism with about 1/300 inheriting TPMT deficiency as an autosomal recessive trait.

Ethnic variation in TPMT activity has been described in the literature. To date, eighteen TPMT alleles have been identified, including four common alleles (TPMT*2, TPMT*3A, TPMT*3B and TPMT*3C) which account for 80–95% of intermediate or low enzyme activity cases.

Purpose: To determine the TPMT allele frequency in Jordanian Pediatric patients with ALL, and to correlate the polymorphic variants with 6-MP tolerance.

Design/Methods: Total of 103 blood samples were collected from paediatric patients diagnosed with ALL between 2000-2007. Age between 1 and 18 years, 57 males and 46 females. Samples were assayed at Erasmus MC Rotterdam, Netherlands by Abdulhadi Alzaben MD. TPMT genotyping was done by two different methods: Restriction Fragment Length Polymorphism (RFLP-PCR) and Real Time PCR (Taqman).

Results: The results revealed that allelic frequencies were 0.97% for TPMT*2 (1 patient), 0.97% for TPMT*3C (1 patient), 0.00% for TPMT*3A and 0.00% for TPMT*3B.

Conclusion: Only two of our patients had heterozygous mutation for TPMT activity. Those two patients did not experience excessive 6-MP toxicity. We do not recommend TPMT genotyping routinely before starting thiopurine drugs for Jordanian children with ALL.

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P-0008 | Hyperdiploidy and Treatment Outcome in Paediatric Acute Lymphoblastic Leukemia – Studying the Relationship in 376 Cases

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Background/Objectives: DNA index is recognized as a strongest predictor of the treatment outcome in paediatric Acute Lymphoblastic Leukaemia (ALL).

Design/Methods: Medical records review of (376) ALL patients (age at diagnosis 1-≤14years), between 2005-2014, with reference to their clinical characteristics and treatment outcome.

Results: 108 (28.7%) patients had hyperdiploid (>1.16) DNA index with median age at diagnosis 48.8 months (min:16.4-max:169.1) vs 53.98 months (min:12.3 - max:179.6) for hypodiploids. 7(6.5%) were ≥ 10 years in hyperdiploids vs 36(13.4%) in the other group (p=0.072). 72(66.7%) were boys in hyperdiploids in contrast to 144(53.7%) in others (p=0.028). Median WBC (10⁹) in hyperdiploids was 6.68 (min:1.05-max:101.87) vs. 11.9(min:0.68-max: 521) in others, with 9(8.3%) had count above 50K in hyperdiploids as compare to 54(20.1%) in hypodiploids (p=0.006). Day14 Bone Marrow were M1 in 96 (93.2%), 6(5.8%) M-2 and 1(1%) M-3 in hperdiploid vs 245(93.5%) M-1, 10(3.8%) M-2 and 7(2.7%) M-3 in other group (p=0.458). 92(86%) were CNS-1, 14(13.1%) CNS-2 and 1(9%) CNS-3 among hyperdiploids vs 223(83.2%) CNS-1, 40(14.9%) CNS-2 and 5(1.9%) CNS-3 in hypodiploids (p=0.798). Amongst hyperdiploids, all were B-cell vs 251(93.7%) B-cell and 17 (6.3%) biphenotype in hypodiploids (p=0.004). In hyperdiploids, 4(4.7%) MLL+ vs 5(2.2%) in others (p=0.261), 7(9.2%) for BCR/ABL vs 12(6.1%) in others (p=0.427) and 14(18.4%) for Tel/AML1 vs 79(41.8%) in others (p<0.001). Trisomies 4, 10 or 17 were positive in 40(95.2%) in hyperdiploids vs 13(14.9%) in hypodiploids (p<0.001). Relapse rate in hyperdiploid group was 11.1% (n=12) vs 15.3%(n=41) in hypodiploids (p=0.329), and 4(3.7%) deaths vs 22(8.2%) respectively. With a median follow-up of 64 months, five year Overall Survival (OS) was 0.952±0.024 vs 0.902±0.021 (p=0.116) and Event Free Survival (EFS) was 0.858±0.039 vs 0.808±0.028 (p=0.226) for hyper- and hypodiploid groups respectively.

Conclusion: Patients with hyperdiploid associated with younger age, male gender, lower WBCs count, no biphenotypic and lower rate of presence *Tel/AML1+*.

P-0009 | Hypoalbuminemia: A Surrogate Marker for Malnutrition and Adverse Outcome in Children with Acute Lymphoblastic Leukemia

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Background/Objectives: To assess the prevalence of malnutrition and malnutrition associated mortality in children with acute lymphoblastic leukaemia.

Design/Methods: A retrospective analysis of 577 patients with Acute lymphoblastic leukaemia aged between birth to 20 years attending the paediatric hemato-oncology unit at KGMU, Lucknow during 1995-2012. The measures used for the assessment of malnutrition were Weight for height, Height for age, BMI Z-scores and Serum Albumin. Multivariate analysis was conducted for the factors of univariate significance.

Results: Wasting was present in 37.8% and stunting was found in 40.6% of children. Hypoalbuminemia was present in 40.1%. Serum albumin was significantly lower in wasted ($p=0.0007$) and stunted children ($p=0.004$) than normal children. Malnutrition was found to be statistically correlated with socioeconomic status (SES). Wasting ($p=0.03$), stunting ($p=0.02$) and low serum albumin ($p=0.002$) were significantly higher in lower SES. Mortality was higher in wasted ($p=0.00$), stunted ($p=0.0006$) & hypoalbuminemic children ($p=0.000$) with statistically linear trend between graded albumin levels & poor outcome ($p=0.000$). The proportion of malnutrition and hypoalbuminemia was higher in children succumbing during induction against the survivors ($p=0.01, p=0.006$). Infection rates were higher in the wasted ($p=0.007$) and stunted children ($p=0.05$) than well nourished children. Hypoalbuminemic patients had 1.7 times higher chances of sepsis ($p=0.01$). The wasted (85% vs 75%) ($p=0.04$) and stunted ($p=0.03$) population also had poor chances of day 28 marrow remission. Significantly higher number of patients who relapsed were wasted and had low serum albumin levels as compared to those who did not relapse ($p=0.01, 0.009$ respectively). Chances of abandoning the treatment was higher in wasted children (44.8% vs 34.3%, $p=0.03$).

Conclusion: There was heavy toll of mortality at our centre and malnutrition contributed to significant morbidity and mortality in our children. Malnutrition and low serum albumin levels were found to be associated with higher incidence of sepsis, mortality, induction failure and relapse. Hence, a low serum albumin level can be used as a surrogate marker of malnutrition and poor outcome in children with ALL.

P-0010 | Osteonecrosis in Children with Acute Lymphoblastic Leukemia: A Report from Children's Cancer Hospital in Egypt (CCHE)

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Background/Objectives: As survival rates for children with acute lymphoblastic leukaemia (ALL) improve, awareness of treatment complications becomes increasingly important. Osteonecrosis (ON) is a serious disabling complication of ALL treatment occurring in 15% to 38% of the patients. The aim of the study was to define the frequency of ON identified by Magnetic Resonance Imaging (MRI) and to study the risk factors for ON.

Design/Methods: Frequency of ON was evaluated retrospectively in 861 patients with ALL, diagnosed at CCHE from January 2009 to December 2012 and followed till December 2015. Patients were treated with St Jude ALL Total Study XV, which constitutes dexamethasone-based maintenance therapy. ON was identified by MRI done during or after treatment.

Results: Out of 861 patients evaluated, 665 were eligible for the study, 65 patients (9.7%) developed ON. The cumulative 5-year incidence of ON was 11.96% (SE, 0.131%). The mean time to develop ON was 21 months from diagnosis. Out of 155 patients aged 10 years and above, 40 patients (25.8%) developed ON. The mean age for patients with ON was 10.7 years. The prognostic factors with significant relationship to ON by univariate analysis were age 10 years and above ($P=0.0001$) and Standard/High risk group ($P=0.0001$). However, gender was not statistically significant.

At the onset of ON, the mean cumulative dexamethasone dose was 796 mg/m² and the mean total corticosteroids dose, calculated as prednisolone equivalence, was 6,431 mg/m². Out of 43 patients who developed ON while still on corticosteroids therapy, 36 patients (84%) required dexamethasone dose modification and/or stopping.

The most common joints for ON were the hip (66%) followed by the knee (27.7%). Surgical intervention was required in 27.6% of the patients with ON.

Conclusion: The frequency of ON among the studied patients was 9.7%. Risk factors with significant association with ON were older age and more intensive corticosteroid therapy.

P-0011 | Time-Lapse between Onset of Fever and Administration of First dose of Intravenous Antibiotic in Paediatric cancer Patients with Febrile Neutropenia: A Single Institutional Experience

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Background/Objectives: The main objective is to evaluate length of time between onset of infection and administration of first dose of intravenous (I/V) antibiotic in paediatric cancer patients with febrile neutropenia (FN) and its impact on outcome.

Design/Methods: A prospective study. A total of 55 paediatric cancer patients with FN admitted in Haematology oncology department of the children's hospital Lahore during September 2015 and 31st January 2016 were enrolled. Data regarding demographics, timings of hospital arrival, first evaluation, intravenous access and administration of first dose of antibiotic was collected. The results were analysed by using SPSS version 16.

Results: Out of total 55 patients, 70% (39) were male, mean age was 1.62 years and 42 (76.4%) admitted through OPD. Majority 24 (43.6%) had fever of 24 hour duration. First evaluation was done (by paediatric doctor) within 30 min of hospital arrival in 28 (50.9%) patients, within 30-40 min in 4 (7.3%), 41-60 min in 8 (14.5%), 60-120 min in 5 (9%) and >120 min in 8 (14.5%) patients. Intravenous access was achieved within 30 min of evaluation in 26 (47.3%) patients, 40-60 min in 11 (20%), 60-120 min in 6 (11%) patients. Majority of patients 47 (85.5%) received first dose of antibiotic at the time of I/V access. Time span between hospital admission and administration of I/V antibiotic varies from 60 min to as long as 5-6 hours. Duration of stay was 3-10 days in 21 (38.2%) and 10-25 days in 18 (32.8%). Forty two (76.4%) patients were discharged and 13(23.6%) died.

Conclusion: Variable length of time was spent by patients with FN within the hospital before receiving first dose of antibiotic leading to longer duration of stay. There is a dire need to take essential steps to avoid unnecessary delay in administration of first dose of antibiotic to these children for better outcome.

P-0012 | A Comparison of Cognitive Status between Children with Leukemia and Healthy Peers

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Background/Objectives: Cognitive functions of the children with cancer may be affected negatively, as a result of cancer therapies' side effects. The aim of our study was to investigate cognitive status of the children with cancer during treatments and to compare with the healthy peers.

Design/Methods: Eight (male: 5, female: 3) children with leukaemia and thirteen (male: 6, female: 7) healthy peers participated in the study. The average age was 9.00 ± 3.62 years in children with leukaemia and 8.46 ± 1.19 years in healthy peers ($p>0.05$). Children's cognitive status was assessed with the Modified Mini-Mental State Exam (MMSE). This test includes orientation, memory, attention and calculation, recalling, and language.

Results: The mean total scores of the MMSE were 23.00 ± 7.92 in children with leukaemia 29.92 ± 4.66 in healthy peers. There were found significant difference between groups in orientation subtest of MMSE ($p=0.001$), and also total scores ($p=0.045$).

Conclusion: During therapies children are staying in hospital for a long time, and they are receiving aggressive therapies especially Methotrexate. Because of these reasons they may have some difficulties in cognitive functions especially in orientation. Rehabilitation programs should be planned to meet the requirements of the children's cognitive influences. There is great need to investigate these influences in larger children populations.

P-0013 | Outcome of Children with Acute Lymphoblastic Leukemia Treated with Intercontinental BFM 2002: Results from a Single Center

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Background/Objectives: Intercontinental BFM (IC-BFM) 2002 is a successful project for improving the outcome of children with Acute lymphoblastic leukaemia (ALL). This randomized trial evaluated the impact on outcome of intensified late reinduction in the context of newly developed risk stratification with some modifications.

Design/Methods: From March 2007 to April 2012, 65 eligible patients aged 1-16 years with newly diagnosed Precursor-B ALL were enrolled. Stratification into 3 risk groups was performed based on the protocol. After the induction and consolidation phase, they were randomized into group A ($n=33$) and B ($n=32$). Standard and intermediate/high risk (HR) group B patients received protocol III two and three times, respectively. They received the maintenance phase according to the protocol. The protocol II \times 1/ \times 2 was prescribed for standard/intermediate and high risk group A patients, respectively. Then, conventional oral methotrexate/6-mercaptopurine maintenance therapy with vincristin/prednisolone (every 35 days) and intrathecal methotrexate (every 105 days) was used.

Results: There was no significant difference in age distribution and median follow-up between the two groups. Ten patients were HR (7 in group A and 3 in group B). Early ($n=2$) and late ($n=4$) relapse was seen in 6 patients of group B. Late relapse developed in one patient of group A. With a median follow-up of 70 months (range 19-107), the estimated 5-yr Relapse Free Survival (RFS) and estimated 5-yr Overall survival (OS) were $87.10 \pm 4.30\%$ and $96.50 \pm 2.50\%$ for all patients. There was no significant difference between OS of group A and B ($96.20 \pm 3.80\%$ vs. $95.50 \pm 4.40\%$, $p=0.96$), but RFS of group A was significantly better than group B ($97.00 \pm 3.00\%$ vs. $77.00 \pm 7.70\%$, $p=0.02$).

Conclusion: IC-BFM 2002 dramatically improved outcome of children with ALL. It appears that protocol II as late reinduction is significantly more effective than protocol III to improve outcome and decrease relapse.

P-0014 | Does the CD45 Antigen Expression in Paediatric Acute Lymphoblastic Leukemia have Prognostic Significance?

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Background/Objectives: To evaluate the prognostic significance of CD45 antigen expression in paediatric acute lymphoblastic leukaemia (ALL).

Design/Methods: We measured the CD45 expression of leukemic blasts in 452 patients with paediatric B-ALL (n = 380) and T-ALL (n = 72). These patients were treated with two different protocols. In all cases, the median fluorescence intensity of the CD45 expression in leukemic blasts and normal lymphocytes were measured within the same sample and the ratio was calculated. The analysis was done separately in B-ALL and T-ALL as mean CD45 expression was significantly higher in T-ALL than in B-ALL (mean +/- SE: T-ALL 0.39 +/- 0.29 vs. B-ALL 0.09 +/- 0.12, p < 0.001). The 75th percentile was used as cut-off to distinguish CD45-high from CD45-low group.

Results: In both B-ALL and T-ALL, we observed no significant association of CD45 expression with age, initial white blood cell count, morphologic remission, BCR/ABL1 positivity, prednisone response and minimal residual disease. The 5-year overall survival (OS) was 73.4% for the CD 45 low versus 64.9% for the CD45 high groups for B-ALL (p=0.96) and the 3-year OS was 75% for the CD 45 low and 37% for the CD 45 high groups for T-ALL (p=0.52). The OS rates for B-ALL were also analysed based on treatment protocols. The 5 year OS rate for one protocol was 73.3% for CD45 low and 70.89% for CD45 high (p=0.2375) and the 2 year OS rate for patients treated with another protocol was 81% for CD 45 low and 66% for CD 45 high groups and this was statistically significant (p=0.03).

Conclusion: These results show that the levels of CD45 antigen expression on leukemic lymphoblasts in paediatric ALL may have prognostic significance based on treatment protocols.

P-0015 | Bet Inhibition as a Novel Therapeutic Approach for the Treatment of MLL-Rearranged Acute Lymphoblastic Leukemia in Infants

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Background/Objectives: Acute lymphoblastic leukaemia with MLL-rearrangement (MLL+ infant ALL) has an overall poor outcome due to drug resistance and high relapse rate. Numerous studies demonstrated that the mechanism of leukemogenesis is mainly ascribable to a broad perturbation of the chromatin structure induced by the MLL fusion. Therefore, new epigenetic strategies targeting the chromatin structure and/or the recruitment of the transcriptional complex represent nowadays the most promising therapeutic approach. The Bromodomain and Extra Terminal (BET) adaptor proteins bind to acetylated chromatin marks, and function as epigenetic readers. Herein we have investigated the effect of BET inhibition in a preclinical study by using the I-BET151 inhibitor.

Design/Methods: A mouse model of human MLL+ infant ALL was generated, by transplanting patient-derived primary samples into immunodeficient mice. Additionally, the biological mechanism of BET inhibition was further elucidated at the molecular level, both in vitro using human MLL+ ALL cell lines, as well as ex vivo in xenograft samples enriched for leukaemia-initiating cells.

Results: We observed that I-BET151 administration reduces the engraftment and the disease burden of MLL+ infant ALL in vivo and prolongs the survival in mice. I-BET151 is able to block cell proliferation and induce apoptosis of MLL+ cells through the downregulation of target genes belonging to the BRD4 and HOXA network. Finally, we have observed that I-BET151 in combination with HDAC inhibitors is even more efficient compared to the single therapy, as these two compounds have a synergic activity.

Conclusion: Taken together our data show that I-BET151 exerts a potent anti-leukemic effect on MLL+ infant ALL. In conclusion, given the aggressiveness of the disease and the lack of a cure for infant patients with MLL leukaemia, this study is extremely novel and particularly relevant, as I-BET inhibitors may represent a promising novel approach for the treatment of this high risk leukaemia.

P-0016 | Inhibition of the MEK/ERK Pathway Sensitizes Acute Lymphoblastic Leukemia Cells to the NEDD8-Activating Enzyme Inhibitor Pevonedistat Via Rebalancing BCL-2 Family Proteins

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Background/Objectives: Acute lymphoblastic leukaemia (ALL) is the leading cause of cancer-related death in children and the relapse rate in adult ALL patients is ~50%, highlighting the need for new therapeutic strategies. ALL cells are sensitive to agents that induce endoplasmic reticulum (ER)-stress/unfolded protein response (UPR). In search for novel strategies, we evaluated the efficacy of pevonedistat[®] (MLN4924), an agent targeting the NEDD8-conjugation pathway leading to inhibition of cullin-RING E3 ligases.

Design/Methods: We used molecular and genetic approaches to target survival pathways using *in vitro* ALL cell models and primary cells, and *in vivo* NOD/scid gamma (NSG) mice engrafted with NALM6/LUC.

Results: We found ALL cells exhibited significant *in vitro* and *in vivo* sensitivity to pevonedistat via ER stress/UPR-mediated cell death mechanisms. Mechanistically, pevonedistat alters protein translation through dysregulation of eIF2 α and concomitant activation of the mTOR/p70S6K pathway, preventing the UPR from halting protein translation following ER-stress. In addition, we observed induction of the MEK/ERK pathway, suggesting phosphorylation of p-ERK1/2 as a compensatory survival mechanism in response to pevonedistat's

cytotoxicity. Supporting this hypothesis, we found significant *in vitro* synergy between the MEK inhibitor selumetinib and pevonedistat (CI=0.017), which correlated with increased Mcl-1 downregulation. Co-treatment with the caspase inhibitor Z-VAD abrogated cell death, but did not prevent degradation of Mcl-1. Co-IPs demonstrated that pevonedistat increased sequestration of Mcl-1 by NOXA and BIM. On this basis, we tested the *in vivo* efficacy of pevonedistat (66 mg/kg) plus selumetinib (50 mg/kg) in NALM6/LUC-engrafted NSG mice. Bioluminescence analysis revealed significant reduction of tumour burden, and Kaplan-Meier analysis showed increased survival in mice treated with pevonedistat plus selumetinib (p<0.05).

Conclusion: Inhibition of the MEK/ERK pathway further sensitizes ALL cells to the NEDD8-conjugation pathway inhibitor pevonedistat by rebalancing Bcl-2 family proteins. Our pre-clinical data demonstrate promising activity of pevonedistat plus MEK/ERK inhibitors with potential for future clinical translation for ALL patients.

P-0017 | Intravenous Pegaspargase – are there more Hypersensitivity Reactions?

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Background/Objectives: When intravenous (IV) infusion of pegaspargase began to replace the intramuscular (IM) injection as the predominant route of administration, there were reports of a suspected greater rate of hypersensitivity reactions (HSRs) with the IV route. Such reactions warrant therapeutic changes for acute lymphoblastic leukaemia. This is a review of the current literature regarding this matter.

Design/Methods: A PubMed search using appropriate terms identified 8 peer-reviewed reports comparing IV to IM pegaspargase. Included were 3 abstract presentations at national meetings. These 8 reports were examined based on number of patients evaluated, the grading of hypersensitivity reactions, and which Common Terminology Criteria for Adverse Events (CTCAE) version was used.

Results: Grade 2 HSRs appear to be more likely with IV than IM administration but the validity of the difference is uncertain. Confounding the analyses are multiple factors including the historically controlled nature of the comparisons and the increased likelihood of reporting adverse reaction when IV infusion replaces IM injection, and when using the current CTCAE version. Grade 3 reactions are ~1% more common with the 2nd doses in regimens that administer only two doses of pegaspargase. Conversely, the hospitalization rate for treatment of HSR appears to be several-fold more frequent with IM injection.

Conclusion: The reports are inconsistent to conclude that the IV HSR rate is more problematic than with IM injection. The most significant problem is the implementation of CTCAEv4.0 during the years covered by the retrospective chart reviews that not only resulted in lower grade HSRs being reported at higher grades but also increased the likelihood of an HSR being reported. Grade 2 HSRs appear to be more likely with IV than IM administration but the validity of the difference based on these studies is uncertain.

P-0018 | Possibilities of Overcoming Drug Resistance of Blast Cells in Children with Relapsed of Acute Lymphoblastic Leukemia

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Background/Objectives: Relapses of acute lymphoblastic leukaemia (ALL) are the main causes of failures in 10-12% of patients. Not always possible to achieve remission using only chemotherapy. Overcoming drug resistance in children with relapsed ALL is a topical problem. Bortezomib (Velcade[®]) can modify the sensitivity of tumour cells to chemotherapy.

Design/Methods: From June 2011 to December 2015 24 patients with relapsed ALL aged 2–21 years were enrolled. Boys were 18 (75.0%), girls – 6 (25.0%). B-cell ALL was in 17 pts (70.9%), T-cell ALL was in 7 (29.1%). First relapse was in 16 (66.7%), initial refractory occurred in 7 cases (29.2%). Isolated extramedullary relapse was in 6 (25.0%), isolated BM in 9 (37.5%) and combined in 9 (37.5%) pts.

Results: Complete remission achieved 20 (83.3%) pts. CR after induction was in 17 (70.8%). After the second course CR was in 3 (12.5%) pts. Three (12.4%) pts didn't achieve CR. The level of MRD was less than 0.001% in 11 (45.8%). DFS in patients with late relapse was 33.3 +/- 27.2%. In patients with early relapse good results were obtained. DFS in patients with isolated BM was 41.7±30.0%, in combined relapse was 31.3±24.5%.

At present 7 pts (29.2%) are alive in CR, 5 (20.9%) had late isolated BM relapse B-ALL, two pts with late relapse of T-lymphoblastic lymphoma. Four (16.6%) pts with BM relapse underwent a SCT.

Conclusion: Thus, the use of bortezomib in combination with standard chemotherapy allowed achieve CR in 83.3% pts. This therapy is more effective for late relapses ALL.

P-0019 | Central Nervous System Relapse in Children with Acute Lymphoblastic Leukemia: Experience of the Moroccan National Protocol (MARALL 2006)

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Background/Objectives: Central nervous system (CNS) relapse is a major cause of treatment failure in acute lymphoblastic leukaemia (ALL). Its management remains problematic especially in developing countries. Our objective is to describe the CNS relapses in children treated by the MARALL 2006 protocol, identify prognostic factors of these relapses, and study the outcome of these patients.

Design/Methods: We conducted a retrospective and descriptive study on children treated for ALL by the MARALL 2006 Protocol, and collected between 2006 and 2015.

Results: Thirty one (5.8%) among the 536 patients with ALL collected during this period had a relapse in the CNS. It was isolated in 23 cases (74.2%) and combined to bone marrow involvement in 8 cases (25.8%). Seventeen patients (54.8%) had a phenotype B (B-ALL) and 9 (29%) had a phenotype T (T-ALL). The median time to relapse was 489 days [18-1222]. The time to onset of relapse was significantly earlier ($p = 0.05$) in isolated relapses. The difference was not significant between phenotypes of ALL, and between the standard risk (ALL/SR) and the high risk ALL (ALL/HR). Nineteen patients (61.3%) underwent curative salvage treatment. Eight patients (33.3%) had a second relapse after a median time of 146.7 days [30-383] from the first relapse. Six relapses were isolated and 2 relapses were combined. Twenty-two patients (70.9%) died. The difference was significant between the death rate among patients who had ALL/SR and those who had ALL/HR ($p=0.03$). The overall survival was better in patients with B-ALL ($p = 0.04$).

Conclusion: This study showed the low incidence of CNS relapse in ALL treated by the MARALL 2006 protocol, and confirms the poor prognosis of neurological relapses especially in case of T phenotype and in case of ALL/HR. However, our results must be confirmed by a larger prospective study.

P-0020 | Outcome of Paediatric Procedural Sedation & Analgesia in a Tertiary Care Hospital for Oncology Patients in Pakistan

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Background/Objectives: Procedural sedation and analgesia (PSA) is pharmacologically induced state which allows patients to tolerate painful procedures while maintaining protective reflexes. It is the standard of care but there is limited data from Pakistan. Our objective was to assess the safety of the procedural sedation and analgesia in Pediatric oncology population at a tertiary care setting.

Design/Methods: A retrospective notes and record review was conducted at the Aga Khan University Hospital Karachi over 4 years from January 2011 to December 2015. Patients were between ages 6 months to 16 years and were in low risk category. The combination of Ketamine and Propofol were used for PSA. Data collected on the standardized hospital PSA form. All procedures were performed by two trained persons.

Results: A total of 3042 diagnostic and therapeutic procedures were performed. Satisfactory level of sedation was achieved for 3016 (99%) of procedures. Indication were Intra-thecal chemotherapy administration in 2283(75%), Bone marrow aspiration and biopsy in 637(21%), PIC line insertion in 122(4.0%). Adverse events occurred in 26 (0.85%) patients including: 13 episodes of hypoxia, 09 episodes of apnea, and 04 episodes of post sedation hallucination. No major events were noted.

Conclusion: Procedural sedation & analgesia for children using Propofol and Ketamine is found safe and effective in our setting.

P-0021 | Parental Satisfaction Survey for Procedural Sedation Analgesia in Oncology Patients of a Developing Country

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Background/Objectives: As paediatric sedation and analgesia (PSA) are becoming safer and more feasible, they have been widely used for diagnostic and therapeutic procedures. Primary purpose is to improve overall parents and patients satisfaction for painful procedures without compromising patient safety. Patient satisfaction is an essential component of the quality of medical care and it generates better clinical outcomes. The aim of this study was to assess parental satisfaction regarding various components of PSA.

Design/Methods: This study was conducted between January 2012- October 2012 in a tertiary care hospital where various oncological procedures were performed under procedural sedation and analgesia. (PSA) The satisfaction regarding PSA administration was determined through a structured questionnaire.

Results: 50 parents were approached to participate in this survey. Of 50 parents 49 parents participated in this survey. This survey was designed to investigate the quality of communication, environment, education, assessment and care provided by sedation team and overall experience. We follow patient on telephone or when they come for clinical visits. Significant associations between each area of satisfaction and parents overall satisfaction existed. Previous sedations, type of sedations, age of child, or any individual provider were not significantly associated with overall satisfaction. Care giver of anxious parents reported overall satisfaction. Response rate was (n=49) that is 98%.

Conclusion: We found overall high parental satisfaction regarding Procedural sedation and analgesia for oncological procedures.

P-0022 | Significance of Day 29 Bone Marrow in Acute Lymphoblastic Leukemia with M 1 Bone Marrow at Day 8/15 in Absence of MRD

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Background/Objectives: Acute lymphoblastic leukaemia (ALL) is most common hematological malignancy among paediatric population. Different protocols like UKALL and COG are used for management and all protocols suggest bone marrow biopsy at day 8 or 15 and then at day 29 during induction phase. On day 29 Minimum residual disease (MRD) status is usually advised. Developing countries where facility of MDR is not available patients of ALL are being treated according to these protocols and bone marrow biopsies are advised on both day 8/15 and day 29. Our hypothesis is "if day 8/15 bone marrow is in remission there is no significance of day 29 bone marrow in absence of MRD facility".

Design/Methods: All patients of ALL admitted form jan 2008 to dec 2013 and survived during induction were included. Induction therapy according to standard arm of UKALL 2003 was given. Bone marrow biopsy was done on day 8 or 15 depending upon regimen and day 29 in all patients. MDR was not available.

Results: Total 282 patients were included. Male to female ratio was 2:1. Age range from 7 month to 17 year. Seventeen (6%) patients were >10 yrs and 265(94%) were < 10 year.30 (10.6%) patients had T cell ALL and 252(89.4) had Pre B ALL. Seventeen (6%) patients had M2 bone marrow and 13(4.6%) had M3 bone marrow on day 8/15 but none of them had residual leukaemia on day 29. 252(89.3%) patients had bone marrow in remission on day 8/15 and none of them had evidence of residual leukaemia on day 29 bone marrow.

Conclusion: In absence of MRD facility there is no significance of day 29 bone marrow if day 8/15 bone marrow is in remission.

P-0023 | Association of Family History with Biochemical Parameters for Deep Venous Thrombosis Development in Acute Lymphoblastic Leukemia: Results from a Developing Country

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Background/Objectives: Deep venous thrombosis is one of the most frequent complications in patients with acute lymphoblastic leukaemia (ALL). Our study aims to determine the correlation of family history with biochemical tests for deep venous thrombosis (DVT) development in ALL patients.

Design/Methods: The study included 71 ALL patients (42 boys, 29 girls) aged 0-18 years, treated between January 1991-2015, at the Pediatric Haematology-Oncology Divisions of Istanbul University Oncology Institute and Bezmialem Vakif University. The files of the patients were retrospectively evaluated and the families were interviewed about family history on DVT.

Results: Seven%9.8 of 71 had developed at least once DVT attack during their treatment. There were 6/42 boys (14.3%) and 1/29 girl (3.4%). Family history was positive in all of the patients, but only 11.9% (7/59) of the patients having positive family history had DVT. There were no statistical difference in total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL) levels between patients with DVT and without DVT. Median Triglyceride (TG) level was 121 mg/dl among patients with DVT. It was 75.5 mg/dl among patients without DVT. This difference between these groups was statistically significant ($p=0.023$).

Conclusion: Our study is too small to attain certain conclusions. However, males might have more risk for development of DVT; family history might have been an important factor in development of DVT and high TG levels might be a risk factor for development of DVT in ALL patients. Studies with larger patient populations are needed to reach absolute conclusions.

P-0024 | Role of rMnSOD as Cytotoxic Agent and Chemotherapy Enhancer in Paediatric Acute Lymphoblastic Leukemia B Cells

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Background/Objectives: An isoform of Manganese-superoxide-dismutase (rMnSOD) was isolated and sequenced for the first time from a human Liposarcoma cells and obtained in recombinant form. The protein showed a specific and selective cytotoxicity on many cancer cell lines. rMnSOD enters cells by means of its 24-aa leader peptide that linked to the oestrogen receptor (ER). A 6-aa sequence, that participates in ER binding, was identified as a molecular carrier by mass spectrometric analysis. The aim of this study was to test the ability of this molecule to inhibit the growth of SUP-B15 cell line and leukemic B-cells and kill them alone and as enhancer of chemotherapeutic drug.

Design/Methods: SUP-B15 cell line and leukemic B cells were cultured in RPMI medium and treated for 5 hours with rMnSOD and Daunoblastine, single and in combination. Cell viability assay was analyzed by MUSE analyzer (Millipore). Apoptotic cell death and cell cycle were analyzed by Annexin-V-FITC staining and PI fluorescence. We analyzed ER expression levels by Real time PCR.

Results: A high level of ER was observed in SUP-B15. Our preliminary data showed that in SUP-B15 cell line rMnSOD induced apoptosis with a reduction of vitality from 61.9% to 31.40% respect to untreated. Treatment with rMnSOD of leukemic cell samples showed in all apoptotic profiles an increase in late apoptosis up to 52%. Better apoptotic induction was observed in prednisone poor responders. Cell cycle analysis showed an arrest in Go/G1 after treatment.

Conclusion: rMnSOD is a promising molecule for the treatment of paediatric B-ALL due to its selective action to cancer cells and to its enhancer action which leads to reduction of drug dose and significantly reducing side effects. Targeted delivery can increase the therapeutic index of conventional chemotherapy, with low doses to kill cancer cells.

P-0025 | Mortality Review of Children with Acute Lymphoblastic Leukemia: Single Center Experience from a Limited Resource Country

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Background/Objectives: Hue Central Hospital plays a key role to treat childhood acute lymphoblastic leukaemia(ALL) in the central zone of Vietnam which covers geographically wide areas. The purpose of this study was to review the causes of death in children with ALL to improve the treatment outcome.

Design/Methods: Medical records of children with ALL who died at HCH between January 2009 and December 2015 were retrospectively reviewed. Data regarding causes of death were collected.

Results: A total of 70 patients who died during 7 years period, a median age was 6 years. The male to female ratio was 2.4:1. 24(34.3%) patients were SR and 46(65.7%) patients were HR. Immunophenotype confirmed that 49(68.1%) had B cell and 20(28.6%) had T cell. The complete remission (CR) rate after induction therapy was 88%. 31(44.3%)patients had good nutrition and 39(55.7%) had poor nutrition status. More than half (65.7%) of the patients were referred from provincial area. The causes of death were 36(50.1%) infection, 25(34.7%) hemorrhage, 19(26.5%) relapse, 13(18.1%) respiratory disorder, 9(12.5%) central nerves disorder and 4(5.6%) tumour lysis syndrome, 2(2.8%) abandonment, 2(2.8%) delay to come back hospital, 1(1.4%) heart failure 1(1.4%) renal failure, 1(1.4%) liver disorder 7(9.7%) deaths occurred before initiation of therapy,18(25%) in Induction, 5 (6.9%) in consolidation, 6(8.3%) in interim maintenance, 10(13.9%) in re-induction and 23(31.9%) in maintenance.

Conclusion: Our results showed that the most common cause of death of childhood ALL was infection and half of the cases died during the maintenance therapy phase even though they had achieved complete remission. In order to improve the survival rate it is necessary to improve the supportive care especially such as infection control or might need to adjust the treatment strength. Further more precise investigation and discussion for these issues are required.

P-0026 | The Influence and Status of TPMT Gene Promoter Variable Tandem Repeat, TPMT and ITPA Genetic Polymorphisms on Mercaptopurine Treatment in Thai Paediatric Acute Lymphoblastic Leukemia

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Background/Objectives: Thiopurine S-methyltransferase (TPMT) and inosine triphosphate pyrophosphatase (ITPA) genetic polymorphisms are significant determinants for clinical outcome and susceptibility to 6-mercaptopurine (6-MP) toxicity during maintenance therapy in paediatric acute lymphoblastic leukaemia (ALL). Recently, modulation of TPMT expression may be caused by a variable number tandem repeats (VNTR) in TPMT gene promoter.

This study aims to explore the influence of genetic polymorphisms of TPMT gene promoter VNTR, TPMT and ITPA genes on clinical outcome in paediatric ALL.

Design/Methods: The genotyping of *TPMT VNTR*, *TPMT*2*, **3B*, **3C*, *ITPA A94C* and *ITPA IVS2+A21C* were performed in paediatric ALL treated in Chiang Mai University Hospital. Oral 6-MP was given during maintenance therapy in a dose of 50 mg/m²/day.

Results: 65 children (male:female = 1:1.1) were enrolled with the median age of 4.95 years (range, 0.58-14.74 years). Forty-nine patients (75.4%) developed grade III-IV of neutropenia according to Common Toxicity Criteria, Version 4.0. 35.4% of patients developed at least one episode of febrile neutropenia during maintenance therapy. We did not find any TPMT variants and ITPA IVS2+A21C mutation in our cohort. The *TPMT VNTR* genotypes were **V4a/*V4a*, **V4b/*V4b*, **V4b/*V5a*, **V5a/*V5a* and **V5a/*V6d*, with frequency of 0.52, 0.02, 0.03, 0.35 and 0.08, respectively. The *TPMT VNTR* genotypes did not affect 6MP dosage, ANC and clinical outcome. For ITPA C94A polymorphism, the mutated allele frequency was 0.23. Patients with AA genotype of ITPA C94A were significantly sensitive to 6-MP therapy, with an average 6-MP dosage lower than those of CA and CC genotypes (36.72 mg/m²/day and 46.39 mg/m²/day, *p* = 0.035). Patients who had ITPA AA and CA genotypes had a significant risk to develop febrile neutropenia than those of CC genotypes (*p* = 0.03).

Conclusion: ITPA C94A polymorphism might be an important determinant for 6MP dose reduction in maintenance therapy in paediatric ALL in Thai children.

P-0027 | Association of Methylentetrahydrofolat Reductase C677T and A1298C Polymorphisms with Methotrexate Induced Toxicities in Children with Acute Lymphoblastic Leukemia

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Background/Objectives: Improvement in the treatment of childhood acute lymphoblastic leukaemia (ALL) has increased the five years event free survival to approximately 85%. Because high toxic drugs are used in the treatment of ALL, main focus of the current studies is reduction of treatment related toxicities. The two commonest polymorphisms in the methylentetrahydrofolat reductase (MTHFR) gene, C677T and A1298C, have been reported to be associated with methotrexate toxicities with still controversial results. The objective of our study was to evaluate the association of MTHFR C677T and A1298C polymorphisms with the occurrence of toxicities during therapy with high doses of methotrexate (MTX).

Design/Methods: Our study included retrospectively 65 children with ALL treated with high doses of methotrexate (5g/m²) during protocol M, part of the ALL BFM 2000 protocol. Genotyping for C677T and A1298C polymorphisms of MTHFR gene was performed using the PCR-

based restriction fragment length polymorphism assay. Toxic effects were analyzed according to the criteria for toxicities from the protocol ALL BFM 2000 (absence or presence of toxic effects) in correlation with the type of present polymorphism.

Results: Subjects with MTHFR 1298 AC polymorphism manifested less hepatotoxicity than subjects with AA and CC polymorphism, *p*=0.023 (OR:0.190 CI:95%). Other toxic effects, which were manifested in less than 5% of the patients (cardiotoxicity, skin toxicity, central and peripheral neurotoxicity) were more common in subjects with MTHFR 1298CC polymorphism, *p*=0.005 (OR:6.095 CI:95%). Infections were more common in subjects with MTHFR 677CT and TT polymorphism without statistical significance. No other toxic effects in correlation with this polymorphisms were registered.

Conclusion: The present study suggests that MTHFR C677T and A1298C polymorphisms have influence on MTX toxicities. Regarding these pharmacogenetic markers, further multi center studies, with larger data, should be performed for future treatment individualization of the childhood ALL.

P-0028 | Ocular Hypertension in Paediatric Patients Treated for Acute Lymphoblastic Leukemia and Non-Hodgkin Lymphoma

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Background/Objectives: In order to identify primary and secondary ocular complications, this study encompassed prospective ophthalmologic evaluations of children and adolescents with Acute Lymphoblastic Leukaemia (ALL) and non-Hodgkin Lymphoma (NHL) at diagnosis, at the beginning and throughout the period of chemotherapy.

Design/Methods: All participating children were evaluated at diagnosis and were treated from June 2013 to June 2015. The standard treatment protocols in Brazil include the administration of a high-dose glucocorticoid resulting in at least 98 days of glucocorticoid use throughout the treatment (prednisone 4g/m² or dexamethasone 600 mg/m²). Intraocular pressure (IOP) was measured when glucocorticoids were just started (D0), on the eighth (D8), the fourteenth (D14) and the twenty-eighth (D28) days of treatment. IOP results exceeding 21 mmHg were considered as ocular hypertension.

Results: We evaluated 33 patients. There were 29 cases (87.9%) of ALL and 4 cases (12.1%) of NHL. Twelve patients (36.3%) were diagnosed with ocular disorders (leukemic infiltration, bilateral papilledema, paralysis of the sixth cranial nerve, retinal hemorrhage, uveitis Herpes zoster and orbital cellulitis). No patients had ocular hypertension before beginning chemotherapy. Seven patients (21%) developed elevated IOP during the first four weeks of chemotherapy. There were a statistically significant differences (*p*<0.001) in IOP variation among all measurements, except between D8 and D14 and between D0 and D28. Every patients obtained satisfactory ocular pressure control when treated with 5% timolol maleate and 10% brinzolamide.

Conclusion: We conclude that ocular disorders occur in patients during the treatment of ALL or NHL. Ocular hypertension has been detected in previously normotense patients. We suggest a protocol including systematic eye examinations and IOP measurements from diagnosis to, at least, the end of the use of glucocorticoid.

P-0029 | Low Initial Peripheral Blast Count Carries Similar Prognosis as That of Good Prednisolone Response in Childhood Acute Lymphoblastic Leukemia

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Background/Objectives: Prednisolone response is one of the most powerful prognostic markers to guide therapeutic decisions in childhood acute lymphoblastic leukaemia (ALL). Patients who present with low peripheral blast count at diagnosis which continues till day 7 of therapy are presumed to be prednisolone responders. In these patients, we lose one prognostic marker while allocating risk-stratified treatment at the end of induction. We aimed to evaluate the significance of initial peripheral blast count in the outcome of ALL in prednisolone good responders.

Design/Methods: Retrospective study conducted in a tertiary care centre from September 2008 to March 2016. Children with ALL were treated with prednisolone prephase followed by standard risk ALL therapy as per institutional protocols. Prednisolone good response (PGR) was defined as an absolute blast count (ABC) of <1000/ μ L in the peripheral blood and prednisolone poor response (PPR) as an ABC of at least 1000/ μ L, after 7 days of oral prednisolone (60 mg/m²/day) and one dose of intrathecal methotrexate. In the PGR groups, 2 subgroups were made wherein children with ABC<1000/ μ L were compared with ABC \geq 1000/ μ L at the baseline. The outcomes were analysed in terms of relapse, event-free survival (EFS) and overall survival (OS).

Results: Out of 152 ALL cases, 136 had PGR and 16 had PPR. In the PGR group, 93 had initial ABC>1000/ μ L while 43 had ABC<1000/ μ L at baseline. Relapse rate was lower in PGR with initial ABC<1000/ μ L as compared to PGR with initial ABC \geq 1000/ μ L (4.8% vs. 8.1%), while it was 35.7% in PPR (*p*=0.006). Four-year projected EFS was 72.2% \pm 16.6% in PGR with initial ABC<1000, 69.6% \pm 7.3% in PGR with initial ABC \geq 1000 and 30.5% \pm 23.0% in PPR. Five-year projected OS was 90.3% \pm 4.6%, 71.3% \pm 7.5% and 60.0% \pm 16.9% respectively in those subgroups.

Conclusion: Initial blast count<1000/ μ L carries good prognosis in children with ALL, at least similar to PGR with initial ABC \geq 1000/ μ L.

P-0030 | Germline Genetic Variants in VDR, RFC and IL15 Genes are Associated with Minimal Residual Disease in Paediatric B-Cell Precursor All

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Background/Objectives: Minimal residual disease (MRD) is the most significant prognostic factor in acute lymphoblastic leukaemia (ALL). We aimed at identification of host genetic variants associated with MRD in patients with paediatric ALL.

Design/Methods: The study included 159 patients treated according to ALL-IC-BFM 2002 and 2009 protocols, with informed consent and approval of local review board. We studied 23 genetic variants potentially involved in metabolism of drugs used in ALL: MDR1 (rs3789243, rs2253046, rs1045642), VDR (rs2228570, rs1544410), NR3C1 (rs6198, rs41423247), GSTP1 (rs1695), GSTM1 and GSTT1 gene deletion, TPMT (rs1800460, rs1142345), MTHFR (rs1801133), TYMS (rs3474033 - alleles TSER*2, TSER*3, and G>C SNP within allele TSER*3), RFC (rs1051266); in anti-tumour immunity: CCR5 (rs333) and MRD-associated variants as revealed by Genome-Wide Association Study: IL15 (rs10519613), NALCN (rs7992226), CCDC85C (rs11160533), 3 intergenic variants (rs9871556, rs3862227, rs4888024). For genotyping High Resolution Melting, TaqMan Genotyping Assays, PCR and PCR-RFLP were used. Flow cytometry or real-time quantitative polymerase chain reaction was used for MRD assessment at day 15, 33 and week 12. The cut off level 10^{-4} was used to identify high vs. low/negative MRD levels.

Results: Three variants were significantly associated with MRD: VDR (rs1544410, MRD_{day15}); RFC (rs1051266, MRD_{day33}), independently and in an additive effect with IL15 (rs10519613); RFC (rs1051266, MRD_{week12}). Risk alleles for MRD-positivity were: A allele of VDR (OR=2.37, 95%CI=1.07-5.21, P=0.03; MRD_{day15}); A allele of RFC (OR=1.93, 95%CI=1.05-3.52, P=0.03; MRD_{day33}); A allele of IL15 (OR=2.30, 95%CI=1.02-5.18, P=0.04; MRD_{day33}). Patients carrying 2vs.1 and 2vs.0 risk alleles in RFC and/or IL15 had significantly higher chance for MRD_{day33}-positive status: OR=3.94, 95% CI=1.28-12.11, P=0.024 (2vs.1) and OR=6.75, 95% CI=1.61-28.39, P=0.012 (2vs.0).

Conclusion: Germline variation in genes related to pharmacokinetics/pharmacodynamics of anti-leukemic drugs and to anti-tumour immunity of the host is associated with MRD and might help improve risk assessment in ALL.

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P-0031 | Does Dexrazoxane Provide Cardiac Protection Against Anthracycline-Induced Cardiotoxicity in Children with High-Risk Acute Lymphoblastic Leukemia?

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Background/Objectives: The role of dexrazoxane in high-risk acute lymphoblastic leukaemia (HR-ALL) is not clear. Currently, risk predictors of anthracycline-induced cardiotoxicity are higher cumulative dose, young age, and female gender. Anthracycline-induced cardiotoxicity often occurs within the first year after anthracycline treatment. The present study was designed to assess the role of dexrazoxane in preventing cardiotoxicity in paediatric patients with HR-ALL.

Design/Methods: Included patients with HR-ALL were from the Maritimes, Canada managed at the Izaak Walton Killam Health Centre between 2009-2015 and received a baseline and follow-up echocardiogram (ECHO) or wall motion ejection fraction (WMEF). After ethics approval, a retrospective population-based cohort study was completed by reviewing patient charts as well as pharmacy and cardiology databases. All patients received treatment based on Children's Oncology Group protocols. Since 2012, all patients with HR-ALL received dexrazoxane as per a new institutional standard. Cases and controls were defined as patients who received anthracycline with or without dexrazoxane respectively. The dose of dexrazoxane:anthracycline was 10:1 for all patients.

Results: There were 16 cases and 22 controls (total n=38). The cases and controls were similar in respect to age and gender and the mean total dose of anthracycline received was $185 \pm 64.8 \text{ mg/m}^2$ and $187 \pm 46.2 \text{ mg/m}^2$ respectively ($p=0.913$). The mean duration from last anthracycline dose to follow-up ECHO/WMEF date was 2.26 ± 1.3 years. On comparison, the mean baseline ejection fractions (EFs) for cases (68.5 ± 9.2) and controls (68.0 ± 8.0) were similar ($p=0.848$). The mean follow-up EFs were not different between cases and controls (65.96 ± 11 vs 68.94 ± 6.9 respectively) ($p=0.358$). Fifteen of the 38 patients had additional ECHOs during therapy with no evidence of cardiotoxicity.

Conclusion: This study suggests that patients with HR-ALL are not at enough risk of early cardiotoxicity to warrant the use of dexrazoxane. Studies in larger populations with longer follow-up would be helpful in better defining at risk populations.

P-0032 | Adverse Events in Children with Acute Lymphoblastic Leukaemia (ALL) Treated with Protocol ALL IC BFM 2002. Single-Centre Retrospective Study

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Background/Objectives: The aim of this study was a retrospective analysis of adverse events in children with acute lymphoblastic leukaemia (ALL) treated with protocol ALL IC BFM 2002 between 2002 and 2015 at Department of Pediatric Oncology, Haematology and Transplantology in Poznan, Poland.

Design/Methods: According to ALL IC BFM 2002 criteria 196 patients (90 [46%] girls, 106 [54%] boys) 1-18 years of age (med. 5.04 yrs) were classified to SR- 52 (26%), IR- 74 (37%) or HR- 69 (35%) groups. Remission on time was achieved by 190 (97%) patients. At a median follow-up was 98 months (range: 44-158 months). Results of the treatment were analysed as 12 years pEFS and pRFS.

Results: Among adverse events 26 (13.3%) relapses were observed within 1.1-69.5 months (med. 23.5 months) from the diagnosis. There were 9 (34.6% [SR-2, IR-2, HR-5]) very early, 5 (19.2% [SR-1, IR-1, HR-3]) early and 12 (46.2% [SR-4, IR-5, HR-3]) late relapses: 12 (46.1%) in BM (SR: 4, IR: 3, HR:5), 4 (15.4%) in CNS (SR: 1, IR:1 HR:2), 1 (3.8%) in testis (HR), 1 (3.8%) in mediastinum (HR) and 8 (30.8%) mixed relapses: 6 BM-CNS (SR: 1, IR: 3, HR: 2), 1 CNS-testicular (IR) and 1 BM-CNS-abdominal (SR). There were 27 (13.8%) deaths: 1 (0.5%) early death due to sepsis; 14 (7.1%) due to treatment complications (9 in I CR [IR: 2, HR: 7], 5 in II CR [IR:2, HR:3]), 11 (5.6%) due to leukaemia relapse/progression (SR:3, IR:3, HR:5), 1 (0.5%) in car accident. In I CR there are 159 (81.1%) patients. 12 years pEFS was 0.65+0.02; RFS was 0.85+0.03.

Conclusion: 1. Majority of children treated with the IC BFM ALL 2002 program achieved long-term remission.

2. BM, CNS and mixed relapses were seen in all risk groups. High rate of deaths was noticed due to treatment complications.

P-0033 | The Prevalence of Thiopurine Methyltransferase Gene Polymorphism in Egyptian Children with Acute Lymphoblastic Leukaemia

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Background/Objectives: Thiopurine methyltransferase (TPMT) gene polymorphism regulates thiopurine therapeutic efficacy and toxicity. *Aim:* Determine the prevalence of TPMT gene polymorphism in Egyptian children with acute lymphoblastic leukaemia (ALL) and its correlation to chemotherapy toxicity.

Design/Methods: Sixty-four patients with ALL, T lineage (27%) and pre-B phenotype (73%), were recruited over a one-year period. They were treated on BFM 90 or CCG 1991 standard risk protocol, experienced myelosuppression toxicity and required interruption and/or modification of thiopurine chemotherapy. Thirty-two patients were on maintenance and another thirty-two were finished their chemotherapy. Seventy healthy age- and sex-matched children served as controls. They were subjected to clinical assessment and haematological panel investigations. TPMT gene polymorphism for G238C, G460A and A719G alleles was detected using PCR followed by RFLP analysis.

Results: Neither the patients nor the controls has had the mutant TPMT variant alleles in either homozygous or heterozygous form. Myelosuppression toxicity in form of different degree of neutropenia was detected in all patients. Most of infection (71%) developed during the course of chemotherapy necessitating hospitalization. As result of myelosuppression toxicity, most of patients need 6-MP dose modification either once (53.1%), twice (15.6%), or \geq three times (25.1%) during their maintenance course. Patients required stopping 6-MP for less than a week (62.5%), up to 2 weeks (28.1%), or $>$ 2 weeks (6.3%).

Conclusion: The studied G238C, G460A and A719G TPMT variant alleles were not detected and were not a determinant cause of mercaptopurine toxicity. Infections and febrile neutropenia were common causes of 6MP dose modification and interruption.

P-0034 | Metabolic Complications During Induction Therapy in Children with Acute Lymphoblastic Leukemia

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Background/Objectives: Patients with Acute Lymphoblastic Leukaemia (ALL) could develop severe complications during treatment, therefore it is important to recognize this risk in each patient. The aim of this study is to describe metabolic complications during the induction treatment in patients with ALL.

Design/Methods: Retrospective study of patients diagnosed with ALL in a Pediatric Haematology-Oncology Unit, from January 2005 to January 2015. Epidemiological and clinical data were reviewed. The statistical analysis was performed by SPSS 22.0.

Results: We analyzed the data of 88 patients with ALL. Most children were boys (60%), median age was 4 years-old (range 0.3-15), 85% were B-cell ALL and 61% were classified as high risk. Hyperleukocytosis was observed in 14% of cases (61.5% T-cell ALL). Metabolic complications were observed in 64% of patients during induction treatment. The most frequent complications were hyperuricemia 11%, hypertriglyceridemia 9% (Triglyceride >1000 mg/dL in 2), hyperglycemia 6%. According to Cairo and Bishop criteria, 10 patients showed high risk to develop tumour lysis syndrome and 2 of them presented acute renal dysfunction. Other complications were hypertransaminasemia 54% (20% grade III-IV), hypercalcemia in 1 patient (calcium 20.4 mg/dL) and SIADH in another patient. Comparing T-cell ALL and B-cell ALL, we found a higher rate of complications in the former group: Hypertriglyceridemia (23%vs7%), Hypertransaminasemia (61.5%vs53.3%) and Hyperglycemia (8%vs5%). None of the patients died of these complications.

Conclusion: More than a half of patients, especially T-cell ALL, could develop hypertransaminasemia and elevation of triglycerides, glucose, calcium and urate plasma levels during induction therapy, mainly related to chemotherapy. This fact, lead to a dose reduction or omission of certain drugs, in order to optimize the treatment on each patient, but the impact of these adjustment should be further evaluated. Some metabolic complications could lead to renal dysfunction or life-threatening situations so a close biochemical monitoring is needed in these children.

P-0035 | Cost-Utility of Protocols of “BFM ALL” and “UK ALL” for Treatment of Children with Acute Lymphoblastic Leukemia in Iran

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Background/Objectives: Nowadays, ALL has been changed to curable disease due to medical promotion. Experts in Iran exert BFM-ALL and UK-ALL protocols in this scope. So, due to lack of necessary resources and economic assessments, there is a requirement to assess the effectiveness and resources used in the protocols. In this study, both the costs and benefits of the treatments in the two protocols are surveyed.

Design/Methods: In this study, the entire direct costs of 130 patients in “BFM ALL” protocol and 93 patients in “UK ALL” protocol calculated over 5 years. All costs were adjusted to the inflation rate in 2015. For calculating utility of the patients, we used standard questionnaire HU13 in format of QALY. The patients and their parents were interviewed. Data were analyzed using software SPSS18 and EXCEL.

Results: According to the results, in UK-ALL protocol (93 Patient;61% Male,39%Female, mean age=7years), in ALL-BFM (130Patient;55% Male,45%Female, mean age=6.5years) There was no difference.

Cost analyze showed that the direct cost per patient, respected the two protocols BFM-ALL was 510,896,313 IRRs (Approximately=12,772 EUR) and UK-ALL was 281,591,023 IRRs (Approximately=7,039 EUR) which showed a significant difference in the total cost of the treatment in the two protocols. In both the costs of inpatient beds and medicine were the most. The average length of hospitalization per patient during treatment was 123 days for ALL-BFM protocol and 96 days for UK-ALL protocol. There was not a significant difference in quality of life in utilizing the methods and these two methods are very similar in different aspects of patients' quality of life.

Conclusion: We think that, primarily, more hospital stay in “BFM ALL” protocol is the cause of increased costs in this protocol. So, by considering similar efficacy in the methods and low costs in “UK ALL” protocol, it seems that “UK ALL” protocol is more preferable.

P-0036 | Cerebrospinal Fluid Toxicity Markers During Treatment are Correlated with Cognitive Performance in Adult Childhood Leukemia Survivors and Can Be Predicted by MTHFR1298 Genotype

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Background/Objectives: Little is known about moderators of toxicity induced by methotrexate (MTX), the corner stone of modern childhood anti-leukemic protocols. Cerebrospinal fluid (CSF) markers of neurotoxicity (Tau) and neurodegeneration (phospho-Tau) during treatment and polymorphisms in MTX-affected enzyme pathways, such as methyltetrahydrofolate reductase (MTHFR), offer an opportunity to study individual differences in susceptibility.

We aim to link CSF phospho-Tau and Tau with cognitive performance in adult childhood leukaemia survivors and MTHFR genotype, respectively.

Design/Methods: CSF-Tau and phospho-Tau were determined at fixed time-points during treatment in children with acute lymphatic leukaemia or non-Hodgkin lymphoma. Fifteen (11.6 – 19.5) years after diagnosis, MTHFR1298 genotype was analyzed in 33 survivors and intelligence (Wechsler Adult Intelligence Scale), memory (Rey Auditory Verbal Learning Test) and executive functioning (Amsterdam Neuropsychological Task) were compared with age- and sex-matched controls without history of cancer.

Results: Mean CSF phospho-Tau during maintenance phase was correlated with TIQ ($r = -0.339$; $p = 0.046$), VIQ ($r = -0.428$; $p = 0.015$) and PIQ ($r = 0.369$; $p = 0.032$).

Compared to wild-types, MTHFR1298A>C homozygotes depicted higher levels of CSF-Tau during the induction phase after intrathecal MTX ($p = 0.011$), especially when administered without folate rescue ($p = 0.007$).

Early developing cognitive domains like long-term memory and attention control were unaffected whereas cognitive flexibility and information processing – only maturing during adolescence – were impaired. This is in accordance with the literature describing increased risk for long-term cognitive dysfunction in very young children.

Conclusion: We demonstrated that 1/MHFR1298A>C homozygosity predicts higher CSF-Tau after intrathecal MTX and 2/CSF phospho-Tau is correlated with intelligence in adult childhood leukaemia survivors.

Pretreatment risk evaluations based on age at diagnosis and MTHFR genotype, completed by CSF Tau and p-Tau during chemotherapy might be a guideline to early identify children at risk for long-term chemotherapy-induced neurotoxicity, allowing timely educational and/or pharmacological interventions

P-0037 | An Unusual Presentation of Acute Leukemia: Epiglottitis

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Background/Objectives: Epiglottitis is an acute and life threatening inflammation in the supraglottic region of the larynx and epiglottis. It is a medical emergency characterized with fever, sore throat, drooling, odynophagia and respiratory distress. We present a patient with epiglottitis who has as an initial presentation of having acute lymphoblastic leukaemia (ALL). Our objective is to describe an unusual presentation of leukaemia and increase awareness epiglottitis.

Design/Methods: A 16-year-old boy admitted to emergency department with 3-day history of sore throat, fever, difficulty in swallowing, hoarseness, and fatigue. The odynophagia was gradually progressive and more for solids than liquids. On physical examination, he was febrile, pale, and had drooling. Indirect laryngoscopy showed a edematous swelling of the epiglottis. Laboratory investigations showed: white blood cell count 2140/mm³ with 300/mm³ neutrophils. Hemoglobin 8,3 gr/dl, platelets 90,000/dL. Serum uric acid and lactate dehydrogenase were 12 mg/dl and 1228U/L, respectively. A peripheral blood smear showed 16% and bone marrow aspiration exhibited 84% blast cells. Flow cytometry and bone marrow biopsy confirmed T-cell ALL. Prednisolone were administered to treat both the epiglottic swelling and malignancy. The magnetic resonance imaging scan of the neck showed swollen epiglottis and thickened aryepiglottic folds. Aerosolized epinephrine, parenteral dexamethasone and ceftriaxone were begun after admission. Blood and throat cultures were negative. The patient received ALL induction therapy with BFM protocol. Within 5th day of the onset of therapy, symptoms resolved dramatically. The leukaemia responded to chemotherapy and he is presently in remission and being followed on an outpatient basis.

Results: Children with ALL usually present with clinical features of cytopenias, organomegalies and bone pains. Although acute epiglottitis due to malignancy is rare, there are few reports of cases with epiglottitis secondary to cytotoxic chemotherapy and neutropenic status.

Conclusion: Our patient had epiglottitis as an initial presentation of malignancy which has been reported in 4 cases, previously.

P-0038 | Neurologic Complications in Children with Acute Lymphoblastic Leukemia: Experience from a Tertiary Care Hospital in a Resource Limited Country

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Background/Objectives: To describe the frequency, clinical profile and outcome of neurological complications in children with acute lymphoblastic leukaemia, admitted in a tertiary care hospital.

Design/Methods: This was a descriptive retrospective study conducted at the Aga Khan University, Karachi on all children below 16 years of age with Acute Lymphoblastic Leukaemia (ALL) and acute neurological complications admitted between October2009 to December 2014. Data was analyzed by using SPSS version 19.

Results: During a 5 year period, 242 children with ALL were diagnosed and treated on BFM based COG protocol. Out of which 42 (17%) suffered a neurological event, with 25(59.5%) being males and 32 (76%) between 1-10 year of age. B precursor ALL was diagnosed in 32(76.2%) and 10 (23.8%) had T-cell ALL. Almost a third of neurological events 15 (35.7%) were observed during induction. Eleven (26.2%) had altered level of consciousness, 27 (64.3%) had convulsions and 8 (19%) had motor weakness/hemiplegia. Systemic chemotherapy (including high dose methotrexate, vincristine & L-asparaginase) & intrathecal methotrexate (19%) seemed to be the most common predisposing factors. Radiological findings suggestive of PRES was found in 4 (9.5%), leuco-encephalopathy in 8 (19%), acute infarct in 7 (16.7%), venous thrombosis in 2 (4.8%) and intracranial bleed in 2 (4.8%). Most of the patients had full recovery by hospital discharge, 4 (9.5%) expired and 2 (4.8%) had neurological deficit on hospital discharge.

Conclusion: Although most patients had full recovery, neurological complications are frequent events during ALL therapy, and require early detection and prompt treatment to limit permanent damage.

P-0039 | Outcome of Children with Acute Lymphoblastic Leukemia from three Urban Centers of Low Middle Income Country

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Background/Objectives: Treatment outcome for children with ALL in developing countries is below that reported for more developed countries. It has also been noted that factors that impact outcome in LMIC differ from those seen in more developed countries. In this study we report the treatment outcome of a cohort of ALL patients from Pakistan. Presenting features and induction outcome for this group of patients have been previously reported.

Design/Methods: Pediatric patients (<18 years) diagnosed with ALL at three children's cancer centers in Karachi during the period September 2009 to August 2012 were prospectively followed. Uniform diagnostic criteria and treatment strategies were applied.

Results: Of the 642 patients enrolled, 66% were males, B-ALL was diagnosed in 78.5%, while 17.5% had T-ALL; 28.8% had a WBC >50 × 10⁹/L. With a median follow up of 20 months, the overall survival (OS) was 72% for all patients. Treatment abandonment was a major cause of treatment failure, and when this was included as a mortality event the OS was 50%. Of the 499 who completed induction chemotherapy only 450 achieved CR; 68 of these subsequently relapsed at a median of 18 months from diagnosis, resulting in a relapse free survival of 56%. Event free survival, with abandonment included as an event, was 40%. On univariate analysis, survival was found not to be associated with age or gender and worse outcome was significantly associated with WBC>50K, T-ALL and CNS-2 status.

Conclusion: The outcome for children with ALL in Karachi is suboptimal. Risk factors impacting outcome includes common associations, but also some unique variables such as treatment abandonment and CNS-2 status.

P-0040 | Paediatric Leukemia Cytogenetics in Botswana

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Background/Objectives: Acute leukaemias are the most common malignancy of childhood in high-income countries and their cytogenetics are relevant in prognosis and risk stratification. However, the majority of children diagnosed with acute leukaemias live in low- and middle-income countries (LMICs), where fewer children survive. Given resource limitations there is less data on cytogenetic alterations in LMICs and whether these contribute to poorer outcomes.

Princess Marina Hospital (PMH) is a government referral hospital with the only paediatric oncology services in Botswana. Due to a lack of advanced diagnostics, consistent blood products and certain chemotherapeutic agents at PMH, all children with acute leukaemias are referred to South Africa (SA) for the intensive phases of treatment.

Design/Methods: This retrospective cohort study reviewed paediatric patients (≤ 18 years) diagnosed with acute leukaemia in Botswana between January 2007 and February 2016. Variables assessed included age, gender, initial leukocyte count and time between caregiver report of initial symptoms and evaluation in SA. Diagnostic cytogenetic studies, including bone marrow karyotype and fluorescence in-situ hybridization (FISH), were obtained in SA.

Results: Forty-six patients were identified for analysis: 30 were diagnosed with acute lymphoblastic leukaemia (ALL) (57% pre-B, 27% T-cell, 3% mature B-cell, 13% unknown); 13 with acute myeloid leukaemia (AML); and three with acute leukaemia of ambiguous lineage. The median time from symptom recognition to evaluation in SA was 47 days (6-278). The median presenting leukocyte count for ALL was 49.0 × 10³/μL (2.13-517.45) and for AML was 41.3 × 10³/μL (2.26-209.50). Twenty-eight patients had cytogenetic information available. The most common translocation in ALL was t(1;19) (4/17, 24%) and in AML was t(8;21) (4/8, 50%).

Conclusion: In this limited cohort study favorable translocations in AML and unfavorable translocations in ALL were observed. Prospective research in LMICs with regional, multinational studies is needed to best determine local cytogenetics and their prognostic and treatment implications.

P-0041 | Revisiting the Four Color Multiparametric Flow Cytometry Panels to Diagnose Paediatric Leukemias and Lymphomas

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Background/Objectives: Acute leukaemia remains an alarming problem even with improvement in current chemotherapy regimens and is still the second leading cause of death in children. Flow cytometry plays a vital role in the diagnosis and detection of this disease.

Previously we investigated the diagnostic potential of a four color panel using 18 antibody leukaemia panel. Some immunophenotypic markers necessary to detect Burkitt lymphoma that is prevalent in Africa were not included. The importance of these markers will positively impact the leukaemia/lymphoma panel in developing countries like Africa.

Design/Methods: The revised assay panel contains five-six reaction tubes each containing four set of antibody mixtures. The flow cytometric assay will be performed in one or multiple steps. The initial step will involve one or two tubes called basic assay tubes. The remainder assay will be performed based on the results from these basic tubes.

Results: The diagnosis of both B- and T-ALL cases by using the revised antibody panel matched with the diagnosis reached by using the extensive (33-37 antibody panel) currently used at the Texas Children's Cancer and Haematology Centers, Texas Children's Hospital.

Conclusion: Preliminary results show promise of using the revised antibody panel for Africa and other developing nations. Strategies to make the flow cytometry cost effective without compromising the diagnosis and patient safety will be discussed.

P-0043 | Variants in MIR-5189, MIR-595 and MIR-6083 Associated with Methotrexate Plasma Levels in Spanish Patients with Paediatric Acute Lymphoblastic Leukemia

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Background/Objectives: Methotrexate (MTX), key drug in childhood B-Acute Lymphoblastic Leukaemia (ALL) therapy, often causes toxicity. Association between genetic variants in MTX transport genes and toxicity has been reported. It is known that these transporters are regulated by microRNAs (miRNAs). Despite miRNA SNPs interfere with miRNA levels or function, studies of miRNA polymorphisms and drug toxicity are almost absent. Regarding B-ALL, we have previously found rs56103835 in miR-323b associated with MTX plasma levels. Nowadays, a large amount of new miRNAs have been annotated. Therefore, the aim of this study was to determine if there are other variants in miRNAs associated with MTX levels.

Design/Methods: Blood samples of 167 Spanish patients with paediatric B-ALL treated with LAL/SHOP protocol were analyzed. We selected the SNPs described in pre-miRNAs with a MAF>1% (213 SNPs in 206 miRNAs) that could regulate MTX transporters. Genotyping was performed with VeraCode GoldenGate platform.

Results: Among the most significant results, we found rs59262801 in miR-5189, rs4909237 in miR-595 and rs78790512 in miR-6083 associated with MTX plasma levels. These miRNAs were predicted, *in silico*, to regulate genes involved in MTX uptake: *SLC46A1*, *SLC19A1* and *SLC01A2*.

Conclusion: In this study we detected 3 SNPs in miR-5189, miR-595 and miR-6083 that might affect *SLC46A1*, *SLC19A1* and *SLC01A2* MTX transport genes regulation and could affect MTX levels in patients with paediatric B-ALL.

This project was supported by RETICS (RD12/0036/0060 and RD12/0036/0036) and Basque Government (IT661-13).

P-0044 | MIR3166, MIR3144 and MIR4745 are Associated with Acute Lymphoblastic Leukemia Susceptibility in the Spanish Population

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Background/Objectives: Recently, several Genome wide associations studies (GWAS) have found genetic variants at *ARID5B*, *IKZF1*, *CEBPE*, *CDKN2A* and *BMI1-PIP4K2A* genes associated with paediatric acute lymphoblastic leukaemia (ALL) risk. These studies were mainly focused in coding regions. However, nowadays it is known that more than 40% of significant variants associated with cancer risk are situated in non-coding regions, where non-coding RNAs are located. MicroRNAs (miRNAs) are non-coding RNA molecules dysregulated in ALL, suggesting that they may have a role in ALL risk. Despite miRNA SNPs interfere with miRNA levels or function, only 3 studies in ALL susceptibility have been done. In those studies, 5 SNPs in 5 miRNAs have shown association with B-ALL. These results suggest that variants in miRNAs could contribute to childhood B-ALL predisposition. Nowadays, a large number of new miRNAs have been annotated. Therefore, the aim of this study was to determine if any of the SNPs in these new miRNAs are involved in B-ALL susceptibility.

Design/Methods: Blood samples of 217 paediatric patients with B-cell ALL in complete remission and 330 healthy controls of Spanish origin were analyzed. We selected the SNPs described in pre-miRNAs with a MAF>1% (213 SNPs in 206 miRNAs). VeraCode GoldenGate platform was used.

Results: Among the most significant results, rs35854553 in mir3166, rs68035463 in mir3144 and rs10422347 in mir4745 showed association with B-ALL risk in the Spanish population with a p-value under 0.005.

Conclusion: Our results suggest that SNPs in miRNAs may be involved in B-ALL susceptibility and give new keys to understand its biology.

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P-0045 | Complications During Maintenance Phase Chemotherapy of Childhood Acute Lymphoblastic Leukemia : A Developing Country's Perspective

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Background/Objectives: Outcome of children with acute lymphoblastic leukaemia (ALL) from developing countries is poor. Although most of the complications arise during the induction and consolidation phases of ALL treatment, complications and deaths occurring during maintenance phase chemotherapy of ALL are not very well accounted for.

Design/Methods: A cohort of 90 children with ALL during the maintenance phase chemotherapy (421 cycles, 3 months each, total 1263 months) were studied for viral infections documented by PCR in relation to morbidity and mortality during this phase.

Results: Of total 90 patients (B-ALL 76, T-ALL 14) entering maintenance phase, there were 15 (16.7%) deaths. Eleven patients died due to infections and 4 due to relapse. Infections were the most common complication observed. Seventy six patients (84.4%) had a documented viral infection (Hepatitis C 26, Hepatitis B 15, Parvovirus B19 25, CMV 2, Influenza A 2, Measles 2, Herpes Simplex 2, Varicella 1, Mumps 1). One patient with CMV infection died due to CMV encephalitis. Fever with or without a focus was present in 58(64.4%) patients and out of these 28(31.1%) had febrile neutropenia. A significant association($p=0.032$;OR=2.83, 95% CI=1.08 to 7.43)between febrile neutropenia episodes with Parvovirus infection was found. Anemia requiring blood transfusion was seen in 42(46.7%) patients, of these 29(69%) were folate deficient, 20(47%) ($p=0.021$) were positive for parvovirus DNA PCR and 13(30%) had both the factors. Fifty eight (64.4%) children had a chemotherapy interruption of more than 7 days (43 due to fever, 10 due to hepatitis, 5 due to social reasons).

Conclusion: With a never ending endeavour to improve the outcome of ALL, one of the target areas is to cut down treatment related deaths during maintenance phase by improving aseptis as infections play a havoc during maintenance phase. Viral infections are a very important and preventable cause of morbidity and mortality in our patient cohort.

P-0046 | Role of Cardiac Biomarkers in Detection of Myocardial Damage in Children with Hematological Malignancies Treated with Anthracyclines

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Background/Objectives: Anthracyclines exposure during treatment of childhood malignancies poses a high risk for development of late cardiotoxicity. Cardiotoxicity is usually diagnosed when patient is symptomatic with progressive cardiac dysfunction. Early detection is important to institute early therapeutic interventions to improve outcome. Aim of present study was to evaluate cardiac troponin T (cTnT), N-terminal probrain natriuretic peptide (NT-pro BNP) and creatinine kinase MB isoenzyme (CK-MB) and echocardiography in the detection of cardiac abnormalities in asymptomatic children treated for hematological malignancies with anthracyclines.

Design/Methods: Serum levels of cTnT, NT-pro BNP and CK-MB were measured in 40 survivors (26 males and 14 females) of hematological malignancies (20 high risk acute lymphoblastic leukaemia and 20 Hodgkin lymphoma patients). All patients had received >200 mg/m² cumulative dose of anthracyclines and were more than 2 years post chemotherapy. 30 healthy children were taken as controls. Echocardiography using M-mode and Doppler measurements were performed on same day as blood investigations. Study was approved by Institute Ethics committee. Informed written consent was taken from parents/guardians of all study subjects.

Results: Serum levels of NT-proBNP were significantly higher in patients compared to controls (48.69 ± 20.36 vs 5.08 ± 3.74 pg/ml; p value <0.01). 6 of the patients had left ventricular (LV) dysfunction with mean NT-proBNP levels of 67.29 ± 22.73 pg/ml which was significantly higher than patients who had normal LV function (mean NT-proBNP levels of 36.19 ± 21.93 pg/ml). Levels correlated inversely with fractional shortening and ejection fraction and positively with the cumulative dose of anthracyclines. No difference was observed between males and females. Serum levels of cTnT and CK-MB were higher in the patients but they were not statistically significant.

Conclusion: NT-pro-BNP is a sensitive test and correlates with cardiac function. It can be used as a useful biomarker for early detection of anthracycline cardiotoxicity.

P-0047 | The Prevalence of Osteonecrosis is High after Treatment for Acute Lymphoblastic Leukemia

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Background/Objectives: Osteonecrosis (ON) is a serious and debilitating complication of childhood acute lymphoblastic leukaemia (ALL). We determined the prevalence and pattern of ON in relationship to clinical indices, fractures, bone mineral density (BMD) and chemotherapy exposure in children following the completion of therapy for ALL.

Design/Methods: Seventy-eight children enrolled in the STOPP study were evaluated for ON by total body magnetic resonance imaging (MRI) after completion of treatment. ON was defined by a decreased signal on T1-weighted and increased signal on STIR images. Clinical parameters and bone health indices were obtained at diagnosis and every 6 months for 6 years.

Results: At a mean of 3.0 years (SD 1.4) following completion of chemotherapy, 28/78 children (36%) had a total of 164 ON lesions at the following sites: 52/164 at the knees (32%), 50 at the tibiae (30%), 33 at the femora (20%), 20 at the ankles (12%), 6 at the hips (4%), 2 at the humeri (1%), and 1 lesion at the shoulder (1%). Multivariable analysis showed age as an independent predictor of ON (every one year increase in age was associated with a 50% increase in the odds of ON, 95% confidence interval 1.1 to 1.9). The following variables were not independent predictors of ON: gender, leukaemia risk category, changes in BMD and body mass index Z-scores in the first 12 months of chemotherapy, height Z-score at diagnosis, cumulative glucocorticoid dose, physical activity, calcium and vitamin D intake, nor the presence of extremity or vertebral fractures.

Conclusion: The prevalence of ON was high in children after the completion of leukaemia therapy and older age was a positive predictor. The variables that normally predict osteoporotic fractures (prior history of fractures, declines in BMD Z-scores and glucocorticoid exposure), were not independent predictors, suggesting that the pathways to osteoporosis and osteonecrosis may be different.

P-0048 | Intravenous and Intramuscular Administration of Asparaginase in Paediatric Patients with Acute Lymphoblastic Leukemia: Treatment Patterns and Perceptions

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Background/Objectives: Asparaginase is an important component of therapy for acute lymphoblastic leukaemia (ALL). In the US, asparaginase may be administered as a course of intramuscular injections, which can be painful and cause anxiety. Intravenous administration may offer a less painful option; however, concerns exist over increased incidence of infusion-related reactions. This study's goal was to assess practices and attitudes of physicians regarding their treatment of paediatric patients with ALL, including route of asparaginase administration.

Design/Methods: This study, conducted between May 20 and June 16, 2015, consisted of a 30-minute, online, quantitative survey targeting US board-certified haematology oncologists with 2-30 years in practice. Inclusion criteria included that physicians spent ≥75% of their time in direct patient care and treated ≥5 paediatric patients with ALL in a typical month.

Results: Data regarding route of administration for asparaginase *Erwinia chrysanthemi* (*Erwinia*) were available for 90.5% (67/74) respondents. Intravenous administration was the standard route of administration for 37% (25/67) of respondents using *Erwinia*. Among respondents preferring intramuscular administration, the most commonly cited reason was standard of practice or protocol (38%, 12/32) while it was ease of administration (68%, 17/25) for intravenous administration. Of 15 respondents who reported using intravenous administration of *Erwinia* for ≥6 months, 67% (10/15) adhered to a 60-minute infusion duration, whereas 27% (4/15) reported using a ≥90-minute infusion duration. Regarding the rate of infusion, 40% (6/15) of respondents reported that they typically start the infusion gradually before ramping up the infusion speed for the remaining dose (1 respondent citing hospital policy; 5 respondents citing improved tolerance/ability to better monitor patients for side effects).

Conclusion: The majority of respondents using *Erwinia* preferred using intramuscular administration, most commonly citing institutional preference/standard of practice. Among physicians experienced with IV *Erwinia* administration, two thirds adhered to a 60-minute infusion, while one third adhered to a ≥90-minute infusion.

P-0049 | Intensive Asparaginase Therapy in Young Adult Patients with Acute Lymphoblastic Leukemia: Treatment Patterns and Barriers to Asparaginase Use

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Background/Objectives: Long-term survival of paediatric patients with acute lymphoblastic leukaemia (ALL) currently exceeds 80%; however, the prognosis for adolescent, young-adult (YA), and adult patients remains poor, with only 30%-45% of patients achieving long-term survival. Several studies suggest that, compared with traditional adult protocols, YA patients have superior overall survival with manageable toxicity when treated with intensive "paediatric-inspired" regimens that include asparaginase. Despite these results, many YA patients with ALL continue to be treated with regimens that include little or no asparaginase. The goal of this study was to assess the views and practices of hematologists/oncologists with respect to asparaginase use in YA patients with ALL.

Design/Methods: This study consisted of a 10-minute, online, quantitative survey targeting US board-certified physicians with 2-30 years in practice who treat YA patients (aged 18-40 years) with ALL, with a 10-minute per-patient chart-audit component for up to 4 charts provided by participating physicians. Inclusion criteria included that physicians spent ≥75% of their time in direct patient care, ≥20% of their time in an academic setting, and that physicians' ALL patient volume (YAs and adults aged >40 years) was >5 over the past 2 years, while personally treating ≥1 YA patient with ALL during that time.

Results: Sixty-three practicing physicians for 189 YA patients with ALL (62% were aged 25-40 years) were included. 60% (114/189) of YA patients were treated with protocols including some asparaginase, but only 29% (55/189) with asparaginase-intensive, paediatric-inspired protocols. Overall, 40% (75/189) of YA patients were treated with protocols not including asparaginase, most commonly hyper-CVAD (77%, 58/75). Of hyper-CVAD users who responded, 50% (18/36) reported the perception of similar outcomes with nonasparaginase regimens as with asparaginase-intensive regimens.

Conclusion: In this study, <30% of YA patients with ALL received asparaginase-intensive, paediatric-inspired regimens.

P-0050 | Challenges in Interaction and Interpretation of Symptoms and Side-Effects in Children with Down Syndrome and Acute Lymphoblastic Leukaemia – A Qualitative Study

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Background/Objectives: The purpose of this study was to explore the experiences of parents of patients with Down Syndrome (DS) and Acute Lymphoblastic Leukaemia (ALL) in relation to the background for the lower treatment intensity of maintenance treatment in patients with DS-ALL.

Design/Methods: A criterion sampling of 14 parents to 10 DS-ALL patients treated on NOPHO ALL2008 treatment protocol from Sweden (n=7) and Denmark (n=3) were selected with various demographic and clinical characteristics. The parents were interviewed together or alone, with or without the child and siblings, and in the family's home or by phone according to parents' wishes. The interviews were conducted in their native language and an interpreter was used in one case. The interview-guide was structured with the topics: side-effects, treatment adherence and cooperation with the physician. The interviews were audio-recorded with parents' permission and transcribed verbatim. The transcribed text was analysed by the research group using qualitative content analysis.

Results: Two main themes emerged in our preliminary analysis: 1) "Difficulties and challenges in interaction and interpretation of a child with DS and ALL", 2) "Great diversity in knowledge on DS-ALL, dose regulation and side-effects during maintenance therapy". Only the first main theme is described in this abstract. Three sub-themes were identified: Enhanced responsibility and challenges for the parent to interpret symptoms and act as spokesperson. The importance of preparation, time and familiar surroundings, and the child's reactions reflecting the cognitive impairment.

Conclusion: The findings indicate that parents of DS-ALL patients may experience a great challenge in the communication and interpretation of their child's symptoms and side-effects. Our study highlights the importance of providing maintenance treatment and care with consideration for the children's extensive need for adjusted care to their cognitive impairment and reliance on their parent as spokesperson.

P-0051 | Comparison of Hypersensitivity Rates to Intravenous and Intramuscular PEG-Asparaginase in Children with Acute Lymphoblastic Leukemia: A Meta-Analysis and Systematic Review

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Background/Objectives: Pegylated-asparaginase (PEG-ASP) is a critical treatment for paediatric acute lymphoblastic leukaemia (ALL) and has traditionally been delivered via intramuscular (IM) injection. In attempt to reduce pain and anxiety, PEG-ASP has increasingly been delivered via intravenous (IV) administration. The objective of this study was to perform a meta-analysis and systematic review to compare and generate pooled hypersensitivity rates for IM and IV PEG-ASP.

Design/Methods: A systematic literature search was conducted for all epidemiological studies that investigated IV and IM hypersensitivity rates for paediatric ALL. Data on hypersensitivity rates by IM and IV delivery among other study characteristics were extracted. Included studies were critically appraised using the GRACE checklist. Pooled estimates and odds ratios with 95% confidence intervals (CIs) for IM and IV hypersensitivity rates were derived based on either a random or fixed effects model.

Results: Four studies satisfied the inclusion criteria and were of adequate quality. The random effects pooled hypersensitivity rates were 23.5% (95% CI, 14.7-33.7%) and 8.7% (95% CI, 5.4-12.8%) for IV and IM, respectively. The fixed effects pooled OR after adjusting for publication bias was 2.49 (95% CI: 1.62, 3.83), indicating a significantly higher risk of hypersensitivity for IV over IM PEG-ASP. This risk is far more pronounced for high risk (HR) patients compared to standard risk (SR) patients (IV vs. IM - HR ↑35.2% & SR ↓2.9%).

Conclusion: Although administering PEG-ASP through IV is preferable for patients, it poses a significantly higher risk of hypersensitivity when compared to IM, especially for HR patients. We recommend paediatric oncologists consider treating patients with HR paediatric ALL with IM PEG-ASP to reduce the risk of hypersensitivity.

P-0052 | Prognostic Significance of Wilms Tumour 1 GENE (WT 1) Expression in Childhood Acute Lymphoblastic Leukemia

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Background/Objectives: Wilms tumour 1 gene (WT 1) is an embryonic zinc-finger transcription factor, which was originally identified as a tumour suppressor gene inactivated in Wilms tumors. In normal tissue, WT1 is expressed during embryogenesis where it plays a pivotal role in the development of the urogenital tract. Alterations of WT1 expression (both under or over-expression) have been described in a number of malignancies and premalignant syndromes. In this study, we focused on evaluation of WT1 expression and its clinical implications in

prognosis of childhood ALL, where WT1 has been least studied and its impact remains most controversial.

Design/Methods: A case-control study was carried out in paediatric oncology unit of Zagazig university children's hospital during the period from January 2011 to June 2013. We examined the expression level of WT1 gene in 44 newly diagnosed children with acute lymphoblastic leukaemia and 20 age and sex matched controls (Patients with hematological problems other than hematological malignancies). Fresh peripheral blood samples were collected from all study participants and submitted for RNA extraction, reverse transcription of extracted RNA and real-time quantitative PCR.

Results: We detected a wide range of WT1 gene expression levels among 44 patients of acute lymphoblastic leukaemia. Statistically, WT1 gene expression level was significantly higher in T-cell acute lymphoblastic leukaemia than in B-cell Precursor acute lymphoblastic leukaemia (P< 0.001) and in those with expression of myeloid markers than those without expression of these markers. Analysis of relapsed cases indicated that abnormally increased WT1 gene expression levels were associated with increased risk of relapse.

Conclusion: We concluded that WT1 gene expression in childhood acute lymphoblastic leukaemia was very variable and much more expressed in T cell ALL and relapsed patients indicating a possible prognostic significance in childhood acute lymphoblastic leukaemia.

P-0053 | CHIP-SEQ Analysis Identifies B-Cell Receptor Signaling Altered by ETV6/RUNX1

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Background/Objectives: In Europe, ~6,900 children are diagnosed yearly with acute lymphoblastic leukaemia (ALL), with 25% harboring the chromosomal translocation t(12;21)(p13;q22), most likely representing the first leukemogenic event. This translocation fuses parts of *ETV6* and *RUNX1*, two essential transcription factors for regulation of hematopoiesis, to create a novel chimeric oncogene *ETV6/RUNX1*. *ETV6/RUNX1* positive cells proliferate to preleukemic clones with a differentiation block in the pro/pre-B stage of B-cell development that, after acquisition of additional mutations, may transform into full malignancy. The mechanism by which *ETV6/RUNX1* disrupts signaling in B-cell precursors is thought to rely on recruitment of corepressors and histone deacetylases to *RUNX1* target sequences in gene promoters resulting in transcriptional repression of genes normally activated by *RUNX1*. However, the precise mechanism of cellular transformation and the identity of *ETV6/RUNX1* target genes are largely unknown.

Design/Methods: *ETV6/RUNX1* oncoprotein binding sites were identified in the *ETV6/RUNX1* positive BCP-ALL cell lines REH and UoC-B6 as well as in primary patient material from children with relapsed *ETV6/RUNX1* positive ALL by chromatin immunoprecipitation followed by next generation sequencing (ChIP-Seq). Binding sites were assigned to potential target genes. Among those genes we selected genes showing in published genome wide gene expression data of REH cells altered expression levels after silencing of *ETV6/RUNX1*.

Results: We were able to identify a core gene set of 1,221 candidate target genes and 100 functionally validated target genes common to all analyzed samples. These 100 genes could be assigned to 24 significantly overrepresented KEGG pathways, with the B-cell receptor signaling pathway showing the strongest overrepresentation.

Conclusion: The results suggest that *ETV6/RUNX1* disrupts the B-cell receptor signaling pathway by a direct deregulation of *GSK3B*, *VAV1*, *CD72*, *CD79A*, *RAC2* and *CD19*.

P-0054 | Phase I Results of Mitoxantrone in Combination with Clofarabine in Children, Adolescents and Young Adults with Refractory/Relapsed Acute Leukemia

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Background/Objectives: Despite excellent outcomes in paediatric ALL, multiply relapsed patients have dismal outcomes. The prognosis for relapsed/refractory AML is also poor. Clofarabine and Mitoxantrone have proven efficacy in children with leukaemia and offer possible synergistic activity.

To determine the MTD and overall response rate of clofarabine in combination with mitoxantrone as reinduction therapy for refractory/relapsed acute leukaemia.

Design/Methods: Patients 0-30.99 yr old with ALL, AML or NHL in relapse OR induction failure were given clofarabine (escalating doses 20, 30, 35 and 40mg/m²/day) Day 1-5, in combination with mitoxantrone 12mg/m²/day on Day 3-6. Dose escalation 3+3 design. CNS prophylaxis with intrathecal liposomal AraC. Patients allowed up to 3 cycles pending response and anthracycline exposure.

Results: Total 18 patients; median Age =13 yrs (8months-23yrs); 11 ALL (3=IF, 6=Relapse 1, 2=Relapse 2), 6 AML (4=IF, 1=Relapse 1, 1=Relapse 2), 1 NHL (=PD). There were 2 Grade III/IV toxicities at Dose Level 4 (Clofarabine 40mg/m²) (1 hepatic toxicity, 1 prolonged myelosuppression) hence 3 additional patients were enrolled at Dose Level 3 (Clofarabine 35mg/m²). Median time to neutrophil recovery =24 days. Fourteen of 17 (82%) leukaemia patients achieved CR after 1 cycle of therapy. Of these, 93% achieved MRD negativity (<0.1%). Patients achieving CR went on to receive alloHSCT with continued remission at a median follow up time of 506 days (range 135-822). 1 year OS for responders =84.6% (CI95: 51.2-95.9).

Conclusion: The combination of clofarabine and mitoxantrone reinduction therapy is safe and well tolerated in children, adolescents and young adults with relapsed hematologic malignancies. The Phase I MTD of this combination has been established at 35mg/m²/dose Clofarabine. Efficacy data from the Phase I portion is encouraging with an 82% CR rate, 93% negative MRD and 84.6% 1 year OS in responding leukaemia patients. An extended multicenter Phase II Study is ongoing.

P-0055 | The Level of Histone Deacetylase 7 in Paediatric ALL and its Effect on Survival

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Background/Objectives: Leukaemia is the most common paediatric malignancy and a major cause of mortality and morbidity in children. Nearly 15,000 children are newly diagnosed with leukaemia in China each year and among them, acute lymphoblastic leukaemia(ALL) accounts for more than 75%. However, chemotherapy-related complications still remain one of the major causes of treatment failure and death. Histone deacetylases (HDACs) have been reported to be altered regulated in many tumors. With increasing focus on precision medicine, HDACs have emerged as promising therapeutic target in paediatric ALL.

Design/Methods: We detected the histone deacetylase 7(HDAC7) expression in bone marrow samples of ninety-two children with newly diagnosed acute lymphoblastic leukaemia at Beijing Children's Hospital using microarray analysis and found out the relationship between the expression level of HDAC7 and the cumulative survival rates and event occurrence.

Results: Here we find that the histone deacetylase 7(HDAC7) is upregulated in bone marrow samples in patients with ALL compared with the normal children. The patients whose expression level of HDAC7 higher than the median have lower cumulative survival rates than the underexpressed patients both in the total samples and the B-ALL patients.

Conclusion: We concluded that HDAC7 may represent as a poor risk factor of survival. HDAC7 has a potent oncogenic effect on paediatric B-ALL, indicating that its deregulation may contribute to the pathogenesis of paediatric ALL.

P-0056 | Prognostic Value of Absolute Lymphocytes Counts at the End of Induction in Childhood Acute Lymphoblastic Leukemia

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Background/Objectives: Absolute lymphocyte counts (ALC) at the end of induction is a power prognostic factor in childhood acute lymphoblastic leukaemia (ALL), while its impact factors were not identified. Previous studies focus on the protocol or ethnicity inference, and in the study, we mainly explore the influence of age on ALC.

Design/Methods: A retrospective study was carried out on the newly diagnosed childhood ALL treated in our department from April 1, 2002 to March 31, 2013. The outcome and ALC at the end of remission (D33 ALC) were reviewed. D33 ALC correlated with 5 year event free survival (EFS), cumulative incidence of relapse (CIR), and treatment related mortality (TRM) were studied. EFS and survival curves were estimated according to Kaplan-Meier method. Cox regression proportional hazards model was used to analyze the possible prognostic factor. Data were analyzed by SPSS 19.0 software.

Results: Totally, 348 cases of ALL were analyzed. The 5-year EFS of patients in low ALC group ($\leq 0.62 \times 10^9/L$, below the 25 percentile,) and high ALC group ($> 0.62 \times 10^9/L$) was $62.0\% \pm 5.8\%$ and $81.8\% \pm 1.5\%$, respectively ($P < 0.001$). The 5 years CIR in low ALC group and high ALC group was $28.0\% \pm 5.6\%$ and $15.3\% \pm 2.4\%$, and the TRM were $12.8\% \pm 3.8\%$ and $2.9\% \pm 1.1\%$, respectively. Only in the patients no more than 6 years old, 5-year EFS of low ALC group were inferior compared to those of high ALC group ($83.0\% \pm 3.2\%$ VS $45.9\% \pm 8.4\%$, $P < 0.001$). And in the patients older than 6 years old, the 5-year EFS of low ALC group and high ALC group were $76.5\% \pm 6.5\%$ and $80.0\% \pm 4.1\%$ respectively ($P = 0.717$). Low ALC was one of the independent risk factor in this study, risk ratio 1.95, 95% CI (1.22, 3.11).

Conclusion: Low ALC ($\leq 0.62 \times 10^9/L$) at the end of induction was an independent factor for poor outcome in children with ALL, especially in those no more than 6 years old.

P-0057 | Successful Treatment of Acute Biphenotypic Leukemia in Children Low-Dose Chemotherapy in Uzbekistan

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Background/Objectives: According to some authors, the optimal therapeutic approach for acute biphenotypic leukaemia may include aggressive chemotherapy and stem cell transplantation, but this is not supported by serious research. The paper assessed the effectiveness of chemotherapy protocol ALL-MB-2008 with low-dose methotrexate in the treatment of acute biphenotypic leukaemia.

Design/Methods: There were 5 patients with biphenotypic acute leukaemia. The average age of the patients was 8.4 ± 1.3 , the ratio of the gender : 2 males, 3 females. All patients had a blast cells linearly mixed immunophenotype (B + myelo), on morphological and cytochemical features of blast cells referred to lymphoblasts. An initial data: all patients spleen was less than 4 cm, initial leukocyte count was less than 30 thousand. One patient had t (9; 22) BCR / ABL p190 and t (9; 22) BCR / ABL p210 PCR, from the 15th day, for induction he received an additional imatinib 300 mg/m² daily inside.

Results: Of the 300 patients with acute leukaemia treated in children's department of the Research Institute of Haematology in Uzbekistan for the period 2014-2016. 5 patients diagnosed with acute biphenotypic leukaemia and treated with ALL-based induction regimen. Early response to the 15th day of treatment in all patients ascertained. All 5 patients had clinical remission after induction course. During induction all 5 patients had severe sepsis, bronchopneumonia. On the 36th day, all patients achieved clinical remission. The patients received consolidation chemotherapy according to plan for the intermediate-risk group with low doses of MTX 30 mg/m² intramuscularly weekly, with additional lumbar puncture with three cytotoxic drugs. A median follow-up of 15.4 months. All patients are in CCR and receive maintenance therapy.

Conclusion: ALL-based low-dose chemotherapy regimen has shown high efficacy in a significant reduction in toxicity. The use of this protocol enabled outpatient treatment.

P-0058 | Diagnostic and Monitoring of Acute Lymphoblastic Leukemia (ALL) in Children: The Role of Nasal Cytology

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Background/Objectives: Recently, it has been reported that the rhinocytogram is important to correct therapeutic approach of allergic and non allergic rhinitis. The presence of blast cells in the nasal mucosa supports the possibility of infiltration by leukaemia. In the present paper we report the role of rhinocytogram in diagnostic and monitoring of ALL.

Design/Methods: Eleven children (age from 5 to 17 years) with ALL were observed to the Pediatric Department of Second University of Naples. Nasal cytology, at diagnosis and after one week of prednisone therapy was performed by anterior rhinoscopy, by scrapings from the middle portion of the inferior turbinate. The slides were stained by May-Grunwald Giemsa and examined by a light microscope.

Results: In all patients we observed a nasal mucosa infiltration by blasts cell from 30% to 90% by rhinocytogram and a percentage of blood blasts cell ranged from 63% to 89%, at diagnosis. It is interesting to note that the rhinocytogram after one week shows a percentage of blasts in the nasal mucosa ranged by 65% to 90% whereas the percentage of blood blasts decreased to 12-32%.

The increasing importance of NC as an adjunct diagnostic tool in nasal diseases has progressively been recognized in the last decades. The modern methods of sampling, staining and interpretation have been sufficiently standardized, so that NC now represents an easy to do procedure, even in routine practice. The use of NC, in addition to the diagnosis of allergic or non-allergic rhinitis is currently providing a useful instrument for research purposes, such as the investigation of conditions less common than allergic rhinitis.

Conclusion: Our preliminary data, even if is needed a larger number of patients, allow us to confirm the importance of nasal cytology in the diagnosis and follow-up of ALL. The nasal mucosa could be a pharmacological sanctuary.

P-0059 | 25-Hydroxy Vitamin D Status among Children with Acute Lymphoblastic Leukemia

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Background/Objectives: Vitamin D status is deficient or insufficient in a significant percentage of children with cancer at diagnosis and end of therapy with prevalence ranging from 14% to 49%. Our aim was to assess vitamin D status and bone mineral density (BMD) in children newly diagnosed with acute lymphoblastic leukaemia (ALL) and to determine whether vitamin D status impact the BMD and the onset of osteonecrosis.

Design/Methods: 25-hydroxy vitamin D serum level was measured at diagnosis in 50 children newly diagnosed with ALL. Serum calcium, phosphorous, alkaline phosphatase and parathormone were also measured. BMD was assessed by lumbar spine DEXA scan which was repeated after 6 months in those with initial abnormal scan and after one year in those with normal scans. Children with insufficient or deficient vitamin D levels were treated with Vitamin D3 at a dose of 50,000 unit/week for 8 weeks followed by a daily maintenance dose of 1,000 unit. The same course of vitamin D therapy was repeated if the vitamin level was still sub-optimal after 8 weeks. History of joint pain or back pain was elicited on follow up, and the occurrence of osteonecrosis was documented.

Results: Vitamin D level was deficient in 5(10%), insufficient in 22(44%) and sufficient in 23(46%). DEXA scan was performed in 40 children at diagnosis; it was normal in 24(60%) and abnormal in 16(40%). There was no correlation between vitamin D levels and DEXA scan results. After 6 months, 6 of those labeled abnormal normalized and 6 labeled as normal at diagnosis became abnormal. At diagnosis and at one year, there was no correlation between Vitamin D levels and DEXA scans with other biochemical markers.

Conclusion: Vitamin D supplementation corrected the vitamin D levels but did not alter the bone mineral density status.

P-0060 | No Impact of Disease and its Treatment on Skeletal Health in Survivors of Childhood Acute Lymphoblastic Leukemia

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Background/Objectives: Acute lymphoblastic leukaemia (ALL) and its treatment are often implicated in adversely affecting bone health. Conflicting data in literature and paucity of studies from the developing world prompted us to study bone mineral density (BMD) profile of childhood ALL survivors.

Design/Methods: BMD lumbar spine (LS) and whole body (WB) were evaluated using dual energy x-ray absorptiometry in 65 paediatric ALL survivors and 50 age and sex matched healthy sibling controls. The comparability of BMD of cases and controls was confirmed by smoothed kernel density plots. The disease, treatment, hormonal and lifestyle related factors modulating BMD were studied using Mann-Whitney U and Student's t test.

Results: At a median duration of 7.2 years from diagnosis, cases and controls had comparable height-adjusted mean BMD Z-scores of LS (-0.67 \pm 1.11, -0.607 \pm 1.05, $P = 0.759$) and WB (-0.842 \pm 0.92, -0.513 \pm 0.97, $P = 0.627$). There was no adverse impact of disease, treatment or endocrine factors on low BMD. Proportion of overweight and obese patients were significantly higher in cases ($P =$) and BMI $> +1$ was associated with normal BMD. In addition, low calcium intake < 800 mg/day (WB, $P = 0.018$) and hypovitaminosis D ≤ 25 nmol/L (HA-WB, $P = 0.046$) predicted low BMD among cases.

Conclusion: BMD in ALL survivors and healthy sibling controls was similar. No adverse impact of treatment particularly prophylactic cranial RT (12.6 Gy) on BMD in our patient profile was reassuring. Counseling for dietary calcium intake and Vitamin D supplementation needs to be actively pursued in survivors.

P-0061 | Neurologic Complications Due to Chemo Therapy in Paediatric Patients with Lymphoproliferative Disorders - Single Center Experience

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Background/Objectives: Lymphoproliferative disorders are common childhood malignancies. Recent therapeutic advances such as polychemotherapy and intrathecal prophylaxis have improved prognosis, but complications have also increased.

Design/Methods: This study presents retrospective analyses of 18 patients with acute lymphoblastic leukaemia (ALL), non-Hodgkin lymphoma (NHL) and Hodgkin lymphoma (HL) who developed neurologic complications due to chemotherapy.

Results: From 2010 up to 2016 the diagnosis of ALL, NHL and HL was established in 137 patients in our Institute. Eighteen patients (13.1%), age between 14 months and 16 years, developed 21 neurologic complications. Among them, 11.9% ALL patients had 13; 29.2% NHL patients had 7, and 3.44% HL patients had 1 complication. Diagnosis was made upon following procedures: computed tomography (14 patients), magnetic resonance (10 patients), lumbar puncture (2 patients), MTHFR c677T mutation (1 patient) and EEG, biochemical analysis and screening for hemostasis were performed in all patients.

The most common manifestation was seizure, which occurred in 11 patients (12 episodes). The reasons for seizures were: sagittal sinus thrombosis (1 ALL patient), posterior reversible encephalopathy syndrome (3 ALL, 2 NHL and 1 HL patient), other cytotoxic effect of chemo therapy (2 NHL and 1 ALL patients), and hygroma developed after the resolution of CNS lymphoma (1 patient). Acute encephalopathy was noticed in two patients with ALL (during the induction treatment and due to hypoglycemia provoked with 6-mercaptopurine). Hemiparesis has occurred in four ALL patients and was caused due to PRES (1 patient), cerebral venous thrombosis (2 patients), and subacute leukoencephalopathy due to methotrexat (1 patient). Severe headache due to sinus venous thrombosis occurred in 2 NHL patients. Complete recovery was achieved in 15 patients (83.3%) and three patients (16.67%) developed neurologic sequelae (delayed speech development and hemiparesis).

Conclusion: Neurologic complications due to chemo therapy are not rare. By better diagnosis and effective treatment the morbidities and mortalities can be decreased.

P-0062 | Powerless and Afraid: What Using Restraint Means to Young Children with Cancer During Painful Medical Procedures

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Background/Objectives: Children's need for support is tied to their experiences of fear during times of trauma and uncertainty. The aim of this paper was to review the use of restraint with young children with cancer, from the child's perspective, during painful medical procedures.

Design/Methods: In two separate Swedish doctoral theses, 20 children (3-7 years of age) with a variety of cancer diagnosis were interviewed about their experiences of everyday life with cancer and experiences of undergoing painful medical procedures. Parents and nurses views were welcomed as complimentary to child data. Interviews were analysed qualitatively by content analyses and phenomenological and life world hermeneutic approaches.

Results: Children and parents described trauma related to the suddenly changed caring role parents' play: from caring parent to health care assistant. Parents helped restrain children and took part in painful and unpleasant procedures and treatments. Nurses described the use of restraint as sometimes necessary due to logistical constraints but also as supportive to the child. Lack of access to parents as protectors was experienced as traumatic by the child. The child felt ashamed, humiliated and powerless, having lost the right to control his/her own body.

Conclusion: From the young child's perspective, restraint is never supportive. Children require a sense of security to overcome fear. When the child seeks security in an adult, the adult's response becomes extremely important. Children need to be guided and be guided by adults, until they think: "I can manage this". Adequate support enables a caring situation characterised by mutual trust. Parents ought to be involved to help alleviate fear, but strategies for collaboration and role definition for parents and health care professionals need to be reassessed.

P-0063 | Induction Remission Response in Acute Lymphoblastic Leukemia Patients; Comparison between UKALL and Lahore Protocol at a Tertiary Care Centre

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Background/Objectives: To conduct a comparative analysis of induction response out come of Lahore Protocol and UKALL (Interim Guideline 2011).

Design/Methods: It is a retrospective descriptive study. Data of 60, ALL patients diagnosed on flow cytometry with age range 1- 16 years admitted in Pediatric Oncology Department, The Children's Hospital & Institute of Child Health, Lahore, Pakistan, (JULY 2014 to June 2015), were reviewed retrospectively for demographics, risk stratification and induction response out come. 30 patients in each group. Both groups were compared in term of early response assessment and end of induction remission.

Results: In Lahore protocol group 73% were male where as in other UKALL protocol group male and females were almost equal i.e 46% and 54% respectively. In both protocols most of the patients belong to age group 1-10 years i.e 90% in Lahore protocol & 73% in UKALL. In UKALL group almost half of the patients 46% were high risk while remaining 54% were having standard risk disease where as in Lahore protocol group 63% patients were having high risk disease.

Among patients who got chemotherapy as per UKALL group of patients, 80% were reported slow responder on day-8 and day-15 of induction bone marrow biopsy (BMB) in high risk and standard risk disease respectively, whereas in Lahore protocol 57% patients found slow responder in early response assessment done on day 8 of induction. Day zero response assessment is a part of Lahore protocol, in this data analysis 20 patients, about 67%, were having poor response to prephase steroids on D0.

On comparison of end of induction remission, it is found that approximately 77%, on Lahore Protocol achieved remission while in other group 63% were able to achieve remission.

Conclusion: Induction response of Lahore Protocol is found better than UKALL, in our setup due contextual arrangement.

P-0064 | Induction Response Assessment in Acute Lymphoblastic Leukemia : Single Centre Experience at a Tertiary Care Hospital

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Background/Objectives: Objective of this study was to determine induction response in Paediatric acute Lymphoblastic leukaemia (ALL) patients, as per UKALL interim guidelines 2011.

Design/Methods: A descriptive retrospective study, conducted from July 2015 to Dec 2015, in Pediatric Haematology/Oncology Department, The Children's hospital, Lahore, Pakistan. Children 1-16 years, diagnosed as ALL, on flow-cytometry were included. Data regarding demographics, clinical presentation, Full blood count, early response assessment (day 8/15 bone marrow), and end of induction response (D29 bone marrow) analyzed. Patients classified (NCI criteria) as standard risk (age1-10yrs, WBC <50,000) or High risk (age >10 years, WBC >50,000).

Results: Total patients were 167. M:F ratio 1.5:1. Majority 88(53%) were of 1-5 years, 50(30%) 5-10 years old. Commonest complaint was fever 155(93%), bone pain 132(79%). Hepatosplenomegaly found in 112(67%), pallor 108(65%), Petechiae/bruises 98(59%). CNS disease at presentation in 2(3%). Baseline hemoglobin <7gm/dl in 72(43%), total Leucocyte Count >50,000 in 40(24%), platelet <50,000 in 91(54%). On flow-cytometry 124(74%) pre-B ALL, 42(25%) pre T ALL and 2(01%) bi-morphic leukaemia.

Standard risk induction (Regimen A with 3 drugs) given in 78(47%), 41/78(52.5%) were rapid early response (RER) and 27/78(35%) slow early responder (SER). End of induction remission documented in 51/78(65%). High risk induction (Regimen B with 4 drugs) given in 89(53%), 57(64%) were RER, 13/76(17%) were SER, 75(84%) achieved end of induction remission. SER escalated to regimen C. Induction was completed in 161(96%), 06(3%) induction failure, and 02(01%) expired due to severe sepsis, during induction.

Conclusion: Induction response is fair especially for patients who received high risk induction. A significant number of the patient presented with massive hepatosplenomegaly and high tumour load at presentation. Prognosis can be further improved by including clinical parameters in risk stratification and better supportive care especially in developing countries.

P-0065 | Pyridoxine Plus Pyridostigmine Treatment for Vincristine-Induced Neuropathy in Paediatric Patients with Malignancies: A Single-Center Experience

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Background/Objectives: Vincristine is a vinca alkaloid used in combination with other agents in the treatment of paediatric malignancies. Neurotoxicity is well-known side effect of vincristine. In this study, we aimed to determine the results of pyridoxine plus pyridostigmine treatment for vincristine-induced neuropathy.

Design/Methods: We retrospectively evaluated 26 patients with vincristine-induced neuropathy between July 2013 and February 2016.

Results: Twenty three patients (88.5%) were acute lymphoblastic leukaemia, 1 patient (3.8%) was Burkitt lymphoma, 1 patient (3.8%) was Hodgkin disease, 1 patient (3.8%) was rhabdomyosarcoma. Of the patients, 46.2% (n=12) were male, 53.8% (n=14) were female. The median age was 68 months and the mean age was 77.2±51.6 months. Drop foot (84.6%), leg pain (88.5%), difficulty in walking (76.9%), ptosis (23.1%), autonomic findings (constipation/urinary retention) (11.5%) were observed. We detected peripheral (66.7%), cranial (3.3%), both peripheral and cranial (20%) and both peripheral and autonomic (10%) types of neuropathy. Areflexia was found in 5/26 patients, hypoactivity in 16/26 and normoactivity in 5/26. In electromyography results, motor nerve neuropathy was determined in 16/26 patients, sensory nerve neuropathy in 4/26 and sensorimotor nerve neuropathy in 6/26. Treatment with pyridoxine (150 mg/m²) plus pyridostigmine (3mg/kg p.o) was started as neuroprotective agents. When therapy response were evaluated on diagnosis, at first month and third month with WHO (sensory/motor) and NCI CTCAE (cranial /sensory/ motor/ paresthesia) scorings, a statistically significant improvement was observed in all of scores in between diagnosis and first month while only motor score was better in between first and third month. The median cumulative dose was 6 mg/m² and the mean cumulative dose was 6,12±2, 6 mg/m² on time of developing neuropathy.

Conclusion: Pyridoxine plus pyridostigmine therapy is shown to be effective clinically. Prolongation of therapy is beneficial as motor score in the third month is better than the score in the first month.

P-0066 | ETV6/RUNX1 Fusion Gene in Childhood Acute Lymphoblastic Leukemia: Cytogenetic Features and Prognostic Implications

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Background/Objectives: ETV6/RUNX1 (also known as TE/AML1) is the most frequent gene fusion in childhood acute lymphoblastic leukaemia (ALL) and is associated with favourable prognosis.

Design/Methods: We performed a retrospective analysis of B-cell ALL patients who were treated in the last five years in our department in order to investigate the incidence, the clinical characteristics and cytogenetic features of TEL-AML1 positive patients.

Results: A total of 51 patients with ALL displayed G-banded karyotypes and were informative for molecular analysis and were included for analysis. Immunophenotype analysis revealed 32 cases (62.7%) as pre-B ALL, 10 (19.6%) as common ALL and 9 (17.7%) as pro-B ALL. The TEL-AML1 fusion gene was identified in 11 patients (21.6%) of which 7 (63.6%) had pre-B, 3 (27.3%) pro-B ALL and 1 (9.1%) common ALL, with median age of 4.16 (range: 3.41-13.16 years). Median leucocyte count was $8.3 \times 10^9/L$ (range $2.6-67 \times 10^9/L$). According to the presenting features, 91% of the TEL/AML1-positive cases were enrolled in the IR group and 9% in the SR. All TEL/AML1-positive cases lacked evidence for BCR/ABL and MLL/AF4 fusion mRNAs.

No structural chromosomal changes were noted in TEL-AML1 positive children. Hyperdiploidy of 47-48 chromosomes was encountered in 18.18% (2/11) of the children with TEL-AML1 rearrangement; however, none of TEL-AML1 positive patients had hyperdiploidy of more than 50 chromosomes. All cases were predilected good responders and they were all very early good responders (minimal residual disease $<10^{-3}$ at day 15. All patients are in continuous complete remission with event-free and overall survival of 100%.

Conclusion: The ETV6/RUNX1 fusion gene is a common genetic anomaly in childhood ALL patients and our results are consistent with literature. Further investigation with a larger sample size and for a longer time is warranted.

P-0067 | Acute Lymphoblastic Leukemia Debuts as Right-Sided Infective Endocarditis in Two Children of Colombian Caribbean Coast

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Background/Objectives: Right-sided infective endocarditis (RSIE) represents 5%-10% of all infective endocarditis (IE) in adults, it occurs less frequently in children than adults and very rarely encountered among patients with leukaemia. (Yen-Ting, Kai-Shen et al 2013) (Keino, Tszuki et al 2015). We report two cases of RSIE without congenital heart disease due *Staphylococcus aureus* in patients with *novo* acute leukaemia.

Design/Methods: This is a case report.

Results: In 6 months We had 2 cases of patients with Acute Lymphoblastic Leukaemia (ALL) who debuted with IE.

Case 1: a 12-years-old girl with a depression, bulimia and suicide attempts without known disease, who presents with vomiting, diarrhea fever and history of trauma in the left trip by falling. Who developed respiratory distress, dizziness, hypotension and shock. Then she presented bilateral pneumonia complicated with pleural effusion and cellulitis in her left hip. Methicillin-Resistant *Staphylococcus aureus* (MRSA) was isolated from blood cultures and the echocardiogram showed a vegetation on the tricuspid valve without regurgitation. For the continuing bicytopenia was performed bone marrow aspiration diagnosed with ALL. She received 6 weeks of treatment with vancomycin and then began chemotherapy cycle.

Case 2: a 5-years-old girl presents fever, dizziness, respiratory distress, leukemoid reaction with bicytopenia. She develops shock with bilateral pneumonia and hepatosplenomegaly, positive blood cultures for MRSA and urine cultures for *Escherichia coli* producing extended-spectrum beta-lactamases. Echocardiography showed vegetation in the tricuspid valve without regurgitation until now she is being treated with vancomycin and meropenem.

Conclusion: IE has an incidence of 0.5% among hematological malignancy complicated with sepsis by *S. aureus*. It is not clear why IE rarely develops in patients with ALL, both has an extremely high risk of mortality, and requires early diagnosis and appropriate treatment.

P-0068 | Should We Routinely Supplement Calcium and Vitamin D for Children with Acute Lymphoblastic Leukaemia (ALL) and Osteoporosis?

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Background/Objectives: Fractures due to osteoporosis can be a presenting feature of ALL or seen as the consequence of treatment (glucocorticoids, methotrexate, mercaptopurine). We are presenting three cases of children with ALL on treatment who developed fractures whilst on maintenance treatment and reviewed literature about the routine supplementation of vitaminD and calcium to these children in developing countries.

Design/Methods: During maintenance treatment as per UKALL 2003 protocol three children presented with fractures with history of trivial fall. A 5 yrs old girl and 2 yrs old boy developed fracture of the lower end of humerus and 12 yrs old boy developed vertebral fracture. Their radiographs showed significant osteoporosis. They were poorly nourished from the beginning.

We reviewed the literature whether any role for routine supplementation of Vitamin D and Calcium.

Results: All three children have had osteoporosis. A 12 yrs old boy has been on maintenance treatment for 6 months developed vertebral fractures, when evaluated for back pain, 5 yrs old girl fractured her left humerus with a trivial fall and 2 yrs old boy developed left humerus fracture. All of them have been started on calcium and vitamin D supplement. Their vitamin D levels were low (18, 21 and 16 ng/mL) at the time of detection of fracture. They did not have any prior X rays. On detailed literature review Bone II study showed routine Supplementation of calcium and vitamin D may have some role in mineralisation of bones in children. However Kaste et al. showed no improvement with supplements.

Conclusion: In developing countries poorly nourished children at diagnosis may benefit from supplementing calcium and vitamin D whilst receiving treatment for ALL. Though there are conflicting reports of benefit of supplementing in mineralisation of the bones further studies required to come to conclusion one way or the other.

P-0069 | The Varicella Zoster Virus Immunoglobulin G and the Varicella Zoster Virus Infection in Children with Cancer Under Chemotherapy

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Background/Objectives: The varicella zoster virus (VZV) is known to be fatal especially for immunocompromised patients receiving chemotherapy for childhood cancer. So we investigated the change of varicella zoster virus immunoglobulin G (VZV IgG) before and during chemotherapy in patients who suffered from chicken pox (CP) or herpes zoster (HZ) to find the relationship between them.

Design/Methods: We reviewed the transition of VZV IgG through medical records in children with cancer who experienced CP or HS during chemotherapy for 10 years in Kyungpook National University Hospital, Daegu, South Korea.

Results: We checked VZV IgG not only when they were diagnosed as cancer but also when they were receiving chemotherapy for 66 patients (VZV IgG (+) : VZV IgG (-) = 40 : 26). Among initial VZV IgG positive group, 28 patients showed sustained positive IgG during chemotherapy, and 6 patients underwent the disease (CP : HZ = 1 : 5). On the other hand, 12 patients showed negative IgG while chemotherapy and 8 patients experienced the disease (CP : HZ = 4 : 4). The seronegative group after chemotherapy showed higher morbidity of CP or HZ compare to seropositive group (p=0.011) (Fig-1). In the case of VZV IgG negative group at diagnosis, 8 patients presented seroconversion to positive IgG and they had no disease of VZV. Among them, 18 patients who showed still negative IgG developed 4 (CP : HZ = 2 : 2) (Fig-2). All together, the seronegative group revealed the tendency of higher morbidity (p=0.034). We treated them using intravenous acyclovir, and no mortality was observed.

Conclusion: Because of higher frequency of CP or HZ in VZV IgG negative group during chemotherapy, it is important to decide when and for whom to carry out VZV vaccination during chemotherapy through regular VZV IgG checking.

P-0070 | CNS Outcomes of Paediatric Acute Lymphoblastic Leukemia with T(1;19)/TCF3-PBX1 in Taiwan Different from Caucasian

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Background/Objectives: t(1;19)/TCF3-PBX1 is one of the frequent translocations in childhood ALL. It has been described to be associated with CNS leukaemia in Caucasian. We sought to examine the CNS outcomes of paediatric t(1;19)/TCF3-PBX1 ALL in Taiwan.

Design/Methods: Between 2002 and 2012, all children with ALL <18 y/o were enrolled in Taiwan Pediatric Oncology Group-2002-ALL studies (Leukaemia 2010). t(1;19)/TCF3-PBX1 was detected by karyotyping and/or RT-PCR assay. As a rule, t(1;19) patients were treated with high-risk (standard-risk in other studies) protocol. All patients received twice triple intrathecal therapy (TIT) in remission induction and TIT alone without cranial radiation during treatment (J Clin Oncol 2014) since 2009. The differences in CNS leukaemia at diagnosis, relapse pattern, and the survivals between patients with t(1;19)/TCF3-PBX1 and those without were analyzed.

Results: Among the 1,173 patients examined, 64(5.5%) had t(1;19)/TCF3-PBX1. t(1;19) patients were older (P = 0.016) and less anemic (P = 0.003). At diagnosis, 3% of t(1;19) ALL had CNS2 and 5% CNS3 compared with 4% CNS2 and 2% CNS3 in non-t(1;19) (P = 0.37). No differences were observed with respect to sex, WBC or platelet counts, and presence of

hepatomegaly or splenomegaly between t(1;19) and non-t(1;19) groups. t(1;19)/TCF3-PBX1 ALL tended to have a better 5-y OS than other B-precursor ALL: 88.5% vs. 82.7% ($P = 0.11$), and 5-y EFS: 83.3 vs. 75.3% ($P = 0.11$). Isolated CNS relapse occurred in 3 of t(1;19) group vs. 42 in non-t(1;19) group ($P = 0.76$); any CNS relapse 4 vs. 44 ($P = 0.41$); isolated BM 6 vs. 191 ($P = 0.08$); isolated testes 1 vs. 10; BM plus testes 0 vs. 1.

Conclusion: t(1;19)/TCF3-PBX1 ALL in Taiwan did not have increased risk of CNS leukaemia either at diagnosis or relapse and thus there is no need to intensify TIT.

P-0071 | Interval between Intra-Thecal Methotrexate and Intra-Venous Cytarabine does not Affect Incidence of Methotrexate Induced Neurotoxicity in Children with Acute Lymphoblastic Leukaemia

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Background/Objectives: Intra-thecal (IT) methotrexate can cause neurotoxicity, manifesting as encephalopathy, stroke-like episodes or seizures. Same day administration of IT methotrexate and IV cytarabine may increase risk of neurotoxicity.

The objective is to compare incidence of methotrexate induced neurotoxicity for same day versus consecutive day IT methotrexate and IV cytarabine dosing schedule.

Design/Methods: At the Royal Marsden Hospital (RMH) during UKALL2003 clinical trial patients received IV cytarabine and IT methotrexate on the same day. In the UKALL2011 trial, dosing was changed to consecutive days. Patients, who developed methotrexate induced neurotoxicity prior to starting maintenance on either trial were identified from the Serious Adverse Events database. Data collected: demographics; time-point of methotrexate induced neurotoxicity; number of IT methotrexate within 24 hours of IV cytarabine and total number IT methotrexate.

Results: Of 271 patients treated on the UKALL2003 protocol, 9 patients developed methotrexate induced neurotoxicity. The incidence per IT methotrexate dose was 0.24% (9/3679). Seven of these patients developed it within 30 days of IT methotrexate and same day IV cytarabine, incidence 0.54% (7/1299).

Of 94 patients on UKALL2011 trial who, to date, have reached the start of maintenance, 1 patient developed methotrexate induced neurotoxicity. The incidence per IT methotrexate dose was 0.10% (1/963) and incidence within 30 days of IT methotrexate and consecutive day IV cytarabine was 0.48% (1/208).

There is no statistically significant difference in incidence of methotrexate induced neurotoxicity between same day dosing (UKALL2003) and consecutive day dosing (UKALL2011) when comparing the number cases per IT methotrexate dose received at a proximate timepoint to IV cytarabine ($p=0.92$, χ^2) or per the total number of IT methotrexate ($p=0.40$, χ^2).

Conclusion: Separating IT methotrexate and IV cytarabine onto consecutive days results in an increased number of hospital visits for patients. The data, so far, does not demonstrate statistically significant reduction in methotrexate induced neurotoxicity with this change.

P-0072 | Monosomy 7 in Childhood Acute Lymphoblastic Leukaemia (ALL)

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Background/Objectives: Monosomy 7 is a rare cytogenetic abnormality in paediatric patients with ALL, with unclear prognostic significance when treated on UK protocols. Traditionally monosomy 7 is identified by karyotype; additional Fluorescence *In Situ* Hybridisation (FISH) can be performed to enhance the cytogenetic description.

Design/Methods: Demographics, relapse and survival outcomes were obtained for all patients age < 19 years with ALL, diagnosed at the Royal Marsden Hospital, England from March 2000 – March 2016. Monosomy 7 was identified by G-banded chromosome analysis. FISH using Vysis probes D7S486 (at 7q31) and CEP7 (at 7 centromere) was performed when possible.

Results: Of 744 patients with ALL, 17 (2.3%) patients had monosomy 7 on G-banded chromosome analysis. Four patients with concomitant, recognised, high-risk cytogenetic abnormalities were excluded.

FISH data were available for 8/13 cases. True monosomy 7 was confirmed in two cases, five cases found chromosome 7 material on marker or ring chromosomes, unidentifiable by karyotype, and hybridisation failed in one case. From five cases without FISH, two had simple monosomy 7 karyotype with no unidentifiable material in the clone. Thus 4/13 had secure monosomy 7.

Event free survival at 5 years was significantly worse for patients with monosomy 7 by karyotype, 2/8 (25%) versus 387/493 (80.2%) for patients without monosomy 7 by karyotype, $p=0.0003$ (χ^2). No significant difference was found in overall survival.

Of the 4 patients with secure monosomy 7, 3 patients have relapsed including one death from secondary Acute Myeloid Leukaemia.

Conclusion: True monosomy 7 in ALL may be more rare than previously supposed based on karyotype alone. It is important to confirm full loss of chromosome 7 by FISH if there is unidentifiable material in the clone.

In this small series, event-free survival was significantly worse for the patients with apparent monosomy 7, and particularly poor if true monosomy 7 is confirmed.

P-0073 | The Isoform II of SRSF1: A Potential Biomarker in the Progression of Paediatric Acute Lymphoblastic Leukemia

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Background/Objectives: Acute lymphoblastic leukaemia (ALL) is the most frequently occurring malignant neoplasm in children. Despite advances in treatment and outcomes for ALL patients, the pathogenesis of the disease remains unclear. Alternative splicing modulates the expression of many oncogene and tumour-suppressor isoforms. SRSF1, a prototypical SR protein has been recognized as an oncoprotein. SRSF1 has been reported to be auto-regulated into multiple isoforms that differ in function in various physiological or pathological conditions.

Design/Methods: Matched, newly diagnosed (ND), complete remission (CR) and relapse (RE) bone marrow samples from 50 patients were collected in order to evaluate the expression patterns of SRSF1 spliced isoforms. The clone formation assay was investigated in leukaemia cell lines.

Results: Both in mRNA and protein level, we identified significant up-regulation of the three main spliced isoforms of SRSF1 and the isoform II is the main variant in the ND samples. Importantly, the expression of three isoforms of SRSF1 returned to normal levels after CR. But the protein isoforms rebound in the RE samples, and the isoform II is high expressed a short-term state prior to morphological or immunological change in the RE cases. We also observed the isoform II can promote significantly to the formation of cell clones.

Conclusion: Our results indicate that the alternative splicing of SRSF1 may play a critical role in leukemogenesis in paediatric ALL, and the isoform II may be a sensitive predictor of relapse and a potential target for the anti-leukemic therapy.

P-0074 | Quality and Quantity of NK Cell Ligand Expression on Tumour Cells Impact Overall Survival of Childhood Acute B Lymphoblastic Leukemia

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Background/Objectives: Consistent with the “missing self” hypothesis, NK cells sensing the loss of self-HLA-class-I (HLA-I) through inhibitory killer cell immunoglobulin-like receptors (KIR) play an important role in tumour immunosurveillance. NK cell function is tuned by inhibitory (iRec) and activating (aRec) receptors, so that quality and quantity of their ligands on the tumour cells can effectively modulate NK cell response. KIR2DL1-3 iRec and KIR2DS1/2 aRec bind HLA-C, KIR3DL1 iRec and KIR3DS1 aRec bind HLA-Bw4 alleles and KIR3DL2 binds HLA-A3/A11 ligands.

To evaluate the role of tumour KIR-ligand/NK-cell interactions on childhood acute B lymphoblastic leukaemia (B-ALL) three-year overall survival (3yOS).

Design/Methods: KIR and KIR-ligand genotype (Luminex) and expression level of HLA-I and HLA-C ligands by flow-cytometry were evaluated at diagnosis in thirty childhood B-ALL and forty-three sex and age matched controls. To evaluate increase/decrease of HLA ligands, mean fluorescence intensity (IMF) of ligands on tumour cells were normalized with the expression on residual healthy lymphocytes.

Results: No differences in the genetic frequency of either iRec/aRec KIRs or HLA-C1/C2, HLA-A3/A11 and HLA-Bw4 ligands were found between controls and B-ALLs. Although, neither SEHOP-PETHEMA-2013 risk-stratification nor day-14 minimal-residual-disease impacted 3yOS, both higher number of iKIR/ligand interactions (> 3 iKIR/ligand interactions) (62.5% vs. 96.2% 3yOS, $p<0.01$) and decreased membrane expression of total HLA-I (77.0% vs. 95.5% 3yOS, $p=0.07$) and HLA-C (75.0% vs. 100% 3yOS, $p=0.019$) on tumour cells negatively impacted patient 3yOS. Cox regression analysis confirms that the number of iKIR/ligand interactions (OR=10.5; $p=0.042$) is an independent prognostic factors in childhood B-ALL.

Conclusion: Although these results should be confirmed in larger series, both the number of iKIR/ligand interactions and the expression level of KIR-ligand on tumour cells could modulate NK cell immunosurveillance of B-ALL, which apparently have an impact on patient survival.

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P-0075 | Children with Acute Lymphocytic Leukemia on Youtube

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Background/Objectives: YouTube is one of the most popular social media channels on the Internet. This exploratory study examines YouTube videos of young children with acute lymphocytic leukaemia (ALL) in terms of information provision, personal experience, and psychosocial support.

Design/Methods: A fixed phrase search, “acute lymphocytic leukaemia”, was entered in the search box on the YouTube site home page, <https://www.youtube.com/>. A wide range of videos on this form of cancer were retrieved. The search results were narrowed by including additional search terms – children, living, fighting, parents, care, and caring – to retrieve cancer narratives and exclude clinical education videos about ALL. Six YouTube videos on children with ALL produced by American hospitals were viewed online.

Details concerning video production (video length, narrators and settings); biomedical aspects of cancer (symptoms, diagnosis and treatment); psychosocial support (parents, siblings, and clinicians); personal experience (e.g. feeling worried) were recorded and examined for themes.

Results: The six YouTube videos of children with acute lymphocytic leukaemia produced by American hospitals are narrated primarily by the patient's parents with participation from the cancer patient, siblings and hospital clinicians. Several symptoms are noted by the parents but are not consistently mentioned. Treatment with chemotherapy is consistently mentioned.

Parental feelings of concern are mixed with their confidence in the skills of the clinicians and the hospital. Children and parents mention caring hospital staff while clinicians express confidence in the treatment regimen and prognosis.

Conclusion: YouTube videos of children with acute lymphocytic leukaemia produced by American hospitals reveal common themes. The overall message is that current treatments for this childhood cancer administered in the hospital by experienced and caring clinicians can provide a positive outcome.

P-0076 | Longitudinal Assessment of Change in the Nutritional Status of Children Treated for Acute Lymphoblastic Leukaemia

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Background/Objectives: Assessment of nutritional status is important to plan appropriate nutritional support for children during chemotherapy. This study was done to assess the nutritional status of children underwent treatment (ALL) from diagnosis through treatment and beyond.

Design/Methods: 195 children, aged more than 2 years at diagnosis were included in this analysis. Weight and height of these subjects taken at diagnosis, beginning of delayed intensification (DI) and maintenance phases (M), end of treatment (EoT) and annually thereafter, were used to calculate Body Mass Index (BMI). Based on CDC- BMI charts, they were divided into undernourished (UN), well-nourished (WN) and overweight/obese (OW-O).

Results: At the time of diagnosis 85(44%) were UN, 96(49%) WN and 14 (7%) were OW-O. The number of under nourished children reduced to 57(29%), 37(19%) and 25(13%) at DI, M and EoT respectively. The incidence of well-nourished children were 59%, 64% and 58% during the same time points. Those who became OW-O increased from 7% at diagnosis to 12%, 17% and 29% at DI, M and EoT respectively.

At one year follow up of 185 children, 16/25 remained UN, 1/25 moved from UN to OW-O. Of the 107 WN, 7 became UN and 11 became OW-O. Of the 53 OW-O 42 remained the same, 9 moved to WN and 2 became UN. During 2nd, 3rd and 5th year follow up of 145, 81 and 34 children, the percentage of UN ranged between 9-15%, WN 47-50% and OW-O 35-43%.

Conclusion: Nutritional status of children change during the course of treatment of ALL and in the post treatment phase. Accurate assessment nutritional status is required to optimize nutritional support for children with ALL.

P-0077 | Relevance Changes in Genes Involved in Acute Lymphoblastic Leukemia Patients

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Background/Objectives: Cytogenetics of B-cell precursor acute lymphoblastic leukaemia (BCP-ALL) is the well-recognized strategy for diagnosis and follow up of the patients with acute lymphoblastic leukaemia. Copy number alterations (CNAs) genes involved in B-cell precursors have been related with poor survival in BCP-ALL.

Design/Methods: In this study, we collected 60 peripheral blood or/and bone marrow samples from BCP-ALL Iranian children patients aged 1-12years. DNA was extracted using Qiagen kit, the next phase, all target genes such as EBF1, PAX5, CDKN2A, CDKN2B, BTG, ETV and others was evaluated for all samples by MLPA (kit p335,MRC Holland), and assessment their correlation with clinical and laboratory finding.

Results: Deletions/amplifications in at least one gene were identified in 60% of the total samples. Finding some relationship between these genes, such as superiority of CNAs involving deletions in CDKN2A/B and pseudoautosomal region 1 (PAR1) area or there are significant relationship between both IKZF1 (P<.05) and CDKN2A (P<.05) among key genes in gene expression and higher risk relapse risk in these patients relationship between IKZF1 and poor outcome.

Conclusion: This study has demonstrated that the pattern of CNA is highly variable according to the primary genetic abnormality in children with B-cell precursor acute lymphoblastic leukaemia. The obtained results corroborate with previous genome-wide studies and aggregate new markers for risk stratification of BCP-ALL in Iran. We showed that (MLPA) provided a reliable method to screen CNA in genes which key role in the development of BCP-ALL.

P-0078 | Venous Occlusive Disease in Children on Chemotherapy Outside Bone Marrow Transplant Setting Responds to Defibrotide

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Background/Objectives: Venous Occlusive Disease (VOD or sinusoidal obstruction syndrome -SOS-) damages small hepatic vessels, especially the sinusoidal endothelium and predominantly occurs in bone marrow transplant (BMT) setting. Diagnostic criteria are modified Seattle (two of following: bilirubin >34.2µmol/l, hepatomegaly or right-upper-quadrant (RUQ) pain, weight-gain >2%) or Baltimore (bilirubin >34.2µmol/l and two of following: hepatomegaly, ascites, weight-gain >5%). Gold standard of treatment is defibrotide (6.25 mg/kg IV QDS), until symptoms resolve.

We report five patients with VOD outside BMT setting responding to defibrotide.

Design/Methods: Patients' ages were 1, 6, 18 months and 14 years (n=2), diagnoses included undifferentiated sarcoma, infant AML (n=2), biphenotypic leukaemia and stage IV neuroblastoma. Patients' criteria were assessed by physical examination and abdominal (Doppler) ultrasound. Defibrotide treatment was administered as indicated above.

Results: Observed symptoms were: ascites with weight-gain (n=5), hepatomegaly (n=4), reversed portal flow with hyperbilirubinemia (>80 µmol/l, n=3), hyperbilirubinemia (35 and 69 µmol/l) without reversed flow, RUQ pain (n=3, not observed 2 patients <1yr).

Three patients responded to defibrotide with normalization of diagnostic criteria. Median duration of treatment was two weeks (range 1-3). In one patient treatment was ceased after one week due to hypertension (>p95), after partial response and further normalisation off treatment. The other patient showed normalisation of the portal flow, however succumbed to multi-organ failure by uncontrollable infection, before the other criteria had normalised.

Four recovered patients restarted chemotherapy regimens with the presumed contributing drug without relapsed VOD, in one patient under defibrotide prophylaxis. The associated chemotherapy agents were: actinomycin D, 6-thioguanine, etoposide and melphalan.

Conclusion: VOD can occur in patients on chemotherapy outside the BMT setting, responds to defibrotide and should thus be part of the differential diagnosis when hepatotoxicity is observed. Symptoms do not tend to occur at chemotherapy restart.

P-0079 | A Case of Acute Myelopathy after Intrathecal Chemotherapy in a Patient with Acute Lymphoblastic Leukemia

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Background/Objectives: Myelopathy is a rare but fatal complication of patients with acute lymphoblastic leukaemia after intrathecal chemotherapy administration. Investigation regarding this condition is still limited.

Objectives: To describe the presentation and evolution of a patient with acute lymphoblastic leukaemia who developed myelopathy.

Design/Methods: Case presentation. A four year-old patient with acute lymphoblastic leukaemia negative for central nervous system infiltration at diagnosis debutes with decreased strength and mobility of the lower limbs and impaired postural tone control after intrathecal administration of Methotrexate and Dexamethasone.

Results: Lumbar MRI showed an enhancement of the meninges at the medular cone and of all the roots of the horsetail. Cerebrospinal fluid cytology and flow cytometry was negative for leukaemia infiltration. Electromyography and somatosensory evoked potentials confirmed the presence of acute-subacute motor axonal polyneuropathy, probably secondary to intrathecal chemotherapy. Treatment with steroids was initiated with mild improve of symptoms. Leukaemia still in remission. Actually patient receives intrathecal Cytarabine for CNS prophylaxis.

Conclusion: Although rare, myelopathy is a possible adverse event of intrathecal or systemic chemotherapy. Risk factors for its development should be established and managed carefully previous to drug administration.

P-0080 | Acute Lymphoblastic Leukemia in Adolescents: Differences in Clinical Findings, Biological Features and Outcome in Comparison with Younger Children

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Background/Objectives: Acute lymphoblastic leukaemia (ALL) is the most common cancer in paediatric age. Children older than 10 years of age (adolescents) have been reported as having a poor prognosis compared to younger children, achieving lower survival rates.

Objectives: To compare clinical and biological features at diagnosis and the outcome of adolescents (10-17 years of age) versus patients younger than 10 years of age.

Design/Methods: From December-2002 to January-2016, 668 eligible ALL patients were diagnosed at our hospital: 500 of them were between 1-9 years-old and 168 were adolescents. They were treated with two consecutive protocols: ALLIC-2002 (63%) and ALLIC-2009 (37%). Adolescents group account for 25% in both studies. We analyzed sex distribution, presence of hyperleukocytosis (>100,000 WBC/mm³), immunophenotype and cytogenetic/molecular findings, assessing the association between patient characteristics in both groups using X2-test. EFSp (SE) was calculated according to Kaplan-Meier and compared using log-rank test.

Results: The analyses showed that adolescent patients presented a statistically significant higher proportion of: WBC count (p=<0.00001), presence of hyperleukocytosis (p=0.0001), T-immunophenotype (p=<0.00001), hypodiploid cases (p=0.0167) and CNS compromise (p= 0.0074) at the moment of diagnosis. However, non-adolescent group disclosed a statistically significant higher proportion of: B-immunophenotype (p=<0.00001), hyperdiploidy (p= 0.0009) and TEL/AML1 (p=<0.00001) cases. Risk distribution showed a higher proportion of high-risk patients in the adolescent group (p=0.013). Regarding response to treatment, not statistically significant differences were observed in response to prednisone, CR and deaths during induction rates. However, adolescents presented a statistically significant superior death in CR

rate ($p=0.0097$) mostly due to infections. EFSp (SE) was 63 (4)% for adolescents and 79 (2)% for the non-adolescent group ($p<0.00001$).

Conclusion: We confirmed that adolescents with ALL present biological features associated with a more aggressive disease and higher morbidity-mortality rates, which results in an inferior survival rate, mainly due to toxic deaths.

P-0081 | Improving Situational Awareness in Elective Paediatric Oncology Theatre Lists Within A Ward Environment

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Background/Objectives: Our aim is to constantly strive for the highest quality care we can achieve and to reduce avoidable error and harm to children through the development of a proactive safety culture. Participation in the RCPCH SAFE (Situational Awareness For Everyone) project has enabled proactive change management and the introduction of a number of safety initiatives within our tertiary oncology day-ward setting.

Design/Methods: Consultation identified a key area of perceived vulnerability to be the satellite twice-weekly elective lumbar puncture, intra-thecal and bone marrow lists. Recent staff changes had created unwarranted variability in practice and a baseline staff survey identified areas for improvement in terms of consistency of delivery of the service.

Results: After initial stake-holder engagement, introducing the tenants of situational awareness several initiatives were embraced:

- 1) Introduction of a "huddle" or morning safety brief prior to each list. Key members of the team now meet for 3-5 minutes prior to commencing the list using a structured aide memoire to discuss safety concerns and identify potential issues.
- 2) Introduction of a multi-disciplinary safety checklist.
- 3) Standardised patient clerk-in paperwork for procedures.
- 4) Introduction of improved two-way communication flow between day-ward and the ward.

Subjective reporting indicates that the overall level of satisfaction with the processes has markedly improved. The formal safety survey will be repeated in 6 months to assess this.

Conclusion: Participation in the RCPCH SAFE project has enabled proactive change management and the introduction of a number of safety initiatives within our tertiary oncology day-ward setting. The main aim of our work to date has been to tighten the processes and procedures to reduce variation and therefore improve patient safety. The new checklist and huddle process are now embedded in our clinical practice and have been met with increased staff satisfaction. Ongoing improvement cycles will measure and modify the checklist as required.

P-0082 | Programmed Cell Death Protein-1 (PD-1) and its Ligands Expression Levels in Children with Acute Lymphoblastic Leukemia and their Implications for Glucocorticoid Resistance

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Background/Objectives: Programmed death-1 (PD-1) is expressed upon activation in mature hematopoietic cells such as T and B cells. Binding to its ligand (PD-L1), PD-1 inhibits T-cell response and plays a role in peripheral tolerance. PD-1 function in tumour cells is not known. But increased expression of PD-L1 was shown in hematological malignancies.

Glucocorticoids have been used in chemotherapy regimens of leukaemia for their lympholytic effect. Glucocorticoid resistance remain as an important problem and the exact mechanism has not been elucidated. Glucocorticoid resistance is determined by blast count of the 8th day of therapy.

We aimed to determine expression levels of PD-1, PD-L1 and its variant in paediatric Pre-B ALL and to evaluate the relationship with clinical parameters and development of glucocorticoid resistance.

Design/Methods: Five paediatric Pre-B ALL patients aged between 1-6 were included to the study. The blood samples were drawn at diagnosis and the 8th day of the glucocorticoid treatment. The RNAs were isolated by using Biotic Stabilized Blood RNA isolation kit. Expression analysis was performed by qRT-PCR and SybrGreen on Light Cycler 480II (Roche). Results were analyzed by Basic Relative Quantification software (2^{-ΔΔCt}-method).

Results: There is an important increase observed in PD1 expression in patient 3 at day 8 compare to day 0. We determined increase in PD-L1 expression at day 8 in the three out of five patients and one of them was striking. Decrease expression in splicing variant of PD-L1 was detected in four out of five patients at day 8. There is no relationship was observed with clinical characteristics of the patients and their glucocorticoid resistance status.

Conclusion: The results showed increased expression of PD-L1 and decreased expression of its variant with glucocorticoid therapy. We did not detected relationship with glucocorticoid resistance status. We are planning to repeat experiments in larger group to confirm our results.

P-0083 | Splenic Infarction and Branch Portal Vein Thrombosis Secondary to PEG-Asparaginase

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Background/Objectives: PEG-asparaginase leads to plasma asparagine depletion and hepatotoxicity causing decreased synthesis of pro-coagulant and anti-coagulant proteins. Thrombotic

complications have been reported in 3-5% of paediatric patients, with majority of the events related to either central nervous system or central venous catheters (CVC).

Design/Methods: Case report of a rare thrombotic event following PEG-asparaginase administration and brief literature review.

Results: An 18-year-old male with a poorly-differentiated lymphoblastic leukaemia (favoring T-cell) was treated with four drug induction regimen (prednisone, daunorubicin, vincristine and PEG-asparaginase). Five days following PEG-asparaginase, Doppler ultrasonography showed an acute occlusive superficial cephalic vein thrombus. Simultaneously, he also developed cramping epigastric/abdominal pain. Computed tomography imaging performed 12 days after PEG-asparaginase administration showed a moderate/large splenic infarct and portal vein branch thrombosis. At our institution, fibrinogen levels, antithrombin (AT) activity, prothrombin time (PT/INR) and activated partial thromboplastin time (aPTT) are monitored following PEG-asparaginase administration in adolescents and young adults. His evaluation two days prior to detection of the splenic infarct showed low fibrinogen (<50 mg/dl), elevated INR (2.8; range 0.8-1.2 sec) and aPTT levels (59 sec; range 28-38 sec). Following imaging studies, additional labs included low AT activity (44%; range 80-130%). Management was supportive with blood products. Eleven days later, imaging studies revealed worsening splenic infarct and a new CVC related acute deep vein thrombosis. Low molecular weight heparin was started (target heparin level of 0.5-1.0 IU/ml). Antithrombin concentrates and cryoprecipitate were administered when AT activity <60% and fibrinogen <50 mg/dl respectively, and PEG-asparaginase therapy was continued. No further thrombotic or bleeding complications were observed.

Conclusion: Adolescents and young adults receiving PEG-asparaginase are at increased risk of thrombosis and bleeding. Monitoring of PT, aPTT, fibrinogen, and AT activity is recommended. In patients with abnormal laboratory evaluation and thrombosis, further PEG-asparaginase can be safely administered with appropriate anticoagulation in combination with AT and fibrinogen replacement therapy.

P-0084 | A Study to Find Out the Problems Faced by Young Adult Survivors of Childhood Malignancies in a Tertiary Cancer Centre

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Background/Objectives: 1. Identify physical problems faced by survivors.

2. Describe psycho social problems of survivors.

3. Find out association between problems faced and selected demographic variables.

Design/Methods: Research Methodology:

A descriptive research design was used. Participants of the study were selected by nonprobability convenient sampling. 71 survivors who came for yearly follow up in the Out Patient Department during 6 weeks period of data collection, who were above the age of 18years and were diagnosed before the age of 15years, were selected. Researcher conducted face to face interview using semi-structured questionnaire. Section I included questions with regard to participant's personal demographic data, family's demographic data. Medical data which was collected from the database. Section II, included questions related to physical, psycho-social problems. General Health Questionnaire 12 to assess the level of psycho-social distress. The data was analysed using descriptive analysis, chi-square was used to show the association between problems and selected demographic variables. Analysis was done using computer software.

Results: Participants had concerns about their growth and development almost 29.6% had concerns of low height, 39.4 were underweight and complained inability to gain weight. About 49.3% had less than 5 physical problems while 46.5% had more than 5 physical problems, only 4.2% reported as having no problems. The General Health Questionnaire 12 score for psychosocial distress was below 5 for 53.5% which indicate no psychological distress whereas 46.5% had GHQ12 score above 5 indicating psychological distress. The association between physical problems and GHQ12 score was statistically significant with 'p' value =0.043 at 0.05 level of significance.

Conclusion: The study shows that majority of young adult survivors of childhood malignancies will have at least one physical problem during his/her lifetime. There should be measures to detect these problems at the earliest level so that quality of life of survivors is not compromised.

P-0085 | Childhood Acute Lymphoblastic Leukemia in Kenya

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Background/Objectives: Acute lymphoblastic leukaemia (ALL) is the most common paediatric malignancy accounting for 25% of childhood cancers. In high-income countries, survival rates have steadily increased to more than 80% over the last three decades. In low-income countries however, survival rates remain low illustrating the global inequalities in health. This study explored treatment outcomes of ALL patients at a Kenyan academic hospital, and the influence of various socio-demographic and clinical characteristics on treatment outcomes.

Design/Methods: This was a retrospective medical records study. All children diagnosed with ALL between 2010 and 2012 were included. Data on treatment outcomes and various socio-demographic and clinical characteristics (age at diagnosis, gender, duration of symptoms, distance to hospital, and health-insurance status) were collected.

Results: From 2010 until 2012, 44 children were diagnosed with ALL. The most common cause of treatment failure was progressive or relapsed disease, which occurred in 16 (36%) children: progressive disease (n=3), and relapse (n=13). Relapses occurred: during treatment (n=10), and after completion of treatment (n=3). Twelve (27%) children abandoned treatment: prior to start treatment (n=0), and during treatment (n=12). Ten (23%) children died during the following phases: prior to start treatment (n=1), induction (n=8), and consolidation (n=1).

Cause of death was: malignancy-related (n=7), treatment-related (n=2), and unspecified (n=1). In total, 6 (14%) children had event-free survival. Age at diagnosis, gender, duration of symptoms, distance to hospital, and health-insurance status did not significantly influence treatment outcomes and event-free survival estimates.

Conclusion: Survival rates of childhood ALL in Kenya are much lower than those in high-income countries. Progressive or relapsed disease was the main reason for ALL treatment failure. These findings warrant urgent attention and future in-depth analysis.

P-0086 | MIR-1206 Micro-RNA Variant is Associated with Methotrexate-Induced Mucositis in Paediatric Acute Lymphoblastic Leukemia

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Background/Objectives: 5-year survival rates of paediatric acute lymphoblastic leukaemia (ALL) have reached 90% in the developed countries. However, toxicity due to chemotherapeutic regimens occurs frequently. Variety in the occurrence and severity of such toxicity is determined by single nucleotide polymorphisms (SNP) in coding genes and recently was found to be associated with SNPs in five microRNA (miRNA) genes. The aim of the current study was to confirm the association of five previously identified miRNA variants in relation to methotrexate (MTX) associated mucositis in a prospective study of Dutch children with ALL.

Design/Methods: Two out of five selected SNPs in *AGO1* and *TNRF6B* had a minor allele frequency ≤ 0.15 and were not considered for analysis. We analysed three out of five SNPs in miRNA genes (*CNOT4*, *mir-1206* and *mir-2053*) with a minor allele frequency > 0.15 in DNA isolated from whole blood of 117 paediatric patients with ALL treated with 5 gram/m² MTX according to the Dutch Childhood Oncology Group ALL-10 protocol. Mucositis was defined as grade ≥ 3 according to the National Cancer Institute criteria (NCI-CTC; grade 3 confluent ulcerations and/or bleeding with minor trauma).

Results: rs2114358 in *mir-1206* was significantly associated with mucositis (OR 3.6 [95% CI 1.1-11.5], $p = 0.024$) in our well-documented homogenous cohort of ALL patients. *CNOT4* rs3812265 was not associated with mucositis (OR 0.69 [95% CI 0.27 - 1.80]). The SNP in *mir-2053* could not be analysed due to Hardy Weinberg disequilibrium.

Conclusion: We confirmed the association of rs2114358 in *mir-1206* with MTX-induced mucositis in our prospective cohort of ALL patients. This indicates that this SNP may be used in future prediction models for mucositis in high dose MTX related treatment in children with ALL.

P-0087 | Invasive Fungal Infections in Children with Acute Lymphoblastic Leukemia: Single Center Experience in Turkey

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Background/Objectives: Invasive fungal infections (IFI) are a major cause of morbidity and mortality in patients with hematological malignancies. The risk of IFI increase in prolonged febrile neutropenia and stem cell transplantation. We aim to present the data of patients with acute lymphoblastic leukaemia (ALL), who developed IFI between the years of 2010 and 2015 at the paediatric haematology department of Erciyes University's Medical Faculty.

Design/Methods: We assessed 166 patients with ALL, aged between 2 and 18 years (mean age of 5 years) in this retrospective study. There were 73 female and 93 male patients. They were grouped as IFI and oral candidiasis. Serum galactomannan, computerized tomography scanning and cultures of tissue, blood or fluids were used to make a definitive diagnosis of IFI.

Results: Among 166 patients with ALL, 21 (12.6%) developed IFI. Furthermore, 110 patients (66.2%) had oral candidiasis. Ten patients (47.6%) with IFI had relapsed/refractory ALL and three of them underwent haploidentical stem cell transplantation. Five patients (23.8%) also had high-risk ALL. We found *Candida* spp in 7 patients (33.3%) with IFI, 10 *Aspergillus* spp (47.6%), 1 *Zygomycetes* (4.76%), 1 *G. capitatum* (4.76%), 1 *A. strictum* (4.76%) respectively. One patient (4.76%) had candidiasis and aspergillosis. All patients received fluconazole as prophylactic antifungal therapy during chemotherapy. Effective antifungal drugs were started after diagnosis of IFI. Nine patients received granulocyte suspensions in addition to antifungal therapy. Eleven patients (52.8%) died because of IFI despite all the therapy efforts.

Conclusion: Since invasive fungal infections (IFI) are a major cause of morbidity and mortality in patients with ALL, further studies are needed to investigate new diagnostic and therapeutic strategies to identify and prevent IFI.

P-0088 | Immunophenotyping Analysis in Cerebrospinal Fluid of Paediatric Patients with Acute Lymphoblastic Leukemia

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Background/Objectives: Cerebrospinal involvement is a frequent complication of haematological malignancies, with an incidence of up to 25% in leukaemias and lymphomas. The diagnostic gold standard to detect cerebrospinal fluid (CSF) involvement is cytologic examination

by light microscopy; unfortunately, this technique is characterized by low sensitivity and low specificity.

Asses the diagnostic accuracy of flow cytometric (FCM) immunophenotyping in comparison with classic cytology for diagnosing central nervous system (CNS) infiltration in ALL.

Design/Methods: One hundred four CSF specimens from paediatric patients with ALL were examined by FCM for immunophenotyping. CSF fluid analysis was performed as part of their routine work up. The results were compared to classic cytology routinely done for all samples. Medical ethical committee of HIMFG approved this study.

Patients. Children with ALL were eligible for inclusion in this study if they met the following criteria 1) they were newly diagnosed with ALL; 2) no prior chemotherapy and radiotherapy had been administered.

Cells for immunophenotyping were obtained from 1 to 2 ml aliquot of CSF collected during the initial diagnostic lumbar puncture. All samples were studied within 6 hours of collection. Monoclonal antibodies against cell surface antigens included CD10 and TdT.

Results: In this work 104 CSF were examined. Nineteen were positive [19/104 (18.2%)] and 85 negative for light microscopy. Twenty-five samples were positive by FCM [25/104(24%). A total of 25/104 positive samples were detected; 14 samples were positive for both FCM and cytology [14/30 (46.6%)]. Eleven samples were positive by FCM and negative by cytology [11/30(36.6%)]. Five samples were positive by cytology and negative by FCM [5/30(16.6%)]. Intraobserver agreement for light microscopy was in our study, with a k index of 0.53.

Conclusion: The diagnosis values of FCM are two-three times more than that of cytology. Immunophenotyping by FCM is recommended for routine diagnosis of CSF infiltration combined with cytology to increase the diagnosis yield.

P-0089 | Dna Methylation Patterns of CIP/KIP Cell Cycle Controlling Genes in Paediatric Acute Lymphoblastic Leukemia Patients: AHMS Experience

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Background/Objectives: Aberrant promoter methylation of tumour suppressor genes (TSGs) is frequently observed in Acute Lymphoblastic Leukaemia (ALL) and is recognized as a critical event in the disease pathogenesis and progression. Hypermethylation of these genes have been reported with a marked variation in the frequencies of methylation patterns. In India, the methylation status of TSGs and their correlation with treatment outcome in paediatric ALL patients has not been reported so far. In view of this, we aimed to investigate the methylation status of putative TSGs: p21 (CIP1) and p27 (KIP1) which also play key role in CIP/KIP cell cycle control pathway in ALL patients.

Aim of the study:

To investigate the frequency of p21 and p27 gene methylation in ALL patients and correlate with the clinical features and patient outcome.

Design/Methods: Total genomic DNA extracted from bone marrow /peripheral blood mononuclear cells of ALL patients was modified by Bisulphite treatment and amplified by methylation specific PCR.

Results: A total of 57 paediatric patients (median age 7 yrs, range 1-12 yrs; M: F 4:1; median TLC-25.6x10⁹/l, range 0.8-810x10⁹/l) were studied. Hypermethylation of p21 (32%) and p27 (10%) genes was observed in our group of patients. This frequency was found to be higher in patients with refractory disease and in patients who relapsed later on.

Conclusion: Hypermethylation of TSGs was a more frequent event observed in our ALL patients as compared to that observed in the West. This might be contributing to the relatively poorer outcome in our ALL patients.

P-0090 | Prognostic Value of Flow Cytometric Minimal Residual Disease Monitoring in Children with Acute Lymphoblastic Leukemia Treated by ALL-MB-2008 Protocol

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Background/Objectives: The aim of the study is to evaluate prognostic significance of MRD data assessed by multicolor flow cytometry (MFC) in ALL patients treated by ALL-MB 2008 protocol in a single center in Russia.

Design/Methods: 191 consecutive unselected children with ALL aged from 1 to 16 years were enrolled in the study. BM samples were obtained at the time of initial diagnostics as well as at days 15 (n=188) and 36 (n=191) of remission induction, and after first consolidation or high-risk block (n=187). MRD was assessed by 6-10-color FC.

Results: FC data at day 15 allowed distinguishing three patients groups with significantly different outcome ($p < 0.0001$). 35.64% patients with MRD lower than 0.1% represented 5-year event-free survival (EFS) of 100%. 48.40% cases with MRD-level between 0.1% and 10% had EFS 84.6 \pm 4.2%. Finally 15.96% patients with very high MRD (more than 10%) belonged to group with poor outcome (EFS 56.7 \pm 9.0%). With the different threshold levels day 15 MRD remained its prognostic value in B-cell precursor ALL, T-lineage ALL, standard risk, intermediate risk and high-risk patients analyzed separately.

At the end of remission induction (day 36) 36 children (18.85%) with MRD higher than 0.1% had significantly worse outcome compared to remaining ones (EFS 49.4 \pm 9.0% and 93.5 \pm 2.1%

respectively, $p < 0.0001$). Day 36 MRD greater than 0.1% was also significant prognostic factor in various patients groups.

From a clinical standpoint it is relevant to evaluate both low-risk and high-risk criteria. Multivariate analysis showed that day 15 MRD low MRD is better for low-risk patients definition while end-induction MRD more than 0.1% is the strongest unfavorable prognostic factor. MRD data obtained after remission induction allowed finding patients with very high risk of treatment failure, although it is not easily applicable for the patients' stratification.

Conclusion: Thus MFC MRD monitoring provides clinically useful data in children with ALL treated by ALL-MB-2008 protocol.

P-0091 | Serotonergic Activity in Acute Lymphoblastic Leukemia Cells: Reduction of Serotonin Secretion Due to Ondansetron in the Cell Line Reh is Associated with Antiproliferative Properties

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Background/Objectives: Cells with serotonergic activity are expected either to be activated by, to release, or at least to be involved in one or more cellular processes which are related to serotonin (5-hydroxytryptamine, 5-HT). Previous reports from our laboratory have indicated that 5-HT concentrations of 1-500 μM are able to induce significant proliferation increases (56-226%) in the B-cell precursor (BCP) acute lymphoblastic leukaemia (ALL) cell line REH. Moreover, the presence of 5-50 μM ondansetron [5-HT receptor 3 (5-HT₃) antagonist] could significantly reduce the proliferation of REH cells by 10-20%. We have here investigated whether the 5-HT secretion would be directly implicated in the described anti-proliferative effects.

Design/Methods: The BCP-ALL cell line REH, derived from a patient with ALL at first relapse, was used in all the performed experiments. After 72h incubation in standard conditions, either in the absence, or in the presence of 5-50 μM ondansetron, all the cell pellets and supernatants were separately collected and tested for their respective 5-HT concentrations. The corresponding 5-HT secretion levels were calculated as described by the 5-HT test provider (IBL-International, Hamburg, Germany).

Results: After 72h incubation in standard conditions, reproducible levels of 5-HT were systematically observed in all the tested supernatants and cell pellets, either in the absence or in the presence of 5-50 μM ondansetron. Moreover, the analysed REH cells showed significant decreases (17-27%) in the resulting 5-HT secretion levels after 72h incubation with 5-50 μM ondansetron. Interestingly, the observed decreases of 5-HT secretion were found to correlate with the previously detected antiproliferative effects of ondansetron in the BCP-ALL cell line REH.

Conclusion: The 5-HT₃-antagonist ondansetron was found to significantly reduce the 5-HT release in cultured REH cells, and the corresponding 5-HT reductions correlated with previously described anti-proliferative properties. These results represent further beneficial effects of ondansetron and further support its actual use in ALL patients.

P-0092 | Detection of the Three Fusion Oncogenes of Childhood Acute Lymphoblastic Leukemia – Experience in a Developing Country

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Background/Objectives: Chromosomal abnormalities, such as t(9;22)(q34;q11) (ABL/BCR), t(12;21)(p13;q22) (TEL/AML1), and t(11q23) (MLL) are independent prognostic indicators in childhood acute lymphoblastic leukaemia resulting in risk adapted therapy. Accurate and rapid detection of these abnormalities is mandatory, which is achieved by karyotyping, fluorescence in situ hybridization (FISH), and real time quantitative reverse transcriptase polymerase chain reaction (RQ-PCR). Risk stratification helps in improving the survival rates and the lack of adequate and appropriate diagnostic facilities in developing countries are identified as one of the causes of low survival rates.

To identify the incidence of common fusion oncogenes of childhood acute lymphoblastic leukaemia

To assess the sensitivity and specificity of the tests used to identify the fusion oncogenes.

Design/Methods: The study was conducted on 35 patients being treated for ALL in our institution. Diagnostic tests of karyotyping, FISH and RT-PCR were performed according accepted protocols and standards.

Results: The adopted diagnostic techniques had a high-individual diagnostic accuracy in detecting the above-mentioned chromosomal translocations. However, the sensitivity of karyotyping for detecting the TEL-AML1 fusion gene and MLL-rearrangements was low.

The frequency of t(9;22)(q34;q11) (BCR/ABL), t(12;21)(p13;q22) (TEL/AML1), and t(11q23) (MLL) was found to be 3%, 6% and 2% respectively.

Conclusion: Higher incidence of TEL/AML1 in the study group highlights the importance of risk stratification, as this decreases the unwarranted toxic effects of chemotherapy in a child with standard risk. Diagnostic accuracy of tests for detecting t(9;22), t(12;21), and t(11q23)(MLL) is generally high, although sensitivity is not optimal for all anomalies. Despite the high-diagnostic accuracy, all diagnostic techniques should be used complementary, because any detection of a significant chromosomal aberration irrespective of diagnostic mode has to be considered in therapy. However, a larger study population would establish the diagnostic accuracy of the three techniques as well as the frequency of these genetic alterations in children with ALL.

P-0093 | Understanding the Role of Procalcitonin (PCT) in Febrile Neutropenic Episodes of Children Undergoing Treatment for Cancers: A Tertiary Centre Data

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Background/Objectives: Infections are major cause of morbidity and mortality in children receiving cancer chemotherapy particularly when they are neutropenic, mainly due to immune deficiency. Between 48-60% neutropenic patients with fever have an underlying infection which can often be life threatening. Before putting the child on empiric antimicrobial regimens for FN, it is essential to know the spectrum of locally prevalent pathogens and their susceptibility patterns. Often these children don't manifest fever even in presence of infection and fever may be present in patients with neutropenia receiving chemotherapy even in the absence of infection. Present diagnostic tools available for diagnoses in FN are often not so robust and do not differentiate between various classes of organisms causing these infections.

Objective: To evaluate the role of PCT, as a sensitive marker for diagnosis of paediatric patients with cancer having FN.

Design/Methods: The analysis is representative of 82 episodes, 3 of the patients had polymicrobial infections and were included for statistical analysis. Blood culture is time consuming and negative blood culture does not exclude bacteremia, which leads to the empirical use of broad-spectrum antibiotic treatment in paediatric patients with neutropenia, even where signs of infection are absent.

Results: Blood-culture was positive in 18.05% of the patients, with majority of patients having gram-negative bacterial infections. On comparison with the focus of infection, high PCT and CRP values were obtained in patients with pulmonary infection than in extra-pulmonary infections. In our study the sensitivity of PCT was high up-to 73.3% at a cut-off of $\geq 0.25\text{ng/ml}$ for ruling out bacteremia, when compared to blood culture and CRP in our patients

Conclusion: The PCT value is certainly helpful in guiding the physicians in clinical decisions and thus the better approach towards the management of paediatrics oncology patients with FN.

P-0094 | Profile of Relapsed Paediatric Leukemias in Dubai, United Arab Emirates

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Background/Objectives: Dubai hospital, Dubai is one of the three main centers which caters for the management of children presenting with cancers in the United Arab Emirates. In the last three years we treated sixty-one children with leukaemia, eleven of whom relapsed. We looked at the profile of these relapsed leukaemia children to give us a better understanding of which of our sub-group of children are relapsing.

Design/Methods: A database was setup in October 2012 to record details of all children presenting to the Pediatric Oncology department of Dubai Hospital for treatment. All children presenting with leukaemia from the years 2013 to 2015 were analyzed.

Results: A total of sixty-one children presented to Dubai hospital with leukaemia's from 2012 to 2015. Out of these fifty three had acute lymphoblastic leukaemia (ALL), seven had acute myeloid leukaemia (AML) and one had biphenotypic leukaemia. 13% of our ALL children relapsed as compared to 42.8% of the AML group. We only had one biphenotypic leukaemia and he relapsed even after second and third line therapy. In the ALL group majority of the relapses were B-ALL (85.7%). The only child with Pro-T ALL relapsed as well. The male to female ratio was 5:2. Only 28.5% of the relapsed children had a presenting white blood count of more than a $100 \times 10^9/\text{L}$. Apart from one child who had hypodiploidy all others had good cytogenetics. Among the AML group all had white cell counts below $50 \times 10^9/\text{L}$ and were males. Two thirds were M5 sub-group with one third being M2.

Conclusion: Pro-T ALL and AML seem to have a worse prognosis in our genetically diverse patient pool from over a hundred nationalities living in Dubai. Good cytogenetics so far does not seem to offer a prognostic significance in our population group.

P-0095 | Mucor Pyelonephritis in a Child with Acute Lymphoblastic Leukemia - A Case Report

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Background/Objectives: Invasive mucormycosis occurs predominantly in immunocompromised patients and is usually disseminated. Rare, isolated involvement of brain, lungs and kidneys has been reported.

Objective: To describe a case of a Mucor pyelonephritis in a child with acute lymphoblastic leukaemia (ALL).

Design/Methods: Case report.

Results: A seven year old Indian girl was diagnosed with intermediate risk pre-B ALL and started on Berlin-Frankfurt-Munster (BFM) based regimen. She developed febrile neutropenia during induction. She was started on broad spectrum antibiotics. With persistent fever, fungal culture was sent, voriconazole started and an ultrasonogram (USG) of abdomen done, which showed a heterogeneous hypoechoic lesion in the upper pole of right kidney suggestive of infection/infarct. CT abdomen showed a non-enhancing, low attenuating focus in upper and mid pole of right kidney, likely evolving abscess with pyelonephritis. It also revealed a non-obstructing cast with central calcification in the right renal pelvis. Fine needle aspiration was consistent with fungal infection, with further speciation not done. Antifungal was escalated to amphotericin B. Follow up USG abdomen showed development of cystic changes at upper pole of right kidney and right hydronephrosis with echogenic content suggestive of a "fungal ball". Renal angiogram showed interventional development of aneurysmal dilation of upper inter-polar hilar division of right renal artery, likely mycotic aneurysm. In view of progressive

fungal infection right radical nephrectomy was done. Histopathological examination showed PAS positive branching hyphae consistent with *Mucor*. Two weeks post surgery the patient recovered and chemotherapy was continued. She is currently in maintenance chemotherapy and doing well.

Conclusion: Although fungal infection is common with children on treatment for ALL, isolated *Mucor* renal pyelonephritis is not frequently encountered and has been previously described only in one child. Our case is unique for its rarity in occurrence, the diagnostic challenges it presented and the successful outcome after treatment.

P-0096 | Outcomes of a Graduated Intensity Treatment for Acute Lymphoblastic Leukemia (ALL) at Butaro Cancer Center of Excellence in Rwanda

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Background/Objectives: While over 85% of children with Acute Lymphoblastic Leukaemia (ALL) can be cured in developed countries, outcomes in developing countries are inferior.²⁻⁵ At Butaro Cancer Center of Excellence, a public, rural-based Rwandan hospital, patients were treated using a graduated intensity protocol as outlined by Hunger (2009).

Design/Methods: Between July 1, 2012 and June 30, 2014, 42 consecutively recruited patients with pathologically-confirmed treatment-naïve ALL were started on level 1 of the Hunger protocol, the same low-intensity regimen for all risk stratifications. Demographics, determinants of delay and prognostic outcomes were collected through December 31, 2014.

Results: Median age of 42 patients was 10.0 (range 0.4 - 40.4 years). At the end of analysis, 28.6% (12) patients were alive without evidence of relapse and continuing treatment, 66.7% (28) had died, and 4.8% (2) were lost to follow up. Twenty-three (82.1%) of the deaths were disease-related, 13.6% treatment-related, and 4.4% unclear. Deaths largely clustered within two months or 6 months following diagnosis, the latter during early maintenance.

The most common cause of chemotherapy delay was thrombocytopenia (21 patients, 50.0%). Prior to induction, 52.4% (22) of patients required blood and 42.9% (18) platelet transfusions. Medication stock outs affected care of 16 patients (38.1%). Socioeconomic delays were infrequent (1 lack of transport, 1 illness of the patient or family member).

Conclusion: In this first published outcomes of the graduated intensity approach to ALL in resource-constrained settings, the majority of failures were relapses as expected given the low intensity of regimen 1. However, treatment-related deaths were acceptably low with one clear case. Many patients still required transfusional support. We are now risk-stratifying patients and advancing to regimen 2 for high-risk patients following an intensive educational program for providers. These results point to the necessity of risk-stratifying and a data-driven approach to care for complex patients in resource-constrained settings.

P-0097 | Outcome and Clinical Significance of Immunophenotypic Markers Expressed in Paediatric Patients with T-Cell Acute Lymphoblastic Leukemia in Developing Countries

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Background/Objectives: T-cell acute lymphoblastic leukaemia (T-ALL); comprising only 15% of paediatric ALL. Although, it is aggressive malignancy and had very poor prognosis the advent of high-dose, multi-agent chemotherapy regimens resulting in significant survival advantage. Deep exploration of T-lymphocyte development in recent years found subgroup of patients with early T-cell precursor acute lymphoblastic leukaemia phenotype (ETP-ALL) has poorer prognosis than other form of T-ALL. This study aimed to evaluate paediatric patients diagnosed and treated for T-ALL at two different Arabic cancer centers regarding their clinic-pathologic, immunophenotypic and cytogenetic features and outcome.

Design/Methods: Retrospective study included all children with T-ALL treated between 2003 and 2013 at two oncology centers in Middle East. Patients divided into (group I) treated with BFM-90 treatment protocol between February 2003& June 2007 and (group II) includes all patients treated thereafter by the total therapy study XIII protocol for high-risk ALL.

Results: Study included 103 patients with median age of 8.9 years. Male to female ratio was 2.6:1. The median initial TLC was $123 \times 10^9/L$. Leukaemia infiltrating central nervous system was detected in 15%. ETP-ALL phenotype found in 16.5%. Five-year overall survival (OS) was $20.7\% \pm 6.5\%$ and $72.9\% \pm 5.7\%$ ($p=0.00$), 5-year disease free survival (DFS) was $47.1\% \pm 13.8\%$ and $77.3\% \pm 6.0\%$ ($p=0.023$) and 5-year event free survival (EFS) was $28.6\% \pm 12.1\%$ vs $71.1\% \pm 6.2\%$ ($p=0.003$) for group I and II respectively.

Conclusion: Outcome of patients with T-ALL significantly improved in patients received treatment protocol of ALL with high-risk criteria. This protocol eliminates the bad outcomes effect of several clinical and immunophenotypic markers. Patient with ETP-ALL phenotype had non-significant inferior outcome compared to non-ETPALL group.

P-0098 | TAL1 Abnormalities in Childhood T-Cell Acute Lymphoblastic Leukemia

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Background/Objectives: T-cell acute lymphoblastic leukaemia (T-ALL) is relatively uncommon, comprising 10% to 15% of newly diagnosed cases of childhood ALL. Although gene fusions generated through chromosomal translocations, deletions, and inversions are the most frequent genetic abnormalities detected in other types of leukaemia, recurrent gene fusions except for *SIL-TAL1* have been poorly defined in T-ALL.

Design/Methods: To discover driver mutations or oncogenic fusion genes, which involved in the pathogenesis of childhood T-ALL, and to identify novel prognostic markers of childhood T-ALL, we performed whole transcriptome sequencing (WTS), targeted capture sequencing for 150 genes related with paediatric ALL, and copy number analysis in 45 cases.

Results: We identified previously known fusion genes, such as *SIL-TAL1* ($n=7$), *MLL-ENL* ($n=2$), *CALM-AF10* ($n=2$), *NUP214-ABL1* ($n=1$) and *FGFR3-FGFR1* ($n=1$). Targeted capture sequencing revealed *TAL1* insertions in enhancer region in 4 cases, which are recently reported that introducing de novo MYB binding site. Since this abnormality lead high expression of *TAL1*, we also analyzed expression data obtained from WTS. All of the cases with *SIL-TAL1* fusions or *TAL1* enhancer insertions showed high expression of *TAL1*. *NOTCH1* mutations were recurrently detected in 76% cases, whereas cases with *SIL-TAL1* fusion or *TAL1* enhancer insertion had significantly lower frequency of *NOTCH1* mutation (52%, $p=0.014$). *CDKN2A/B* deletions were also frequently detected in 84% cases by copy number analysis, but there was no correlation with *TAL1* over expression.

Conclusion: *SIL-TAL1* fusions and *TAL1* enhancer insertions were mutually exclusive, and closely related with *TAL1* over expression. These alterations accounted for 24% cases of paediatric T-ALL, which is characterized by lower frequency of *NOTCH1* mutation. Consistent with other reports, frequent translocations were not observed in T-ALL, and thus, our finding further illustrated the genetic differences between T-ALL and other hematological malignancies.

P-0099 | High Dose Chemotherapy and Autologous Peripheral Blood Stem Cell Transplantation for Paediatric Acute Lymphoblastic Leukemia: A Single Institute Experience

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Background/Objectives: The role of autologous peripheral blood stem cell transplantation (aPBST) remains unclear for acute lymphoblastic leukaemia (ALL). We analyzed the outcome of high dose chemotherapy and autologous peripheral blood stem cell transplantation (HDCT and aPBST) in children with ALL and further compared the outcome of those who received post-aPBST maintenance chemotherapy to those who did not.

Design/Methods: The outcome of children who received HDCT and aPBST for ALL between August 1997 and April 2013 at Seoul National University Children's Hospital was retrospectively reviewed. High dose chemotherapy consisted of carmustine $250 \text{ mg/m}^2/\text{day}$ on day -8 and $200 \text{ mg/m}^2/\text{day}$ on day -3, etoposide $200 \text{ mg/m}^2/\text{day}$ and cytarabine $2,000 \text{ mg/m}^2/\text{day}$ between day -7 and day -4, and cyclophosphamide 50 mg/kg/day between day -2 and day -1. From the year 2001, all of the patients received additional post-aPBST maintenance chemotherapy, which consisted of monthly pulses of oral prednisolone and intravenous vincristine, weekly oral methotrexate, and daily oral 6-mercaptopurine.

Results: Ten patients underwent HDCT and aPBST for ALL at median age of 4.9 years old for cytogenetic abnormalities ($n=5$), infant ALL with $t(4;11)$ ($n=1$), ectopic myeloid phenotype ($n=1$), and bone marrow relapse ($n=3$). Two patients had transient grade 2 adverse events which were seizure and pneumonia. Three patients who did not receive post-aPBST maintenance relapsed and died of disease. There was no transplant-related mortality. At median 72 months from aPBST, the event-free survival (ESF) of the patients who received post-aPBST maintenance chemotherapy and those who did not was 100% and 40% respectively. The overall survival (OS) of the total study population was 70% at median 72 months from aPBST.

Conclusion: HDCT and aPBST, especially with post-aPBST maintenance chemotherapy, have been effective as an alternative therapy for children with high risk ALL when patients lack appropriate allogeneic donors.

P-0100 | Standing Together: Everyday Life of Mothers of Children with Leukemia

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Background/Objectives: Aims and objectives: To gain insight into everyday living mothers of children with leukaemia.

The main objective of this study was trying to know the life stories of a mother dealing with leukemic child and see in its true colors.

Background: When a child is being clinically diagnosed with leukaemia, parents face with a real terrible shock that usually results in a huge change in their normal life. Both parents especially mothers should tackle a new life by supporting and backing their leukemic child through some activities such as home-based treatment.

Design/Methods: One-time individual in-depth interview was the procedure that the researchers went through while considering grounded theory as the basis of their study. Sixteen mothers took part in this study and the interviews were carried out in two oncology ward in Tehran University Hospitals.

Results: Standing together with a leukemic child is one of the things that occur in a mother's everyday life when she knows about her child's severe illness. This mother gets so close to her child and she makes one with her/him. In this way, on the one hand, the mother's quality of life suffers and in the long run it causes weariness. On the other hand, it ruins other roles of mother.

Conclusion: The mothers' life was exposed to wide inevitable changes after the illness of the child. Such a life style affected not only the mother but also the child and other family members widely. The perception of the mothers' life will help the health care worker to have a better imagination of their problems, to establish a better and closer communication with them and to offer more accessible supportive resources and more effective approaches.

P-0101 | Determination of Thiopurine Methyltransferase (TPMT) Status in Children with Acute Lymphoblastic Leukemia to Customize Thiopurine Dosage

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Background/Objectives: Daily mercaptopurine constitutes one of the standard "backbone" of Acute Lymphoblastic leukaemia continuation regimens. We determined the TPMT genotype in children with acute lymphoblastic leukaemia before commencing thiopurine therapy to customize the dosage of mercaptopurine.

Design/Methods: This is a prospective study of 45 children newly diagnosed as acute lymphoblastic leukaemia by flow cytometry from January 2014 to March 2015. The TPMT genotype status of the child was detected by peripheral blood TPMT Genotyping PCR (Qualitative) and RFLP Analysis. The analysis was done for five genotypes TPMT* 1 Wild Type, TPMT* 2, TPMT* 3A, TPMT* 3B and TPMT* 3C. The prevalence of TPMT polymorphisms was correlated with the tolerated dose of mercaptopurine.

Results: A total of 45 samples were analysed for TPMT genotype status. The incidence of TPMT deficiency in our study population was 2.2% (1/45). 97% of our study population with ALL were found to have TPMT* 1 Wild Type genotype consistent with normal enzyme activity. 2.2% of the study population had no enzyme activity with heterozygous genotype for TPMT. The average tolerated dose of 6-mercaptopurine during consolidation phase in the normal enzyme activity group was 32 mg/m²/day as against the tolerated dose of 10 mg/m²/day in the TPMT deficient group. The average dose of 6-mercaptopurine tolerated during the maintenance phase was 27 mg/m²/day as against the recommended dose of 75 mg/m²/day.

Conclusion: The TPMT deficient children tolerate lesser dosage than the non-deficient children and hence clinically would help in optimizing the dosage of 6-mercaptopurine in an individual. However, the absence of TPMT mutations did not seem to account for the reduced tolerance of 6-mercaptopurine in our non-deficient population. This opens up further studies of variant genes other than TPMT involved in transformation of 6-mercaptopurine and polymorphisms in genes of folate metabolism to be evaluated in the Indian population.

P-0102 | The Prevalence of Sleep Problems in Children with Acute Lymphoblastic Leukemia

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Background/Objectives: Management of sleep problems may be an important tool to improve quality of life (QoL) in children with acute lymphoblastic leukaemia (ALL). To design effective intervention studies, insight is needed in the extent, nature and risk factors of sleep problems. This study aims to describe the prevalence of sleep problems during ALL treatment.

Design/Methods: This study is part of a longitudinal study assessing sleep, fatigue and QoL in children with ALL. Preliminary data on child sleep of the first assessment three months after diagnosis are described here. Sleep was assessed with parent-proxy and self-report (≥ 8 years) questionnaires (Children's Sleep Habits Questionnaire, Adolescent Sleep Habits Questionnaire and Sleep Self Report). Total questionnaire scores were compared to age-appropriate Dutch norms using T-tests or Mann-Whitney U Tests. Scores of one standard deviation above the norm were considered clinically relevant (chi-square tests).

Results: Sixty-six children (84%), mean age 6.6 years, completed the first assessment. Parent-proxies (n=65) were assessed in 24 toddlers (2-3 years), 32 school-aged children (4-12 years), and 9 adolescents (13-18 years). Self-reports (n=15) were assessed in 8 school-aged children (8-12 years) and 7 adolescents. Parents reported significantly higher sleep scores (i.e. more sleep problems) compared to norms in all age categories (p<0.01). Self-reported sleep scores were not statistically different from norms. Parents reported clinically relevant disturbed sleep in 46% of the toddlers (p<0.01), in 38% of the school-aged children (p<0.01), and in 33% of

the adolescents (p=0.11). Adolescents self-reported clinically relevant disturbed sleep in 29% (p=0.71). Clinically relevant scores were not reported by school-aged children.

Conclusion: Parents and children reported differently about sleep outcomes. Sleep problems were most prevalent in toddlers but were common among all ages. In a larger sample, sub-analyses will allow to describe risk factors for the development of sleep problems in children with ALL.

P-0103 | Expression of Phosphorylated AKT and PI3 Kinase (PI3K) Isoforms in Childhood Acute Lymphoblastic Leukemia

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Background/Objectives: Acute lymphoblastic leukaemia (ALL), the commonest malignancy in childhood, represents 30% of all childhood cancers. Although more than 80% of ALL cases are curable, there is still a significant number of resistant or relapsed disease. The identification of genes and molecular pathways that are involved is crucial for targeted therapy design. The intracellular signaling pathway PI3K/AKT induced by growth factors and plays an important role in triggering many biological processes of the cell. Recently, it has been found that changes in the expression and mutations in molecules of this pathway are involved in tumorigenesis, which makes them an attractive target for cancer therapy. The objective of this research was the study of the expression of P110 β , P110 δ and P-Akt proteins in ALL diagnosis and in remission, as well as in solid tumors without bone marrow involvement.

Design/Methods: Proteins were extracted from bone marrow lymphoblasts of 32 children with ALL at diagnosis, lymphomononuclear cells from 21 children with ALL in complete remission, and from 20 children with solid tumors without bone marrow involvement. An amount of 200 μ g of proteins was analyzed with Western blot and the detection of P-Akt, P110 β and P110 δ was completed with Amersham ECL Prime. The analysis of the results was made with Image Lab.

Results: The expression of P110 δ was high in ALL diagnosis with statistically significant difference compared with ALL cases in complete remission (0.33 \pm 3.78 vs 1.06 \pm 2.05, p=0.03) after induction chemotherapy. The comparison between ALL groups (diagnosis and remission) and controls group did not reveal statistically significant difference. Additionally, the statistical analysis did not show significant difference of the expression of P-Akt and P110 β between all these three groups.

Conclusion: The significant high expression of P110 δ found in ALL diagnosis needs further investigation especially in regard with the significant decrease after complete remission is achieved.

P-0104 | The Bone Marrow Findings of FDG-PET/CT in Children with Acute Leukemia: Retrospective and Single Institute Experience

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Background/Objectives: Background: Fluorine-18 fluorodeoxyglucose positron emission tomography combined with computed tomography (FDG-PET/CT) is a promising diagnostic procedure for the detection of extramedullary disease in acute myeloid leukaemia. But a few report were described the accumulation of FDG in bone marrows of acute leukaemia(AL) children. Objectives: To assess the FDG-PET/CT findings of bone marrows in children with AL.

Design/Methods: We analyzed FDG-PET/CT findings of 6 children with AL and 22 children without neoplastic disease (w/oND) retrospectively. Six AL children were three acute lymphoblastic leukaemia and three acute myelogenous leukaemia, median age was 7 years old, range 2-17 years old. Twenty two w/oND children were 7 necrotizing lymphadenopathy, 3 thrombocytopenic purpura, and other inflammation diseases, median age was 6.5 years old, range 7 months-16 years old. We evaluated the accumulation of FDG by maximum standardized uptake value (SUVmax) and our visual quantitative score (0:no accumulation, 1:mild accumulation, 2:strong accumulation) of bone marrows. We divided into eleven sections of the bone marrow in a whole body : vertebrae, pelvis, proximal humerus, center humerus, distal humerus, proximal forearm, center forearm, distal forearm, proximal femur, center femur and distal femur. We compared the data at each section between AL and w/oND by using Mann-Whitney U-test.

Results: Children with AL had significantly higher SUVmax than w/oND at all 11 sections. The visual scores of proximal humerus, center humerus, distal humerus, proximal forearm, center forearm, distal forearm, proximal femur, center femur and distal femur were significantly higher in AL than w/oND. But the visual scores of vertebrae and pelvis didn't have significant difference.

Conclusion: High FDG accumulation in the bone marrows in children with AL were seen at extremities. Sometime we experience the difficulty of diagnosis when a bone marrow aspiration is dry. These FDG-PET/CT findings will have the potential of a diagnostic tool in such a difficult case of acute leukaemia in children.

P-0105 | Butein Kills Acute Lymphoblastic Leukemic Cells In Vitro and In Vivo through FOXO3A and Caspase-Dependent Apoptotic Pathways

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Background/Objectives: Acute lymphoblastic leukaemia (ALL) is a common hematological malignancy in children. Discovering and developing effective chemotherapeutic drugs are needed for ALL. In this study, the anti-leukemic effect and the potential molecular mechanisms of butein on ALL were investigated.

Design/Methods: We examined the rate of apoptosis of CEM-C7 (T-ALL), CEM-C1 (T-ALL), MOLT-4 (T-ALL), RS4-11 (B-ALL) cell lines and primary ALL blasts exposed to various concentrations of butein for 24 h using the flow cytometry. We tested the expression of the caspase-3, poly ADP-ribose polymerase (PARP), nuclear Forkhead Class box O3a (FOXO3a) and BCL-2 interacting mediator of cell death (BIM) using western blot assay. We established the xenograft mouse model to examine the anti-leukemic effect of butein *in vivo*.

Results: Butein was found to significantly induce the cellular apoptosis of ALL cell lines and primary ALL blasts in a dose-dependent manner. It also activated the cleavage of caspase-3 and PARP. We also found that butein promoted FOXO3a localization, enhanced the binding of FOXO3a on the BIM gene promoter and then increased the expression of BIM. Moreover, we showed that FOXO3a knockdown significantly decreased the apoptosis by butein, whereas overexpression of FOXO3a enhanced the butein-induced apoptosis. However, overexpression of FOXO3a mutation (C-terminally truncated FOXO3a DNA-binding domain) decreased the apoptosis by butein through decreasing the expression of BIM. Furthermore, treatment with butein was highly efficacious *in vivo*, with enhanced reduction of tumour burden in a xenograft model of ALL.

Conclusion: Our results therefore demonstrate the therapeutic potential of butein for ALL via FOXO3a and caspase-dependent apoptotic pathways.

P-0106 | Detection of Susceptibility to Childhood Acute Lymphoblastic Leukemia (ALL)

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Background/Objectives: Currently, there are no known means to predict susceptibility to, and prevent ALL. We have separated, evaluated and patented a group of proteins dubbed 'Protein X' from a certain *Aspergillus Flavus* (AF) and developed methods for screening, and identifying patients in remission of ALL distinguishing them from "normal" controls.

Design/Methods: Mononuclear leukocytes (MNL) of ALL patients in remission and controls were separated. Controls were normals, sickle cell and patients with tumors. Epstein Barr virus (EBV) was obtained commercially. Materials for control were aflatoxin, *Mycocladus Corymbifera* (MC), avian leukosis virus and cell line CRL-2312. Pre/post exposure MNL were co-incubated with 'Protein X' ± EBV ± irradiation, for periods of 1-72 hours. Controls were treated identically with appropriate substitutions. MNL were examined for genetic markers, NF-κB and ALL cell surface markers (CSM). Changes expressed as percentage of control. Using ELISA, plasmas were tested for antibodies against 'Protein X' ± EBV.

Results: Upon 1-72 hours exposure of MNL from ALL to 'Protein X' ± EBV, these developed CSM of ALL. Addition of EBV ± radiation to 'Protein X', enhanced these effects in MNL of ALL and not controls. Changes were statistically significant and separated ALL from controls. NF-κB revealed enhancement in ALL and not controls. Aflatoxin indiscriminately induced changes in CSM of both normal and ALL while supernatant CRL-2312 or MC had no effect. ELISA, using 'Protein X' ± EBV, distinguished ALL from controls. Gene array and biomarkers confirmed transformation to leukemic markers with 'Protein X' in cells from ALL but not controls.

Conclusion: These studies reveal, *in vitro*, upon exposure to 'Protein X', unlike normals, MNL from ALL in remission, can develop CSM/genetics typical of ALL. These techniques have potential for screening for ALL and may have implications for its etiology and prevention.

P-0107 | IKZF1 Gene Deletions is More Powerful Prognostic Factor Than Genetic Risk Group Stratification in Paediatric Acute Lymphoblastic Leukemia Patients Enrolled in ALL-MB 2008 Protocol

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Background/Objectives: Recently new stratification strategy for paediatric B-cell precursor ALL (BCP-ALL) based on cytogenetic risk group and copy-number alterations (CNAs) was introduced (A. Moorman *et al.*, *Blood*, 2014).

To estimate new diagnostic strategy on childhood BCP-ALL patients enrolled into Russian multicenter trial ALL-MB 2008.

Design/Methods: 142 BCP-ALL patients were included in the current study. Median of follow-up period was 5 years. CNAs were estimated by SALSA MLPA P335 ALL-IKZF1 probemix and SALSA MLPA P202 IKZF1 (IKAROS) probemix (both MRC-Holland, The Netherlands).

Results: Following CNAs were detected: *IKZF1* deletions were found in 15 (10.6%) patients, *CDKN2A/B* deletions in 44 (31.0%), *BTG1* deletions in 12 (8.4%), *EBF1* in 2 (1.4%), *PAX5* in 46 (32.4%), *ETV6* in 39 (27.5%), *RBI1* in 11 (7.7%), *PARI* region in 9 (6.3%). Totally 111 (78.2%) patients were allocated to the genetic good risk (GGR) group, 31 (21.8%) to the genetic poor risk (GPR) group. Patients referred to the GGR group had higher EFS than patients in GPR group (0.89±0.03 vs 0.59±0.11, p=0.002) and lower cumulative incidence of relapse (CIR) (0.07±0.03 vs 0.39±0.11, p<0.001). However in multivariate analysis genetic risk group stratification was not statistically significant, while presence of *IKZF1* deletions, WBC count at diagnosis more than 50*10⁹/L and M3 status of bone marrow (BM M3) at day 15 were

significantly associated with decreased EFS and higher CIR. *IKZF1* deletions retained their prognostic significance in different subsets of patients: in the 'B-other' group, in BM M3 at day 15, in MRD-defined risk groups, in ALL-MB 2008 ImRG patients, but not in SRG or HRG.

Conclusion: We could not confirm that stratification for genetic risk groups was independent of other factors. It might be protocol-dependent. In contrast, *IKZF1* deletions led to unfavorable outcome in the whole cohort of patients and various subgroups.

P-0108 | Outcomes of Paediatric Relapsed Philadelphia Chromosome Positive All in the UK

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Background/Objectives: The BCR/ABL1 fusion gene in childhood acute lymphoblastic leukaemia (ALL), although rare, has historically carried a poor prognosis, with relapsed disease generally being considered incurable. With the advent of new targeted treatments, particularly tyrosine kinase inhibitors (TKIs), the outlook for children with relapsed Philadelphia chromosome positive (Ph+) ALL has changed, but the outcomes have been difficult to quantify given the small numbers of patients.

Design/Methods: We identified 8 children diagnosed between 2004-2013 across 3 centres in the UK with relapsed Ph+ ALL. Their demographics at diagnosis, treatment including chemotherapy regimen, TKI and haematopoietic stem cell transplant (HSCT) were recorded. Data was also recorded on survival.

Results: There were 6 males and 2 females in the cohort, and the median age at diagnosis was 9 years. Five patients were stratified as high risk based on post-induction MRD and the remainder were treated as standard risk. Five patients were treated on the EsPhALL protocol and 3 on the UKALL with 1 of the latter group also being treated on Dasatinib at diagnosis. All but 1 patient received HSCT in first complete remission (CR1), and of the 7 patients who achieved CR2, 4 received a second HSCT in CR2. Six patients received a Imatinib as part of their treatment, 3 during induction, 2 post induction and 1 post HSCT.

The median CR1 duration in the group was 18.5 months (range 11-89 months) and median CR2 duration was 8 months (range 1-48 months). At the time of follow up, 4 patients were still alive, including 1 with ongoing disease and the other 3 in CR. Of the 2 patients who did not receive Imatinib as part of their treatment, 1 is currently in CR and the other died prior to achieving CR2.

Conclusion: The outcomes for relapsed paediatric Philadelphia positive ALL have improved since the advent of TKIs.

P-0109 | Weekly Hemogram May not Be Mandatory for Paediatric Patients with Acute Lymphoblastic Leukemia (ALL) on Prophylactic Cranial Irradiation (PCI) in Developing Countries: An Observational Study

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Background/Objectives: Pediatric patients with ALL undergo PCI as part of consolidation phase of chemotherapy. Hypothesis is that irradiation of flat bones may depress the bone marrow and result in low blood cell counts. Resource-constraint in developing countries may prevent weekly evaluation of patients by hemogram. Patients may also feel it difficult to get weekly hemogram due to long-waiting time, poor logistics and disadvantaged social circumstances. Hence we decided to observe the patients on PCI for any symptoms of low blood cell counts or alteration in blood counts on hemogram.

Design/Methods: Due to huge crowd and resource-constraint, prospective documentation of patient condition and hemogram report was not feasible in our set-up. We retrospectively collected the demographic and clinical data of twelve patients with ALL who have undergone PCI in the department of Radiation Oncology, Kidwai Memorial Institute of Oncology, Bangalore between July 2014 and March 2016. Data on hematological, clinical and laboratory adverse events developing during and immediately after the completion of therapy were collected by retrospective recall of treating physician.

Results: Patients were aged between 2 and 14 years (median age of 8 years) with 6 each of male and female children. None of the twelve children with ALL on PCI had any symptoms of fatigability, palpitation, fever, cough, diarrhea or bleeding diathesis. Neither patients complying with prescribe hematologic investigation nor in-compliant patients had significant drop of blood cells count or present to review during or immediately after radiotherapy with symptoms or signs of low blood cells count.

Conclusion: Recommended weekly hemogram may not be mandatory in patients with ALL undergoing PCI as part of MCP 841 protocol. Selected patients can undergo PCI without weekly hemogram. Further large-scale studies are needed to identify the sub-set of patients who may not need weekly hemogram or at risk of clinically significant fall of blood cells count.

P-0110 | Predictors of Dexamethasone-Induced Neuropsychological Side Effects in Children with Acute Lymphoblastic Leukemia

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Background/Objectives: Dexamethasone is highly effective in the treatment of acute lymphoblastic leukaemia (ALL), but may lead to serious neuropsychological side effects. Despite the standard dose, the severity of side effects varies widely between patients. We hypothesized that neuropsychological side effects are influenced by glucocorticoid sensitivity at the tissue level or by dexamethasone serum levels. In this study we determined whether neuropsychological side effects could be predicted by a very low dose dexamethasone suppression test (DST) as diagnostic test for glucocorticoid sensitivity or by dexamethasone trough levels.

Design/Methods: Fifty patients (3-16 years) treated with dexamethasone courses according to the maintenance phase of DCOG ALL protocols were included. In the salivary very low dose DST, a post-DST cortisol level of <2.0 nmol/L was considered a hypersensitive response. Neuropsychological endpoints consisted of the parent-reported Strengths and Difficulties Questionnaire (SDQ-Dut) and Sleep Disturbance Scale for Children (SDSC) before and during a dexamethasone pulse. Dexamethasone trough levels were measured during dexamethasone (6mg/m²) treatment.

Results: Patients with a hypersensitive response (N=13, 26%) had more dexamethasone-induced behavioral problems (median delta: 1.0 (inter quartile range: 0.0,2.0) versus 0.0 (-0.5,1.0), P=0.01), sleeping problems (4.5 (0.0, 13.5) versus 0.0 (-3.0, 2.0), P=0.03), and/or somnolence (3.0 (1.0, 6.0) versus 1.0 (-0.5, 2.5), P<0.05). The positive predictive value of the DST for psychosocial problems and sleeping problems was 50% and 30% respectively. Dexamethasone levels were not associated with neuropsychological side effects.

Conclusion: The very low dose DST and dexamethasone trough levels could not accurately predict neuropsychological side effects. However, patients with glucocorticoid hypersensitivity experienced significantly more dexamethasone-induced depressive symptoms. Future studies should further elucidate the glucocorticoid sensitivity dependent mechanisms by which neuropsychological side effects are influenced.

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P-0111 | Evolving Profile of Childhood Leukaemia at Kamuzu Central Hospital, Lilongwe

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Background/Objectives: The prevalence and spectrum of childhood leukaemia in Sub-Saharan Africa is poorly understood. Under-diagnosis and lack of effective cancer registries pose significant challenges. There is a widely held belief that childhood leukaemia is comparatively rare in Malawi. Previous retrospective data from Kamuzu Central Hospital (KCH) showed that leukaemia represented 2% of the childhood cancer burden. We describe the substantial, relative contribution of Leukaemia to the paediatric cancer burden at KCH in Lilongwe Malawi.

Design/Methods: Between July 2015 and March 2016, all children referred to KCH cancer center, were assessed for the possibility of leukaemia. All leukaemia diagnoses were confirmed morphologically using peripheral blood smear and bone marrow evaluation. Immune histochemistry was used to evaluate one case. BCR-ABL status was assessed in one case. Data was collected on the demographics, baseline clinical and haematological features, World Health Organization (WHO) leukaemia classification, and 28 day survival.

Results: Excluding Kaposi Sarcoma, 23/113 (20%) new childhood cancer diagnoses at KCH, during the study period were leukaemia. We registered 12 (52%) cases of Acute lymphoblastic leukaemia (ALL), 7 (30%) cases of Acute myeloid leukaemia, (AML), 2 cases of Acute promyelocytic leukaemia (APL), 1 case of Burkitts leukaemia and 1 case of BCR-ABL positive chronic myeloid leukaemia (CML). The median age was 9 years (range 2.7 to 15.4 years) and 10 (45%) patients were male. The median white cell count (WCC) was $66 \times 10^6/L$ (range 3-380[KW1]). CNS involvement occurred in 2/23 patients (8%); both had AML. One [KW2] (4%) patient was lost to follow up. Day 28 survival was 13/23(56%). Three patients died within 48 hours of admission. Of the 12 evaluable patients, 9 (90%) achieved complete remission at end of induction.

Conclusion: Contrary to traditional views, leukaemia is one of the more common types of childhood cancer in Malawi, with different subtypes represented within the spectrum.

P-0112 | Feasibility, Safety, and Efficacy of An Anthracycline Containing Induction Protocol for Childhood Acute Lymphoblastic Leukaemia in Malawi

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Background/Objectives: The success achieved in treatment of Acute lymphoblastic leukaemia (ALL) in high income countries has not been replicated in low income countries (LICs). Mortality is highest during induction. Low-intensity treatment (which excludes anthracyclines) are recommended for use in LICs to reduce toxicity, but may compromise chances of cure. There is a paucity of data documenting the toxicity of anthracycline-containing induction protocols in LICs. We share our experience of treating childhood ALL at Kamuzu Central Hospital, in Lilongwe Malawi.

Design/Methods: Between July 2015 and March 2016, all children diagnosed with ALL or lymphoblastic lymphoma (LBL) were treated on a modified UKALL 2011 regimen B protocol. Short course Dexamethasone [KW1] 10mg/m²/day was given for 14days. Daunorubicin was substituted for Doxorubicin 20-25mg/m²/day. Asparaginase was available for only 5 (38%) children. Data was collected on the demographics, baseline clinical and haematological features, toxicity, and remission status at the end of induction. Supportive care was standardized with allopurinol and IV fluids to prevent tumour lysis syndrome and Cotrimoxazole and Ciprofloxacin to prevent infection. All leukaemia diagnoses were confirmed morphologically using peripheral blood smear and bone marrow evaluation.

Results: Thirteen children with ALL or LBL, were commenced on this induction protocol. Median age was 9 years (range 2.7-15.4) and 7 (54%) were male. Ten (77%) patients were NCI high risk for age (6/13 46%) and/or WCC (8/13, 60%). One (8%) patient was lost to follow up. Ten (83%) of 12 evaluable children survived to the end of induction. Of the two deaths, one died from sepsis and the other from unexplained cardiac arrest. Grade 4 toxicity (sepsis) was observed in 1/11 (9%) evaluable children. Remission was achieved in 9/10 (90%) of evaluable patients by end of induction.

Conclusion: Anthracycline containing ALL induction protocols appear to be feasible, safe and effective for children in poor resource settings, such as Malawi.

P-0113 | The Results of Intensive Chemotherapy Protocols in Children with High Risk Acute Lymphoblastic Leukemia (CCG-106 B, CCG-1882- Augmented BFM and CCG-1961)

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Background/Objectives: Introduction-Aim: Treatment failure rates are high in the children with Acute Lymphoblastic Leukaemia (ALL) having negative risk criteria (high white blood cell count: >50,000/mm³, >10 years, bulky disease, immunophenotypic characteristics, specific cytogenetic findings and slow response bone marrow in 7th day >25% blast, M3 response. In this study, the results of three CCG protocols for children with high risk ALL.

Design/Methods: Patients-Methods: Between January 1987 and January 1994, CCG-106 B chemotherapy was used to 32 children with ALL who have high risk characteristics. In 96.7% of the patients, complete remission was reached. Relapse was developed in 29% (9/32) of the patients. Five patients were lost with the progressive illness. Twenty patients (64.5%) are being followed for over 20 years without treatment. Between December 1992 and November 1997, CCG-1882 regimen C (Augmented BFM) was used in 16 children with ALL having high-risk characteristics. In this protocol, marrow bone response (M3) in 7th day was taken into account and intensive post-induction chemotherapy continued in this branch (Augmented BFM). In all patients complete remission was reached. Relapse developed in 4 patients (26.7%). 73.3% of the patients were followed for nearly 20 years without illness. Between September 1997 and March 2016, CCG-1961 regimen C, regimen D protocols were used in 32 children with ALL having high-risk characteristics. 93.8% of the patients entered into remission and relapse developed in 21.9% (7/32) of these children. Currently, 1 patient is under treatment and 25 patients are being followed without treatment for 6-189 months.

Results: With the usage of high-risk ALL protocols that we started to use after 1987, 65-70% of our patients obtained a long life-term without illness, which was previously 70% relapse frequency in patients.

Conclusion: Our patients obtained a long life-term without illness and our results are very close with the results reported by other centers.

P-0114 | Investigation of Dominant Hand Functions and Motor Proficiency Test Results between Hospitalized Children with Leukemia and Healthy Peers

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Background/Objectives: Children with cancer have a lot of functional impairments as a result of diagnosis, receiving therapies, hospital staying, and immobilization. The aim of our study was to investigate hand functions and motor proficiency in hospitalized children with leukaemia during treatments and compare with the healthy peers.

Design/Methods: Seventeen (female: 7, male: 10) children with leukaemia and sixteen (female: 9, male: 7) healthy peers participated in this study. The average age was 9.70 ± 3.86 years in children with leukaemia and 8.43 ± 1.67 years in healthy peers ($p>0.05$). Hand function was assessed by Nine Hole Peg test with dominant hand. Children's motor proficiency was assessed by the Bruininks - Oseretsky Motor Proficiency Test (BOT-2) - Short Form. This measurement consisted of fine motor precision, fine motor integration, manual dexterity, bilateral coordination, balance, running speed and agility, upper-limb coordination, and strength subtests.

Results: It was found that significant differences in Nine Hole Peg test between groups; the placing and removing pegs time with dominant hand in children with leukaemia was more than that healthy peers performed ($p=0.001$, $p<0.001$, respectively). The mean total scores of the BOT-2 were 49.70 ± 14.20 points in children with cancer, 60.31 ± 10.26 points in healthy peers ($p=0.021$). In addition, there were found significant differences between groups in subtests of BOT-2: manual dexterity, balance and strength ($p=0.035$, $p=0.036$, $p=0.005$, respectively).

Conclusion: According to the study results, hand function and motor proficiency of children with leukaemia affected negatively. Because of this the rehabilitation program of children with cancer should include motor functions, especially manual dexterity, balance, and strength parameters are needed much attention.

P-0115 | A Case of CD20 Negative Epstein-Barr Virus-Related Post-Transplantation Lymphoproliferative Disorder (EBV-RELATED PTLD) after Hla-Haploidentical Transplantation for Acute Lymphoblastic Leukemia (ALL)

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Background/Objectives: A CD20 negative EBV-related PTLD is a life-threatening complication in patients after hematopoietic stem cell transplantation (HSCT).

Design/Methods: A 14-year-old boy with ALL achieved complete remission after the 2nd line reinduction therapy including clofarabine, etoposide and cyclophosphamide. After 2 cycles of reinduction therapy, he had received haplo-HSCT from his father. The conditioning regimen included total body irradiation (12 Gy), melphalan, etoposide and ATG. His GVHD prophylaxis were short methotrexate, prednisolone and tacrolimus. The neutrophil engraftment was confirmed at day31.

Results: At day39, plasma EBV DNA was detected. He was treated a weekly dose of rituximab and the dose of immunosuppression reduced. However, blood EBV-DNA load increased up to 4.9×10^3 copies/ μ g DNA at day 46 concomitant with development of severe lympho-adenopathies. The atypical lymphocyte counts in peripheral blood were elevated up to 26% at day 48. The surface marker of these EB virus infected B cells were CD20-negative/CD19-positive. Donor-lymphocytes infusion (DLI) was performed at day 49 (CD3-positive cells: 3.8×10^5 cells/kg) and $56 (4.4 \times 10^5$ cells/kg). According to emergence of EBV-specific cytotoxic T cells after DLI, his adenopathies gradually reduced in size and blood EBV DNA load completely cleared by day 93. After DLI, no sign or symptom attributable to graft-versus-host disease was observed. The patient was disease-free for 8 months after HSCT.

Conclusion: DLI is effective for CD20-negative EBV-related PTLD, however the clinical symptoms should be carefully monitored after DLI from the HLA haploidentical donor.

P-0116 | Cluster of Differentiation 97 as a Biomarker for Detection of Minimal Residual Disease in Common Acute Lymphoblastic Leukemia

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Background/Objectives: Acute lymphoblastic leukaemia (ALL) is a biologically heterogeneous disorder. Clinical parameters, immunophenotype, cytogenetic and minimal residual disease (MRD) are among currently used factors in risk stratification and therapy determination of ALL patients. Minimal residual disease (MRD) is gaining importance nowadays both for therapy efficacy, follow up and relapse risk estimation. Recent studies have high lightened potential markers that may improve the sensitivity of MRD detection by flowcytometry. CD97 is one of these markers which show over expression in paediatric ALL. In this study we aimed to assess the value of CD97 as biomarker for detection of MRD in paediatric ALL.

Design/Methods: This cohort study was conducted on thirty newly diagnosed patients with B-lineage ALL. They were 16 males and 14 females with mean age of 8.38 ± 4.21 and a range from (1-18) year. 20 patients were low risk group and 10 patients were high risk group treated according to modified CCG 1991. A panel of monoclonal antibodies was used with special emphasis on CD10, CD19, CD34 and CD97 at diagnosis and at day 14 post induction of chemotherapy for detection of MRD.

Results: Three patients (10%) presented with total leucocytic counts (TLC) $\geq 50 \times 10^3/\text{mm}^3$ while twenty seven patients (90%) had TLC $< 50 \times 10^3/\text{mm}^3$. Mean multiparameter flow cytometry of CD19/CD97, CD34/CD97 and CD10/CD97 at day 0 was 57.15 ± 21.74 , 57.73 ± 21.20 and 57.87 ± 20.77 while at day 14 was 6.09 ± 2.50 , 10.67 ± 8.89 and 5.97 ± 2.44 respectively p value < 0.001 . CD97 was expressed in 81.5% of patients at diagnosis and wasn't detected at day 14 p value < 0.001 . one patient had blast counts $> 5\%$ by light microscopy while twenty nine patients had MRD > 0.1 by multiparameter flow cytometry at day 14 p value < 0.001 .

Conclusion: CD97 can be used for MRD tracing in paediatric ALL.

P-0117 | The Role and Mechanism Study of Lncrnas Involved in Glucocorticoid Resistance in Paediatric Acute Lymphoblastic Leukemia

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Background/Objectives: Glucocorticoids (GCs) are key components in the treatment of childhood acute lymphoblastic leukaemia (ALL) and most ALL therapeutic failures can be explained by cellular resistance to GCs. However, the mechanisms of GC resistance are poorly understood. LncRNAs are involved in normal hematopoiesis and leukaemia development, whereas the roles of LncRNAs in GC resistance are still unknown. Our goal was to investigate the role of LncRNAs involved in glucocorticoid resistance in paediatric acute lymphoblastic leukaemia, and also elucidate the mechanism preliminarily.

Design/Methods: In this study, LncRNA microarray was performed on GC-resistant cell line CEM-C1 and GC-sensitive cell line CEM-C7 to screen the differential expression of LncRNAs. Five up-regulated and five down-regulated LncRNAs were randomly chosen for validation by Real-time PCR. GO-Pathway analysis was done to investigate potential signaling pathways regulated by the LncRNAs.

Results: The microarray revealed that 4286 LncRNAs differed ($p < 0.05$ and fold change > 2.0) in GC-sensitive cell from those in GC-resistant cell. 826 LncRNAs changed more than 5-fold,

while 356 LncRNAs changed more than 10-fold. Among them, 203 LncRNAs were up-regulated and 153 LncRNAs were down-regulated. Expression of ten selected LncRNAs was validated by Real-time PCR. GO analysis indicated that differentially expressed LncRNAs were involved in apoptotic process related GO terms. Pathway analysis revealed that these LncRNAs were involved in apoptosis, cell cycle, mTOR and some other signaling pathways.

Conclusion: Our study showed that LncRNA expression profile was altered in GC-sensitive and GC-resistant cells, indicating that differentially expressed LncRNAs may play important functional roles in GC resistance of ALL. And these LncRNAs may be involved in GC resistance by regulating signaling pathways associated with cell proliferation, differentiation and apoptosis. Our study provides new biological foundations for further mechanism study in GC resistance and also provides a new strategy for therapeutic development of ALL.

BONE TUMOURS

P-0118 | Non-High Dose -Methotrexate (HD-MTX) Based, Dose-Dense (DD), Combination, Chemotherapy(CT) in 83 Metastatic Osteosarcoma Patients: A Tertiary Care Centre Experience from India

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Background/Objectives: Despite the improvement in survival for localized osteosarcoma, patients with metastatic disease at presentation have a poor prognosis. Considering, complexities associated with HDMTX administration (pharmacokinetic monitoring, in-patient treatment, unpredictable, & substantial toxicity and cost), an alternative regimen devoid of these lacunas and comparable outcome is worthy of exploration.

Design/Methods: This prospective study evaluated OGS-12 regimen comprising DD-CT with Doxorubicin, Ifosfamide, & Cisplatin. Histological response (HR) to chemotherapy, survival and toxicity analysis was carried out for outcome measures. Baseline parameters were correlated with outcomes and toxicity.

Results: There were 326 patients enrolled from 2011-2014, of which 83 (26%) were metastatic. Majority was nutritionally challenged and having high risk features (elevated serum LDH, SAP, high tumour burden). Amongst 83 metastatic patients, 69 were analyzable for histological response and 29(42%) were good responders. At a Median follow-up of 21 (4-49) Months, median overall survival (OS) and progression free survival(PFS) was 29 months (22-36 months) and 15 months (12-18 months) respectively. Estimated 3 year OS & PFS is 43% & 24.4%. Median post relapse survival is 8(4-11 months).

The protocol was well tolerated; significant grade 4 hematological toxicity were febrile neutropenia-19(27.5%), thrombocytopenia-29 (42%), anaemia-43(62%); there were no significant grade 3 non hematological toxicity observed. In uni and multivariate analysis ECOG-performance status, surgery performed, baseline vitamin B12, HR were significantly associated with OS and PFS.

Conclusion: Non-HD MTX based, DD, OGS-12 regimen was proven as low cost, outpatient based, well tolerable and efficacious, treatment in metastatic, high risk, nutritionally challenged osteosarcomas. Aggressive treatment including surgery and metastectomy had shown better results. Potential prognostic markers in the current study, merits further exploration in larger cohorts with long follow up for reproducibility.

P-0119 | Outcome of Children and Adolescents with Primary Bone Tumors - 10 Years Single Center Experience in Bratislava, Slovakia

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Background/Objectives: Since primary bone tumors belong to challenging group of childhood cancer the aim of our study was to perform 10 years retrospective analysis of our patients with primary bone tumors treated at our center in terms of time to diagnosis, chemotherapy regimens in the 1st and 2nd line, surgery, toxicity and survival. In Slovakia annually there are about 140 newly diagnosed patients with cancer, the incidence of bone tumors is about 8-10 children per year.

Design/Methods: We have analysed the cohort of 45 patients with primary bone tumors treated at single center Bratislava in period 1/2006-12/2015. There were 22 patients with Ewing's sarcoma, primary metastatic disease has occurred in 28 pts (36.4%) patients, 11 cases (50%) with primary involvement of vertebrae or pelvis. Twenty three patients had osteosarcoma, in 5 patients primary metastatic disease was present, 20 patients had primary involvement of femur or tibia. Patients were treated according protocols: EURO EWING 99, COSS 96, EURAMOS-1.

Results: In group of Ewing sarcoma: 15 patients (68.2%) are survivors, 5yOS of the whole cohort is 58% (+/- 12.5). Five years OS/EFS in patients without metastases were 65/64% (+/- 17/+/-14) as for group of patients with metastases 5yOS/EFS were 43/37 (+/-18/+/-17). In group of osteosarcoma patients: 12 patients (52.1%) are survivors, 5yOS of the whole group was 57% (+/- 11), Patients without metastases had 5yOS 62% (+/-12) and 5yEFS 51% (+/-12), 5yOS/EFS of patients with metastases 40% (+/- 22) 2yEFS 8% (+/- 7).

Conclusion: The dismal outcome of patients with primary bone tumors are in concordance with published data of large groups. Remaining challenges in Slovakia are centralized pathology, primary bone tumour bank, optimizing nad harmonizing biopsy and definitive surgery, active participation and enrollment to large international groups.

P-0120 | Nephrotoxicity in Children Receiving Chemotherapy - 'Omics and Biomarkers

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Background/Objectives: Nephrotoxicity is a common adverse side effect in children receiving treatment for cancer, and with drugs such as cisplatin, ifosfamide and high dose methotrexate, can be a significant and dose limiting toxicity. No novel markers of renal injury other than measure GFR have found routine use in clinical practice and clinical trials.

Design/Methods: Here we described work exploring historical and contemporary markers of renal injury within this group, including a systematic review of markers of tubular damage, epidemiology of serum and biochemical changes and a consideration of clinical markers including magnesium supplementation. Further research considers a recently completed metabolomic analysis of paired urine and serum samples from paediatric patients receiving ifosfamide, and pharmacogenomics of cisplatin induced renal injury.

Results: Changes with serum and urinary markers of renal injury are well established, but few have been validated in clinical trials or through longitudinal research. Animal models however have demonstrated that several markers demonstrate clear clinical utility and prognostic value. An ongoing controversy remains the reversibility of kidney injury and factors that confer increased risk, such as concurrent nephrotoxic agents.

Conclusion: Both renal and serum markers of acute kidney injury should be included in future randomised clinical trials to determine their clinical utility and value as both in both the diagnosis of acute kidney and prognostic value in predicting long term outcomes.

P-0121 | Hypoalbuminemia and High WBC are Poor Predictors of Survival in Head and Neck Ewing Sarcoma Family of Tumors: An Updated Analysis of 59 Patients

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Background/Objectives: To evaluate prognostic factors and treatment outcome in Ewing sarcoma family of tumors (ESFT) in head and neck region.

Design/Methods: This is single institutional data review of 59 consecutive patients of ESFT in head and neck region treated between June 2003 and September 2014 with uniform chemotherapy protocol. All patients received neoadjuvant chemotherapy, surgery and/or radiotherapy as local treatment followed by adjuvant chemotherapy.

Results: Median age was 12 years (range: 1-45) with male: female ratio 38:21. Most common sites of disease were maxilla and maxillary sinus in 19 (32%), skull base in 13 (22%) and mandible in 12 (20%); six patients (10%) had baseline metastasis. Of the 59 patients, 49 were eligible for local therapy: 2 underwent surgery alone, 12 underwent surgery with adjuvant radiotherapy, while definitive radiotherapy was primary local treatment modality in 35 patients. After median follow-up of 49.3 months (range: 3.1-152), 5-year event-free-survival (EFS) and overall survival (OS) was 46.1±7.8% and 60.4±7.3%, respectively. In the cohort of patients with localized disease (n=53), the outcome was equivalent for local treatment modality (Surgery ±radiotherapy versus radiotherapy alone) for both EFS (5-year value of 50.4% vs 53.5%, respectively; p=0.52) and OS (5-year value of 71.6% vs 60.2%, respectively; p=0.7). Further in this cohort of localized disease, multivariate analysis showed that baseline serum albumin of ≤3.5 g/dl and white blood cell (WBC) count of >11,000/μl independently predicted inferior outcome for both EFS (hazard ratio of 5.85 and 5.82, respectively) and OS (hazard ratio of 4.14 and 4.96, respectively).

Conclusion: Definitive radiotherapy as local treatment modality results in similar outcome as compared to surgery in head and neck ESFT with localized disease. Baseline serum albumin and WBC counts predicts inferior EFS and OS. Local radiotherapy can be an alternative to mutilating surgery in head and neck ESFT.

P-0122 | Pretreatment Neutrophil to Lymphocyte Ratio is a Predictor of Event Free Survival in Ewing Sarcoma Family of Tumors – An Analysis of 330 Patients

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Background/Objectives: Ewing sarcoma family tumour (ESFT) is a systemic disease and inflammatory in nature. Inflammatory biomarkers have been identified as prognostic marker in various malignancies including sarcoma. Here we have evaluated the prognostic implication of pretreatment neutrophil to lymphocyte ratio (NLR) in ESFT.

Design/Methods: We have calculated baseline NLR from peripheral blood parameters in 330 patients of ESFT treated with uniform chemotherapy protocol in our institution from June 2003 to Nov 2011. Treatment protocol consists of neoadjuvant chemotherapy followed by surgery and/or radiotherapy as local treatment modality and adjuvant chemotherapy. NLR was dichotomized as high and low with high NLR defined as value over the median. Data was censored on 30th Jan 2016.

Results: Median age was 15 years (range: 1-55) with male: female ratio of 239:91. Forty-one percent (n=136) patients had metastasis at presentation. Most common sites of tumour were long bones in 133 (40%), thorax in 66 (20%) and abdomen-pelvis in 57 (17%) patients. Ninety-seven (29%) patients had systemic symptoms at presentation. Median NLR was 1.48 (range: 0.08-7.22). High NLR was associated with older age (p=0.004), female sex (p=0.02), high WBC count (p=0.02), and low serum albumin (p=0.02). In the whole cohort, high NLR (>1.48) emerged as independent prognostic factor predicting inferior EFS (Hazard ratio-1.62, p=0.005) along with metastasis at presentation (p<0.001) and high lactate dehydrogenase level (p=0.001), in multivariate analysis. In the cohort of localized disease, high NLR didn't predict inferior EFS whereas in cohort of metastatic disease, high NLR independently predicted inferior EFS (Hazard ratio-1.76, p=0.02), in multivariate analysis.

Conclusion: High pretreatment NLR emerged as independent prognostic factor predicting inferior EFS in patients with ESFT, especially in those with metastasis at presentation. It is an easily available and cost effective biomarker. Prognostic nature of NLR should be evaluated in a prospective study and if proven, should be included in prognostic model to tailor therapy.

P-0123 | Delayed Methotrexate Clearance in Children, Can We Predict it with Small Changes in Creatinine Values?

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Background/Objectives: Methotrexate is a mainstay chemotherapy agent in Osteosarcoma and Leukaemia protocols. Decreased renal excretion leads to prolonged drug exposure, increasing the likelihood of toxicity. Children's Oncology Group protocols utilizing high dose methotrexate identify delayed clearance by regularly monitoring serum levels. Serum monitoring is currently not feasible worldwide and many institutions use changes in serum creatinine values to identify delayed clearance. The Pediatric Risk, Injury, Failure, Loss, End Stage Renal Disease (pRIFLE) acute kidney injury (AKI) classification system has been proposed as a quantifiable way to identify changes in kidney function that put children at risk of increased morbidity and mortality.

Objectives: To evaluate associations in serum creatinine, using the pRIFLE AKI classification system, and delayed methotrexate clearance.

Design/Methods: A retrospective review was performed on 127MTX infusions in patients with Leukaemia and 147MTX infusions in patients with Osteosarcoma from 2009-2014. Data was collected including creatinine values pre, during, and post infusion, dose, total clearance time, 24 hour MTX level, and 48 hour MTX level. The Schwartz equation was used to calculate creatinine clearance and pRIFLE criteria were applied to each dose visit to determine the presence of AKI during or following the infusion. Statistical analysis was performed using t-tests and linear regression analysis.

Results: There was no significant difference between the occurrence of AKI in infusions with delayed clearance and infusions without delayed clearance in both patients with leukaemia and patients with osteosarcoma (p=0.84).

Conclusion: Using the pRIFLE AKI classification system allows small changes in serum creatinine (Cr) to be quantified even while Cr values remain within a normal range for age. However, we found no association with Cr and delayed methotrexate clearance. Our study suggests that creatinine monitoring is not a good early marker of poor MTX clearance and other options for monitoring for delayed MTX clearance should be considered.

P-0124 | Istratutumab (MM-141), A Bispecific Antibody Targeting IGF-1R and ERBB3, Potentiates the Activity of Standard of Care Chemotherapy in In Vivo Models of Ewing Sarcoma

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Background/Objectives: Insulin-like growth factor 1 receptor (IGF-1R) signaling has been implicated in the pathogenesis of Ewing sarcoma (EWS). High IGF-1 and IGF-1R expression has been identified in 70-80% of primary untreated EWS tumors by quantitative RT-PCR and immunohistochemical staining, respectively. In addition, the EWS-FLI-1 fusion protein most commonly associated with EWS oncogenesis upregulates IGF-1R signaling. However, clinical trials evaluating monospecific IGF-1R inhibitors have demonstrated limited efficacy. ErbB3, a member of the ErbB receptor tyrosine kinase family, can activate pro-survival AKT signaling and may represent a resistance mechanism to monospecific IGF-1R blockade. Istratutumab, an IGF-1R and ErbB3 directed bispecific antibody, inhibits ligand activation of these signaling pathways and degrades IGF-1R and ErbB3 receptor-containing complexes from the cell surface, leading to inhibition of downstream pro-survival signaling. Here we tested the activity of istratutumab, alone and in combination with chemotherapy, in EWS models.

Design/Methods: Expression of IGF-1R and ErbB3 was evaluated in a panel of 7 EWS cell lines by quantitative flow cytometry. The *in vitro* effects of istratutumab on expression of downstream pro-survival signaling effector proteins were tested by western blotting. Anti-tumour activity of istratutumab, alone and in combination with the common relapse regimen irinotecan + temozolomide (irino-tem), was tested in *in vivo* EWS xenograft models.

Results: IGF-1R and ErbB3 were expressed in all EWS cell lines tested. In addition, istratutumab monotherapy down-regulated pAKT and pS6 in 60 and 100% of EWS cell lines *in vitro*, respectively. Co-treatment of istratutumab and irino-tem significantly inhibited tumour growth (p<0.005) compared to either irino-tem or istratutumab treatment alone, and significantly delayed the time to tumour progression (p<0.05).

Conclusion: Our findings demonstrate that co-inhibition of IGF-1R and ErbB3 signaling with istratutumab can potentiate the effects of a standard-of-care relapsed chemotherapy regimen in EWS tumour models and warrants further investigation as a potential therapy for EWS patients.

P-0125 | Assessing the Value of Bone Marrow Aspirate and Trephine in Identifying Metastatic Involvement in Children with Ewing Sarcoma: A Retrospective Single Centre Experience

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Background/Objectives: Bilateral Bone marrow aspirates and trephines are part of the initial staging evaluation of patients with Ewing sarcoma. However, the utility of performing this

invasive investigation in addition to imaging with MRI and Technetium 99 bone scan has not been assessed.

Aim: To assess the value of performing bone marrow aspirates and trephines in identifying metastases compared to imaging, particularly Technetium 99 bone scan.

Design/Methods: Retrospective review of 48 children aged 16 and under with Ewing sarcoma treated in our institution between August 2000 and September 2014.

Results: There were 25 males and 23 females (M: F= 1.08:1) in our series. 54% of patients were over 10 years old while 12.5% of patients were under 5 years old; the remaining 33.3% were aged between 5 and 10 years. Using imaging alone, 65% (n=31) had localised disease while 35% (N=17) had metastatic disease. 81% of patients (n=39) had bone marrow aspirates and trephines performed, of which 3 were positive for disease; one of these patients had a pelvic primary and the marrow was positive on the left side which was the location of the primary site. 43 patients (90%) had a bone scan, of which 10 were positive for bony metastases. All three patients who had bone marrow positivity also had metastatic lesions on bone scan. 4 patients with metastatic bony lesions did not have a bone marrow performed, while the other 3 did not have evidence of disease in the bone marrow aspirate or trephine.

Conclusion: Although our numbers are small, there is a high correlation between bony metastases identified by Technetium 99 bone scan and bone marrow aspirate and trephine positivity. Further prospective evaluation is required to determine whether a bone marrow examination adds any value to the initial staging of Ewing's sarcoma over imaging and whether it can be omitted from the staging assessment.

P-0126 | Systemic Hyalohyphomycosis Infection Following Freshwater Swimming in Paediatric Ewing Sarcoma Patient on Chemotherapy: A Case Report

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Background/Objectives: Neutropenic patients with cancer are at high risk for bacterial and fungal infections. Fresh water swimming may put neutropenic patients at risk for particular bacterial infections such as *Aeromonas* or *Vibrio* species. Fungii are considered uncommon causes of disseminated infection in patients with intact skin. *Fusarium* species can be found in water and can enter the body through preexisting onychomycosis or impetigo lesions.

Design/Methods: A twelve year old boy undergoing treatment for Ewing Sarcoma of the chest wall presented with fever, fatigue and neutropenia (ANC 0) 48 hours after swimming in a lake. He had no history of prior skin lesions. Chemotherapy with doxorubicin, vincristine and cyclophosphamide was given six days prior to presentation. He was started on cefepime and vancomycin with no response. He developed left thigh pain and within two days, had multiple necrotic, painful papules on his legs and trunk, all with central necrosis and circular lesions of liquefaction. Antimicrobials were changed to meropenem, daptomycin, linezolid, posaconazole (300mg/d) and caspofungin. He underwent skin biopsy, then liposomal amphotericin b (5mg/kg/d) and granulocyte transfusions were started. Weeks later, after count recovery, he developed a groin mass that spontaneously ruptured. All skin lesions resolved after 3 months of posaconazole and 4 weeks of ambisome treatment. CT showed stable chest wall tumour.

Results: Biopsy revealed subcutaneous fat necrosis, vascular thrombosis and numerous septate fungal hyphae, branching mostly at acute/right angles, with focal angioinvasion. Serum galactomannan, blood, wound cultures were negative for bacteria, fungi or AFB. Lung biopsy showed inflammation only.

Conclusion: In addition to waterborne Gram negative rods, opportunistic molds that belong to Hyalohyphomycetes, such as *Fusarium*, should be included in the differential diagnosis of painful necrotic skin lesions in the neutropenic host following freshwater exposure. Prompt anti-fungal therapy and granulocyte transfusions until counts recover are essential in improving outcomes in this patient group.

P-0127 | Effects of Chemotherapy on Weight of Children and Adolescents with Osteosarcoma

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Background/Objectives: Osteosarcoma is the most common primary malignant bone tumour. Signs of malnutrition and severe malnutrition occur frequently in children and adolescents with osteosarcoma due to symptoms associated with the treatment and can lead to loss of appetite, further contributing to weight loss and increase the risk of complications. The main objective of this study was to assess the nutritional status of patients with osteosarcoma at diagnosis and after the first chemotherapy cycle.

Design/Methods: A retrospective longitudinal study with children and adolescents 0-19 years diagnosed with osteosarcoma from January 2009 to January 2014 at the Institute of Oncology Pediatric / GRAACC / UNIFESP. Evaluation of nutritional status was performed using measures and anthropometric indices. The latter were calculated from the anthropometric measurements of weight and height.

Results: Among 34 patients who were evaluated in the study, 53% were male. The average age was 8 years, and 27 patients were older than 10 years. As the BMI of patients younger than 10 years old, 57% had a BMI below appropriate on admission and 71% after the first chemotherapy cycle (p = 0.05). Among patients older than 10 years old, 62.5% had a BMI below adequate on admission, and after chemotherapy the incidence increased to 75% (p = 0.06). Among the gastrointestinal symptoms after chemotherapy, 20 (59%) patients experienced vomiting, 18 (53%) nausea, 15 (44%) mucositis, 13 (38%) constipation, 10 (29%) odynophagia, 7 (20%) xerostomia, 5 (15%) diarrhea, 5 (15%) change in taste and 2 (6%) dysphagia. Considering it is a retrospective study, there were no records of gastrointestinal symptoms on admission.

Conclusion: It was concluded that there was deterioration of nutritional status during the period between the first assessment and the first chemotherapy cycle, emphasizing the children under 10 years of age for this outcome.

P-0128 | Evolution of Nutritional State of Paediatric Patients in Osteosarcoma Treatment

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Background/Objectives: Pediatric patients with osteosarcoma are at increased risk of malnutrition. Nutritional monitoring is essential for promoting proper growth and development of children and adolescents. The main objective of this study was to evaluate the evolution of the nutritional status of patients with Osteosarcoma during the period of treatment.

Design/Methods: A retrospective and longitudinal study with information collected from the database of oncologic patients aged 7 to 45 years old diagnosed with Osteosarcoma followed by the nutrition team, from January 2009 to January 2014 in the Pediatric Oncology Institute / GRAACC / UNIFESP. The following data were collected from the patients reports: weight, height and assessment of nutritional status were measured on admission and last visit, considering up to a year of oncology treatment and nutritional monitoring. For the assessment of nutritional status the z score BMI/A was considered according to the WHO, in addition to TSFT and MUA percentile according to Frisancho criteria. The sample was subdivided according to the monitoring period, as follows: group A (up to 9 months), B (10 to 14 months) and C (>14 months), the results were expressed as mean and standard deviation.

Results: Among 34 patients included, 52% were male. On admission, 34% of patients had BMI/A below adequate. However, considering the TSFT and MUAC measures, this finding was observed in respectively 67% and 73% of this population. In the final evaluation, it was observed some mean improvement in the anthropometric indicator from -0.85 z-score to -0.29 BMI/A.

Conclusion: It was concluded that there is improvement of the nutritional status based on anthropometric parameters (BMI/A) and follow-up measures (TSFT and MUAC) for the period of nutritional monitoring. Dietary intervention at the time of cancer diagnosis might favored these results because the degree of nutritional impairment was identified at an early stage.

P-0129 | Feasibility of Outpatient Administration of Interval-Compressed Regimen for Children with Ewing Sarcoma

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Background/Objectives: Interval-compressed regimen with cycles of chemotherapy given every 2 weeks emerged recently as the standard of care for children with Ewing Sarcoma (ES). We developed institutional clinical practice guidelines based on the administration of this regimen given in the outpatient settings. This study intended to evaluate our institutional experience with this regimen.

Design/Methods: We conducted a retrospective review of patients with ES who were treated using interval-compressed protocol of 14 cycles of alternating cyclophosphamide, doxorubicin, vincristine (VDC) and ifosfamide, etoposide (IE) with maximum dose of doxorubicin of 375mg/m². Cycles were followed by G-CSF administration until count recovery. Patients treated using our guidelines from June2013 to June2015 were eligible. Patients younger than 3 years at time of diagnosis, those with multiple sites of metastasis, and patients who presented to our center with relapse were not eligible for treatment with our guidelines and thus were excluded from this analysis.

Results: Twelve patients with localized ES or lung-only metastasis were eligible. By the time of analysis, 153 cycles were administered to these patients. Eight cycles for 6 patients were administered on inpatient basis while the rest (N=145) were administered in the outpatient chemotherapy unit. The median number of cycles per patient was 14 (range, 5 to 14). Ninety cycles (59%) were administered on time per CPG. The median interval between cycles was 17.8 days (range, 14 to 20). The median interval between induction and consolidation cycles were 14 and 17 days, respectively. Neutropenia was reported at time of next cycle in 12 cycles. Toxicity profile was similar to what was reported in the literature using the same regimen in the inpatient settings with transient gross hematuria reported in 1 patient only.

Conclusion: Our study showed that the outpatient administration of interval-compressed regimen is well-tolerated and feasible.

P-0130 | Epidemiology of Ewing Sarcoma in the North of England, 1990-2011

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Background/Objectives: Ewing sarcoma (ES) arises in bone and soft tissue sites. The purpose of this study was to describe the incidence and survival outcomes for ES in the north of England.

Design/Methods: Details of 190 patients diagnosed with ES from 1990-2011 were extracted from two population-based registers in the north of England: the Yorkshire Specialist Register of Cancer in Children and Young People (ages 0-29 years) and Northern Region Young Persons Malignant Disease Register (ages 0-24 years). Information on diagnostic tests including positivity for CD99 and *EWSR1* gene rearrangements was extracted. Follow-up for all individuals was to 31.12.2015. Overall survival (OS) and event free survival (EFS) was calculated using Kaplan-Meier estimates. Log-rank tests were used to compare differences.

Results: The majority of patients were male (59%) and diagnosed between 10-19 years of age (60%). One-hundred and twenty (68%) were classified as ES of the bone and 70 (32%) in soft tissue sites. Thirty-five percent of patients relapsed, with median time to relapse from diagnosis of 1.6 (95%CI 1.2-2.0) years for ES of the bone and 2.1 (95%CI 1.4-3.0) years for soft tissue ES. Around half of all cases were positive for CD99, whilst *EWSR1* rearrangements were reported in 111(58%) of cases.

Overall incidence was 3.6 per million persons per year with higher rates for ES of the bone (2.3 per million persons per year) compared to soft tissue (1.3 per million persons per year). Five-year OS estimates were 53.5% (95% CI 46.0-60.4%) and equivalent EFS estimates 45.1% (95% CI 37.8-52.1%). Survival trends revealed a lack of any improvement over time ($P=0.638$).

Conclusion: ES in the north of England is more common in males than females, and most frequently diagnosed in bony sites. Time to relapse was shorter in those with ES of the bone compared to soft tissue ES.

P-0131 | Askin Tumour, Nine Patients, Five years Experience

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Background/Objectives: Askin's tumour is a primitive neuroectodermal tumour (PNET) of the chest wall described the first time in 1979 by Askin. Its a rare entity usually treated as other Ewing family tumors, with chemotherapy, surgery and radiotherapy.

Our aim is to report 5 years' experience with Askin Tumour treatment in two different centers (paediatric and adult oncology Units) and describe clinical characteristics, evaluate response to treatment and report toxicity.

Design/Methods: We reviewed the records of 9 patients (p) with Askin tumour admitted and treated at Hospital de Niños Ricardo Gutierrez and Hospital Militar Central between January 2009 and December 2013.

Results: Nine p were included. Median age: 15 years (r: 9-25 years). Male 5. Localized disease 6p. Metastatic disease: 3p (2 lung and 1 lung and bone). Four p had left rib tumour. All patient received chemotherapy as initial treatment (according to EuroEwing 99 trial).

Local treatment: surgery alone 3 p (with complete resection and 100% necrosis), surgery and radiotherapy 4 p and radiotherapy alone 1 p.

One patient died before local treatment because of sepsis.

Four of 6 p with localized disease are alive at 1,3,4 and 5 years. One died because of a second tumour (LMA) and 1 because of local relapse and lung metastasis after 1 year of remission.

All patients had grade IV hematologic toxicity during induction.

Global OS for 9 patients 44%.

EFS/OS for localized patient: 66%.

OS for metastatic patients: 0%

Conclusion: Askin tumour is a rare disease that needs early diagnosis and intensive chemotherapy regimens. Patients with localized disease can be cured with chemotherapy and local treatment. Radiotherapy could be avoided in patient with complete resection and high necrosis response. In our experience no patient with metastatic disease achieved long survival and all progressed in a short time despite treatment.

P-0132 | Four Variants in 14q32 Mirna Cluster are Associated with the Risk of Osteosarcoma in the Spanish Population

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Background/Objectives: A recent genome wide association study (GWAS) in osteosarcoma risk identified significant associations in extragenic positions, suggesting that non-coding regions could play an important role. The deregulation of microRNAs (miRNAs) has already been associated with osteosarcoma. Consequently, genetic variants affecting miRNA function could contribute to the risk of the disease. In fact, two variants in miRNAs have already been associated with osteosarcoma risk. Considering that a large number of new miRNAs has been annotated, this study aimed to evaluate the involvement of new variants in pre-miRNAs in relationship to the risk of osteosarcoma.

Design/Methods: All the SNPs in pre-miRNAs with a MAF>0.1 in Caucasian populations described in databases until May 2014 were selected. A total of 213 SNPs in 206 pre-miRNAs were analyzed in a cohort of Spanish patients (n=74) and their corresponding controls (n=160) using GoldenGate Veracode technology. R v2.11 software was used for statistical analyses.

Results: The most remarkable finding was the association detected between 4 SNPs in 4 pre-miRNAs located at the 14q32 miRNA cluster and osteosarcoma risk. Interestingly, miRNAs of this cluster were found to be underexpressed in osteosarcoma in previous studies. This down-regulation was correlated with MYC overexpression. Therefore, genetic variation in these miRNAs could lead to their downregulation, which in turn could lead to MYC overexpression. This result supports that this region is a hotspot for the development of the disease.

Conclusion: Variants in the 14q32 miRNA cluster could be associated with the risk of osteosarcoma in the Spanish population.

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P-0133 | Treatment of Children with Ewing Sarcoma in Saint Petersburg, Russia

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Background/Objectives: There is no national protocol for Ewing Sarcoma (ES) in Russia. However, our hospitals were allowed to follow recommendations of the Euro-EWING-99 protocol. Our study is to assess the results of treatment in patients with ES who were treated according to Rosen's VACD regimen (vincristine, actinomycin-D, cyclophosphamide and doxorubicin) from 1992 to 2000 and the Euro-EWING-99 protocol since 2001.

Design/Methods: We provided retrospective analysis of 71 patients (56% male, median age 13 years (4-17 years)) from 1992 to 2015. The median follow-up was 31 months (4-199 months). The primary site was extremity in 39 patients and axial/other in 32 patients (43.8% pelvis). Fifty five patients were treated according to Euro-EWING-99 protocol and 16 patients by Rosen's regimen. There are 25 patients with metastases (68% pulmonary metastases) in Euro-EWING group and 4 patients with metastases in Rosen's. Overall survival (OS) and event-free survival (EFS) rates were estimated by Kaplan-Meier analyses and Log-rank test.

Results: The 5-year OS was statistically superior ($p=0.0024$) for patients treated according to Euro-EWING-99 protocol compared to Rosen's group (48.8±8.5%, median OS 58 months and 18.7±9.8%, median OS 18.5 months respectively). The 5-year EFS for patients of Euro-EWING-99 group (EFS, 37.2±8.2% v 18.7±9.8% for Rosen's group; $p=0.05$) was also significantly higher. In Euro-Ewing-99 group, the 5-year OS in patients with localised ES was 61.2±11%, median OS 139 months. The 5-year EFS in patients with pulmonary metastases was 21.8±12.6%, median EFS 37 months. The difference in OS of patients with localised ES based on primary site was not statistically significant in our group (axial ES 74.6±12.8% v extremity ES 42.1±17.7%; $p=0.217$).

Conclusion: Using Euro-EWING-99 protocol has improved treatment results in both hospitals. The primary site of localised ES had no impact to the treatment results, but there were only 8 patients with pelvic tumour in our group.

P-0134 | Role of Bone Marrow Aspiration and Biopsy in Diagnostic Staging of Paediatric Ewing Sarcoma

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Background/Objectives: Ewing sarcoma (ES) is the second most common primary malignant bone tumour in children and adolescents (Esiashvili N et al. J Pediatr Hematol Oncol 2008). ES tumors can occur in bones of the extremities, pelvis, chest wall as well as soft tissue². Pediatric Ewing sarcoma (ES) treatment protocols at present indicate the need for bilateral bone marrow aspiration and biopsy (BMAB) as part of the initial staging work-up. There are no established recommendations that assist in evaluating the need for BMAB procedure in patients identified as having non-metastatic ES according to conventional imaging (CI). Here we aim to report our institutional experience of positive BMAB findings in patients who were considered non-metastatic on standard imaging studies.

Design/Methods: Medical records at a large regional cancer center were retrospectively reviewed from January 2010 to January 2015 after IRB approval. Data was collected for patients with newly diagnosed non-metastatic ES on imaging studies and less than 20 years of age at the time of diagnosis.

Results: A total of 139 patients were identified for chart review. Ten patients were excluded from the analysis because their BMAB were not done at initial staging. Eleven patients were identified to have bone marrow (BM) disease. Among these 5 (45.5%) had metastatic disease on bone scan (p=002), and 1 (0.09%) had both pulmonary and bone metastases. Six patients (54.5%) with BM disease were non-metastatic on CI.

Conclusion: Patients with metastatic disease on bone scan have a higher risk of bone marrow involvement and should get BMAB on initial staging. There is BM involvement without the presence of metastatic disease. BMAB should be performed at the initial staging for all newly diagnosed paediatric patients with ES.

P-0135 | Ewings Sarcoma of the Head and Neck Region: Outcomes of Multimodality Treatment

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Background/Objectives: To evaluate treatment response and prognostic factors for patients of non-metastatic Ewings sarcoma (ES) of the head and neck region treated with curative intent at the Tata Memorial Hospital, Mumbai, India.

Design/Methods: From January 2009 to December 2014, 25 patients with histologically proven ES in the age group of 2 months – 50 Yrs (Median 17 Yrs) were retrospectively evaluated. Prognostic factors like patients age, sex, skeletal/ extra-skeletal origin, primary site (para nasal sinus/non paranasal), tumour size, regional nodal status, performance status, haematological and biochemical parameters (hemoglobin, total count, lactate dehydrogenase, alkaline phosphatase and albumin), response to chemotherapy (CTH) and type of local treatment were evaluated.

Results: Fourteen (56%) were males, Twelve (48%) patients had extra-skeletal disease with a mean size of 6 cms. All patients received multimodal treatment in the form of EFT 2001 systemic CTH and local treatment comprising of surgery (Sx) or radiation therapy (RTh) or both. After a median follow-up of 30 months, the 2 year local control (LC), disease free survival (DFS) and overall survival (OS) were 84%, 84% and 85% respectively. All patients were disease free at completion of planned treatment. At last follow up, 20 (80%) patients were alive

and disease free. Two patients had local relapse only while one had both local relapse and distant metastases. On univariate analysis patients undergoing Sx and RTh had superior LC and OS compared to RTh alone (70% vs. 100%; $p=0.09$ and 64% vs. 100%; $p=0.07$) respectively. None of the prognostic factors were statistically significant. All patients tolerated treatment well without any grade III or IV toxicities.

Conclusion: Multimodality treatment using a combination of CTh, Sx and RTh results in optimal disease control with acceptable toxicities.

P-0136 | Development of Computational Tools to Interpret Tumour Necrosis in Resected Osteosarcoma

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Background/Objectives: Tumour necrosis remains the most important biomarker for patients with non-metastatic high-grade osteosarcoma. We hypothesize that failed international efforts to successfully employ this biomarker in treatment assignment relates in part to the late availability of data and the inability to explore whole tumour response with current techniques. We propose to develop computational tools to predict tumour necrosis with MRIs performed early in treatment using image pattern recognition algorithms.

Design/Methods: Osteosarcoma resection specimens are prepared for histologic evaluation of response by decalcifying and then taking sections from the estimated widest and longest tumour surface area. To maintain orientation, whole tumour specimens are overlaid with a grid/tumour map identifying the sections, and histology slides of individual sections are then labeled according to their place on this grid. Each section is a single slide, while each individual patient case may require 20-50 slides depending on tumour size. For this study histopathology slides have been digitalized using an Aperio Scanscope® retaining the cellular detail and ability to magnify images.

Results: Fifty resection samples and their representation tumour map, from patients treated over a 20-year period have been identified. Digital images have been stitched together by inverting, orienting and scaling individual section slides to their appropriate place in a digital tumour map. Computer algorithm to complete this task automatically has been developed along with tools to upload data to a web page and tools to allow image manipulation to visualize either a portion of an image or the whole tumour map.

Conclusion: In order to develop an algorithm to interpret MRI findings that correlate to histopathological data we will identify a co-planar tumour area for both digital data sources. We have successfully completed the first step in this process by re-creating a digital histopathology whole specimen image reflecting the tumour grid used in preparation of histology slides.

P-0137 | Higher Gemcitabine Dose was Associated with better Outcome of Osteosarcoma Patients Receiving Gemcitabine-Docetaxel Chemotherapy

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Background/Objectives: We evaluated the efficacy of gemcitabine and docetaxel chemotherapy (GEM+DOC) in Korean patients with recurrent or refractory osteosarcoma.

Design/Methods: Data of 53 patients (40 male, 13 female) from 9 institutions who received gemcitabine (675 or 900 mg/m² on days 1 and 8) and docetaxel (100 mg/m² on day 8) were retrospectively reviewed.

Results: The median age at GEM+DOC chemotherapy was 15.7 years (range, 7.6-43.8 years). Tumour sites were lung (n=30), bone (n=14), lung+bone (n=7) and lung+elsewhere (n=2). A total of 188 courses of GEM+DOC chemotherapy were administered (median 3 courses; range, 1-10 courses). Response was evaluated in 28 patients and there were 3 complete response (CR, including 2 metabolic CR), 1 partial response (PR) and 4 stable disease (SD). Objective response rate (CR+PR) and disease control rate (CR+ PR+SD) were 14.3% and 28.6%, respectively. A higher dose of gemcitabine (900 mg/m²) was associated with better disease control (50.0% vs. 12.5%, $P=0.03$). With a median follow-up of 14.9 months (range, 0.6- 122.5 months), 1-year overall and progression-free survival rates were 56.6±6.8% and 22.9±6.1%, respectively. Surgery ($P=0.001$), higher gemcitabine dose ($P=0.0003$), number of tumour recurrences ($P=0.002$) and tumour sites ($P=0.0007$) influenced the survival. For the 28 patients who received palliative GEM+DOC therapy, disease control ($P=0.002$) and higher gemcitabine dose ($P=0.04$) were associated with better survival.

Conclusion: A higher dose of gemcitabine was associated with better outcomes in osteosarcoma patients receiving GEM+DOC chemotherapy. Further studies are necessary to investigate the efficacy of more aggressive and higher doses of GEM+DOC chemotherapy in osteosarcoma.

P-0138 | Pretreatment Neutrophil-to-Lymphocyte Ratio and Lymphocyte Recovery: Independent Prognostic Factors for Survival in Paediatric Sarcomas

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Background/Objectives: Pretreatment neutrophil-to-lymphocyte ratio (NLR) and lymphocyte recovery have been shown to be associated with prognosis in several types of cancer in adults. However, evidence in paediatric cancer is scarce. The aim of our study was to retrospectively evaluate whether pretreatment NLR and late lymphocyte recovery (absolute lymphocyte count of <800 cells/uL at day 15 post initial chemotherapy) as prognostic factors in children with paediatric sarcomas.

Design/Methods: Study participants were identified from a retrospective cohort of 100 children treated for osteosarcoma (n=55), Ewing sarcoma (n=23) and rhabdomyosarcoma (n=22) between 2002 and 2015 at Rebagliati-Hospital, Peru. Data for the haematological variables were obtained from clinical records and were analyzed together with other known prognostic factors in the univariate and multivariate analyses.

Results: The median follow-up time was 37.5 months. The 5-year overall survival (OS) rates in children with osteosarcoma, Ewing sarcoma and rhabdomyosarcoma were 55.8% (±9.4 Standard Error, SE), 61.2 (±18.2, SE) and 66.1% (±17.2, SE) in localized disease; and 19.1% (±9.4, SE), 16.75 (±10.3, SE) and 17.8 (±15.4, SE) in metastatic disease, respectively. In multivariate analysis, NLR>2 was an independent prognostic factor for OS in patients with osteosarcoma (HR 2.27, 95%CI 1.07-5.30; $p=0.046$) along with metastatic disease and poor histological response after neoadjuvant chemotherapy; as well as in patients with rhabdomyosarcoma (HR 4.76, 95%CI 1.02-22.24; $p=0.0237$) along with metastatic disease. Late lymphocyte recovery was an independent prognostic factor in osteosarcoma (HR 3.34, 95%CI 1.37-8.12; $p=0.008$) and rhabdomyosarcoma (HR 3.89; 95%CI 1.01-14.89; $p=0.0338$). Additionally, pre-treatment lymphopenia<1000 cells/uL significantly correlated to inferior OS in all groups ($p<0.05$).

Conclusion: Our study confirms that NLR and lymphocyte recovery are independent prognostic factors for paediatric sarcomas, implying an important role of immune system in survival. Clinical utility of these prognostic biomarkers should be validated in larger paediatric studies.

P-0139 | Osteosarcoma with Several Bone Lesions at Diagnosis: Experience of the OS2006 Study

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Background/Objectives: We aimed to describe the clinical characteristics and outcome of patients with osteosarcoma and several bone lesions.

Design/Methods: Description of all patients prospectively enrolled in the French OS2006 study between April-2007 and March-2014, for a newly diagnosed high-grade osteosarcoma with at least one synchronous distant or regional bone lesion in addition to the primary. MRI of the primary site and technetium bone scintigraphy (TBS) were mandatory at diagnosis, Positron Emission Tomography (PET) was optional.

Results: From the 518 study patients, 21 patients (median age=13.7; range, 5.7-37) had several bone lesions: 10 with a unique lesion in addition to the primary, and 11 with multifocal lesions. Bone metastases were localised in a bone contiguous to the primary tumour in 6 patients. Pulmonary metastases were associated in 10/21 patients. TBS and PET were both performed in 11/21 patients: secondary bone lesions identified on TBS were associated with a strong PET signal in 6 and a weak signal in 2, whereas both tests were negative in 2 patients and PET signal was weak in 1 patient with bone lesions diagnosed on MRI. A complete remission was obtained in 12 patients after polychemotherapy combined with local treatment of primary site and metastatic lesions. Only 5 patients (4 with a unique lesion and 1 with 2 regional lesions) are alive free of event with more than 2 years of follow-up, leading to a 2-year EFS of 24% (95%CI, 11%-45%), not significantly different from that of patients with lung metastases only ($p=0.52$). Overall survival was 36% (95%CI, 19%-56%).

Conclusion: Multiple bone lesions are rare in osteosarcoma and not always evidenced by PET. The prognosis of these patients remains poor, but in our study it was no worse than that of patients with lung metastases only. Number and sites of bone lesions may influence patient outcome.

P-0140 | Outcome and Prognostic Factors for Localized Ewing Sarcoma Family of Tumors: Children's Cancer Hospital 57357 Egypt (CCHHE) Experience

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Background/Objectives: The survival of patients with Ewing sarcoma family of tumors (ESFT) has improved dramatically as a result of the combined modality treatment with chemotherapy, surgery and/or radiotherapy. The objective of our study was to determine the outcome and prognostic factors of ESFT patients treated at our institution.

Design/Methods: We retrospectively reviewed the records of 155 patients treated between January 2008 and December 2014 according to Ewing Sarcoma institutional protocol (Adopted from POG#9354/CCG#7942, arm A). All patients received neoadjuvant chemotherapy, surgery and/or radiotherapy for local control followed by adjuvant chemotherapy.

Results: The median age at diagnosis was 11 years. The primary site of the disease was in the appendicular skeleton in 54% and in the trunk in 46%. In terms of local control eighty patients underwent surgery only, 50 received radiotherapy and 25 underwent surgery followed by radiotherapy. The median follow up period was 34 months (range from 4 months to 8 years). The 5 year overall survival (OS) and relapse free survival (RFS) were 74% (SE 4.3%) and 73.6% (SE 4.2%) respectively. In univariate survival analysis good response to neoadjuvant chemotherapy (P= 0.027), surgical resection (P= 0.001) and appendicular site (P= 0.04) were associated with better outcome. Upon multivariate analysis only complete surgical resection was the only independent prognostic factor.

Conclusion: In this institutional study, the modality of local control, primary tumour site and histologic response to neoadjuvant chemotherapy were predictors of outcome. These factors should be considered in designing risk adapted treatment protocols for localized Ewing sarcoma family of tumors.

P-0141 | A Systematic Review of Chemotherapy in Metastatic, Refractory or Relapsed Ewing Sarcoma in Patients Less Than 30 Years of Age

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Background/Objectives: Outcomes in metastatic, relapsed or refractory Ewing Sarcoma (ES) are poor, necessitating development and evaluation of new treatment regimens. This systematic review evaluated the evidence for the effectiveness of current regimens in metastatic, refractory or relapsed ES in patients under 30 years of age.

Design/Methods: Bibliographic databases were searched for ES and chemotherapy regimens. Two reviewers assessed papers for inclusion. Data were extracted by one reviewer and checked by a second. Response outcomes (overall response - OR, complete response - CR, partial response - PR, progressive disease - PD) were extracted and summarised.

Results: Searches yielded 326 citations of which 19 studies met inclusion criteria. No randomised controlled trials (RCTs) were identified. Publication dates ranged from 1998-2015. Total number of patients was 376; study sizes ranged from 6-37. There was considerable heterogeneity concerning patient population, previous treatment, re-induction schedule and response assessment, precluding synthesis of results. Study quality was highly variable. Irinotecan/temozolomide (4 studies; 64 patients) had OR of 46% (19% CR, 27% PR) with PD in 48%. Topotecan/cyclophosphamide (5 studies; 108 patients) demonstrated OR of 42% (6% CR, 36% PR) with PD in 13%. Gemcitabine/docetaxel (2 studies; 20 patients) had OR of 30% (CR 15%, PR 15%) with PD in 35%. Single agent irinotecan, docetaxel and topotecan had OR of 25%, 11% and 6% respectively. Toxicity varied across regimens: irinotecan/temozolomide caused treatable diarrhoea, vomiting and haematological toxicities; topotecan/cyclophosphamide caused severe myelosuppression associated with 5 treatment-related deaths; gemcitabine/docetaxel caused mild myelosuppression.

Conclusion: Evidence for the efficacy of chemotherapy regimens in this patient group is very limited. Comparison of regimens is not possible because of the uncontrolled nature of all the studies, with potentially substantial confounding factors, e.g. patient selection. Prospective phase III RCTs - such as the ongoing rEECur trial - are urgently needed to inform clinical decision making to improve outcomes.

P-0142 | Total Pleuropneumectomy as Salvage Therapy in Children Suffering from Refractory Sarcomas with Multiple Pleural Localizations

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Background/Objectives: Refractory paediatric sarcomas with pleuropulmonary localizations (locoregional or metastatic extension) have a dismal prognosis without any curative treatment because of the impossibility to obtain local control. The purpose of this study was to determine if radical pleuropneumectomy could be a therapeutic option in these cases.

Design/Methods: We retrospectively reviewed 5 cases of paediatric refractory bone or soft tissue sarcomas with pleuropulmonary locoregional or metastatic extension, in whom a salvage pleuropneumectomy had been performed between 2005 and 2009.

Results: Children were 9 to 15 years-old at the time of procedure. Underlying disease included 2 metastatic Ewing sarcomas (ES), 2 metastatic osteosarcomas (Os) and one primary undifferentiated chest wall sarcoma with lung and pleura extension. Pleural localizations had occurred either at time of initial diagnosis (1 ES and 1 undifferentiated sarcoma) or at relapse (within 2 to 4 years of diagnosis). All patients received preoperative chemotherapy. Due to pleural spread, the only alternative to pleuropneumectomy was a palliative treatment. Thoracotomies and sternotomies allowed complete resection in 1/5 and marginal in 4/5. No post-operative complication occurred. Mean post-operative average hospital stay was 11 days (range 8 to 16). Chemotherapy could be started within 15 days after procedure. Six months after the procedure, Lansky score >80% was observed in all but one patient. Two patients died, respectively 3 and 10 months after surgery due to multimetastatic relapse. Three are still alive in complete remission 4, 6 and 7 years after surgery. Pulmonary function assessments showed good respiratory function at 3 months (5/5), 3 years (3/3) and 5 years (3/3).

Conclusion: In case of primary or relapsing paediatric sarcoma with unilateral pleuropulmonary extension not accessible to conservative local treatment, a total pleuropneumectomy is a valid salvage therapy allowing long survival. Procedure is well tolerated in children, allowing satisfying long term respiratory function.

P-0143 | The Best Strategy as a First Line Treatment through Paediatric Iranian Population with Osteosarcoma

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Background/Objectives: Based on using two different chemotherapy schemes (high dose methotrexate protocol and regimen without methotrexate) and rare evidences around outcomes of treatment in Iranian paediatric osteosarcoma population, this study designed to prepare a solution that which of the protocols can be the best strategy (with low outcomes and challenges through high survival rate) as the first line treatment?

Design/Methods: This retrospective single center study designed with paediatric patients less than 15 years old who diagnosed as osteosarcoma cases between April 2007 and April 2015. Patients randomly categorized into two groups that used high dose methotrexate protocol (n=20) or regimen without high dose methotrexate (n=21). The statistical significance in the two sided study was defined by a P-Value < 0.025. For defining the population, descriptive statistics were used. The comparison between discrete variables was analyzed by the χ^2 test or Fisher's exact test, also Mann-Whitney test was used for analyzing continuous variables. All of the analysis was done by SPSS version 22.

Results: Out of 41 enrolled patients, 20 cases (14 out of 20 children with HD MTX and 6 out of 21 children with non-HD MTX) died. The median time of overall survival rate for patients with osteosarcoma who treated at MPCTRC was 30 months (range 21 days to 6 years). The median time for Disease Free Survival (DFS) through considered cases was 6 months (maximum 56 months). The median time of first event (DFS) for cases who used HD MTX was one month (maximum 19 months) and for cases who administered by non-HD MTX was 11.5 months (maximum 56 months).

Conclusion: The author's suggestion is that non-HD MTX regimen can have more efficacies through improving the survival rate of paediatric cases of osteosarcoma. We assume that the answer of the subject is protocol without high dose methotrexate.

P-0144 | Bones Sarcomas in Children: Results of Treatment

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Background/Objectives: Advances in diagnosis and treatment of childhood cancer have dramatically increased long-term survival and it is now evident that the disease and its treatment can significantly impair long-term health.

Design/Methods: Ninety eight children and adolescents at the mean age of 10,9 years (51 males, 47 females) with osteosarcoma (OS), Ewing's sarcoma (ES), and other tumors were treated between 1999 and 2013 years. Histologically, 36 patients had OS, 59 - Ewing sarcoma. Nine patients had solitary metastases, 21 - multiple. Nine patients had distant metastases at lungs, bones were involvement in 3 cases, combine lesion were in 9 cases. Treatment consisted of neoadjuvant chemotherapy, the radiotherapy of the initial tumour and metastasis left after the induction and/or oncologic surgery and adjuvant chemotherapy. The local control of the tumour consisting of the surgical ablation of the primary lesion and metastases, if the technical opportunity of this stage is available, including limb-sparing procedures. The most common late effects we had observed were: scoliosis, muscular hypoplasia, osteopenia, limb-length discrepancy in spite of usage of growing endoprosthesis, poor joint movement, musculoskeletal deformity. Twenty three patients had from 5 till 11 late effects. An individual rehabilitation program consist with combined early mobilization, physical exercise, kinesiotherapy, aquatic rehabilitation and orthopaedic correction, laser therapy, massage, gait training.

Results: In our research we have analyzed the 2-year disease free survival (DFS). Thus, 2-year DFS for patients with bone sarcomas were 71,5±4,7. DFS for patients with metastases were 48,7±9,3%. DFS for patients underwent limb-sparing procedures were 74,3±6,7%.

Conclusion: More aggressive systemic chemotherapy and surgery improves DFS. Long-term survival is possible, even for patients with metastatic disease. All long-term survivors of childhood cancer therapy should attend a specialized late effects clinic yearly.

P-0145 | Long-Term Outcome in Patients with Pelvic Ewing Sarcomas

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Background/Objectives: With improved survival rates of patients with Ewing sarcoma the quality of long-term survivorship needs to be addressed. The pelvis is one of the most common primary sites for Ewing sarcomas, and comprises 1/5 of all diagnoses. In this study, general recovery and restitution of function following intensive bone tumour treatment were

analysed by assessing the clinico-functional outcome and physical activity using self-reporting and objective measurement tools.

Design/Methods: Long-term outcomes of 125 former patients with pelvic Ewing sarcoma, registered between 1980 and 2009 in consecutive clinical trials of the GPOH, were assessed using the TESS, SF-36, BSI, and RSES questionnaire scales, and the accelerometer StepWatch Activity Monitor (SAM). To compare results with healthy subjects, 61 non-random peer controls were selected. Median observation time was 12.5 years from primary diagnosis (range 3.7–30.6).

Results: Absolute values from the questionnaire scores indicated no major significant clinical findings in former patients. Compared to controls, unfavourable outcomes were however seen on physical-based TESS, PCS (SF-36) ($d > -0.50$) and BSI-S scales ($d = 0.46$) ($P < 0.001$), compared to mental-based MCS, BSI-A, BSI-D, RSES scores ($d < 0.35$). Former patients were less active than the control group (9,304 vs. 12,053 steps per day; $d = -0.75$; $P < 0.001$), and on average did not reach the recommended level for active life-styles ($> 10,000$ steps). Comparing local therapy modality, scores for SAM, TESS, PCS were 10,368, 95.0, $T = 52.2$ for patients treated with surgery ($N = 14$), 8,687, 89.3, $T = 45.7$ in patients with combined modality treatment ($N = 71$), and 10,072, 92.9, $T = 48.5$ for patients with definite radiotherapy ($N = 39$) ($P = 0.164$; $P = 0.073$; $P = 0.064$).

Conclusion: Survivors of primary pelvic Ewing sarcoma exhibited moderately reduced self-reported, mainly physical-based, outcome scores compared to controls; this was confirmed by an objective measurement of reduced physical activity. Continuous long-term observation will be important in order to identify disease-specific prognostic factors for these patient-orientated outcomes, and to reduce potential late effects of treatment.

P-0146 | Endocannabinoid/Endovanilloid System as New Therapeutic Target in Osteosarcoma

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Background/Objectives: Osteosarcoma (OS) is the most common primary malignant tumour of bone and it affects predominantly children and adolescents, exhibiting high invasion and metastasis rate. Available treatments results in significant morbidity (cardiac toxicity, infertility, renal dysfunction) and chemo resistance. Therefore novel therapeutic approaches are needed to treat osteosarcoma more efficiently and improve patient's life quality. We studied the involvement of the Endocannabinoid/endovanilloid (EC/EV) system in OS because of its well known anti-tumour potential and its emerging role in bone metabolism.

Design/Methods: We treated 7 OS cell lines (Saos-2, MG-63, 143B, HOS, MNNG/HOS, KHOS/NP e Hs888Lu) with agonist and antagonist of the EC/EV system (JWH-133 [100 nM, 1 μM e 5 μM], AM630 [10 μM, 50 μM e 100 μM], RTX [2.5 μM, 5 μM, 7 μM], I-RTX [2.5 μM]) and evaluated by Quantitative PCR, Annexin V Assay and Count & Viability Assay the effect of these compounds on cell survival and proliferation. Student T-Test has been used to evaluate the statistical relevance of the assays. P value < 0.05 have been considered statistically significant.

Results: TRPV1 stimulation with RTX [2.5 μM] and CB2 with JWH-133 [100 nM] induces apoptosis in all OS cell lines together with an over expression of p53 onco-suppressor gene in MG63 and HOS cell lines and a marked down regulation of the survival factor ERK2 in MNNG/HOS, 143B, Hs888Lu and KHOS/NP cell lines; whereas the blocking of CB2 receptor with AM630 [10 μM] induces apoptosis only in 5 of the cell lines we used.

Conclusion: Taken together those results suggest a possible and desirable application of EC/EV compounds in the treatment of all different forms of OS

P-0147 | A Pictorial Review of Paediatric Skull Base Lesions

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Background/Objectives: The skull base anatomy is complex. Paediatric skull base lesions are uncommon and have a wide differential diagnosis which includes benign and malignant entities which can be a challenge to diagnose. Radiology plays a key role in the diagnosis of these lesions as many can be difficult to biopsy. It is important to identify and not to over-investigate benign conditions. Assessing their location and extent is vital for treatment planning.

Design/Methods: In this pictorial review we will clearly illustrate the anatomy of the skull base and the multimodality imaging features of a number of the different pathologies encountered.

Results: Neoplastic skull base lesions including Langerhans cell histiocytosis, Chordoma, Burkitt lymphoma and neuroblastoma metastases will be discussed and illustrated. Benign entities including CHARGE syndrome, fibrous dysplasia, aneurysmal bone cyst and osteomyelitis will also be reviewed.

Conclusion: Paediatric skull base lesions are complex and can be challenging to diagnose. Following this review the reader will have a greater knowledge of the anatomy of the skull base and the key imaging features of pathologies that can occur.

P-0148 | Prognostic Factors Affecting Outcome of Resectable Paediatric Ewing Sarcoma Family of Tumors in Chest Wall

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Background/Objectives: Ewing sarcoma family of tumors (ESFT) is the most frequent malignant tumour of the chest wall in children and young adults. Complete resection is the goal, and if this is accomplished with adequate margins, it may allow the patient to avoid radiation therapy with its potential long-term complications.

The aim of this study was to evaluate the role of different prognostic factors on the outcomes of primary ESFT of the chest wall treated by surgery.

Design/Methods: Retrospective analysis of twenty-two patients treated at the Children's Cancer Hospital Egypt (CCHE-57357) between July 2007 and December 2014. All patients received chemotherapy (including Vincristine, Adriamycin, Cyclophosphamide, Etoposide, and Ifosfamide) and surgery, with or without radiotherapy. Patients' outcomes were evaluated in relation to age, gender, pleural effusion, tumour size, presence of lung infiltrates, initial metastases, surgical margins and histologic response to treatment.

Results: With a median follow-up of 28.5 months, the 5-year relapse-free survival (RFS) and overall survival rates were 50.1% and 55.6%, respectively. Upon univariate analysis, RFS was significantly related to the surgical margins only ($P = 0.035$), but not to the other prognostic factors; age ($P = 0.66$), gender ($P = 0.96$), pleural effusion ($P = 0.93$), tumour size ($P = 0.762$), presence of lung infiltrates ($P = 0.488$), initial metastases ($P = 0.207$), and histologic response to treatment ($P = 0.215$). Median age of patients was 8.2 (range 5 months to 16 years). All patients underwent surgery of primary tumour in the chest wall, where wedge resection was done in ten patients. Postoperative radiotherapy was given in 8 cases. Local and systemic recurrences occurred in 9 patients (40.9%) (Two patients developed local relapse, and seven patients developed systemic relapse).

Conclusion: Multi-modal treatment of paediatric ESFT of chest wall results in long-term survival. Complete surgical resection is the only prognostic factor proven to be affecting the relapse-free survival of our patients.

P-0149 | MAPK Pathways Regulation by DUSP1 in Osteosarcoma Development: Potential Markers and Therapeutic Targets

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Background/Objectives: Osteosarcoma (OS) is the most frequent primary bone tumour that affects children and adolescents. OS is highly aggressive with high risk of metastasis and, the implementation of new drugs has not been successful. The identification of biomarkers or new therapeutic targets can help in advances of OS treatment. MAPKs are major signaling transduction molecules that play an important role in regulating cellular responses. DUSP1 is a phosphatase that desphosphorylates the MAPKs. Both MAPKs and DUSPs have been implicated as major modulators of critical signaling pathways that are dysregulated in various diseases. In previous studies of our group, we found that *MAPK7* gene expression contributed for worst overall survival and treatment response, and *MAPK7* can modulate growth, proliferation, migration, invasion and chemosensitivity in OS cell lines. Thus, the purpose is to find prognostic markers and/or therapeutic targets for increasing the potential options for diagnosis and treatment in OS.

Design/Methods: We analyzed gene expression of MAPK pathways that participate in *MAPK7* regulation, and *DUSP1* gene using paired 28 pre/post-chemotherapy and 12 metastasis OS samples. To understand the *DUSP1* role in the pathogenesis of OS, we assessed the function of *DUSP1* in four OS cell lines through a series of cellular assays combined with gene silencing technique.

Results: Our findings showed increased *MAP2K6*, *MAP4K3* and *DUSP1* gene expression in post-chemotherapy OS samples presenting poor prognosis. We also found that the suppression of *DUSP1* gene expression resulted in decreased proliferation, migration and invasion in OS cells.

Conclusion: These results suggest that members of MAPK family may be possible prognostic markers in OS and that *DUSP1* has a relevant role in the OS pathogenesis. Our findings could be attractive for the development of new strategies of OS treatment, including MAPK family members as possible target for treatment of conditions that are resistant to current OS treatment.

P-0150 | Shell We Change Chemotherapy Regimen in Non Metastatic Osteosarcoma Patients According to the Tissue Necrosis after the First Line Chemotherapy

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Background/Objectives: Tumour necrosis following preoperative chemotherapy in patients with osteosarcoma is a predictor of overall survival. The purpose of this study was to determine

if there is a better prognosis if primary chemotherapy regimen is changed postoperatively in low histological responders in osteosarcoma patients.

Design/Methods: 23 patients with nonmetastatic osteosarcoma were managed with preoperative and postoperative chemotherapy and operative resection during 1995-2015. Sections of each operative specimen were examined, and the histological response to chemotherapy was graded.

Results: First line chemotherapy was epirubicin 90 mg/m²/day; ifosfamide 1 mg/m²/day x3 and cisplatin 100 mg/m²/day in all of the patients.

The chemotherapy regimen was changed to high dose mtz regimen in 5 patients with grade 1 and 2 response; and in 18 patients the first line chemotherapy was not changed among them there were 6 poor responders (grade 1 and 2) and 12 good responders (grade 3).

In all of the patients the overall survival in 5 years is 82.6%; in poor histological responders is 72.7% and in grade 3 responders is 85%.

The survival in poor responders that chemotherapy regimen was not changed postoperatively is 66.7% (n=6) and in poor responders that chemotherapy regimen was changed postoperatively is 100% (n=5). Statistical analysis could not be done because of inadequate number of the patients but as seen, there is a clear difference.

Conclusion: The histological response to preoperative chemotherapy is an important clinical predictor in osteosarcoma. This indicator should be used to identify patients who are at high risk for poor prognosis. This study could not establish statistically if such patients may be candidates for more intensive therapy or not because of inadequate number of the patients. But there is a clear increase in survival when the chemotherapy regimen was changed to more intensive chemotherapy postoperatively in poor responders.

P-0151 | Askin Tumours

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Background/Objectives: Askin tumour was defined by Askin and Rosai in 1979. Although once accepted as distinct entity, Ewing sarcoma, Askin tumour and primitive neuroectodermal tumour (PNET) are all considered as members of the Ewing family of tumours; and when localised to the thoraco-pulmonary region, these are termed as Askin tumours. The frequency of Ewing sarcoma and PNET among childhood tumours is 2%.

The aim of this study is to examine the incidence, characteristics, survival and the factors affecting the survival in our Askin Tumour patients.

Design/Methods: This is a retrospective review of 91 paediatric patients with Ewing Sarcoma family tumours treated between 1996 -2015. Data collected from the charts and survival analysis was performed using Kaplan-Meier method.

Results: Of the 91 patients, Askin tumour was diagnosed in 16 patients (17.5%). Median age was 12 years (9-17.5 years) There were 11 male and 5 female patients. Only five of the patients were metastatic. (3 bone and one lung) Presenting symptom was respiratory insufficiency in 9 (56.2%); mass in thorax in 5 (31.2%) patients. The tumour was diagnosed by chance in 2 case.

All of the patients had received neoadjuvant chemotherapy. (ifosfamide, etoposide, vincristine, doxorubicine, cyclophosphamide and actinomycin.) After 3-4 cycles of chemotherapy, surgery had been performed. Radiotherapy was used in all cases except one. During the follow up, 2 patients had relapsed, 2 died with progression, 1 with infection. Two patients are still in chemotherapy. The others are in complete remission.

The 5 year overall survival is 65% and disease free survival is 60%.

Conclusion: Askin tumour should be considered as an aetiological possibility in tumours located at the thoracopulmonary region, Patients with such tumours should be treated with neoadjuvant chemotherapy and wide local excision whenever possible. Radiotherapy should not be omitted because of the possibility of microscopic rest.

P-0152 | CYP Genes and Osteosarcoma: Their Role in Tumorigenesis, Pulmonary Metastatic Microenvironment and Treatment Response

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Background/Objectives: Osteosarcoma (OS) is the most common malignant bone tumour in children and adolescents. The present study investigated the expression of CYP (Cytochrome P-450) genes in OS, and their role in microenvironment to OS establishment and treatment response, since the CYP enzymes mediate the metabolic activation of precarcinogens and participate in the inactivation and activation of anticancer drugs. The aim was also to investigate if chemotherapy modulates CYP genes expression in OS cell lines.

Design/Methods: We investigated the expression of CYP1A2, CYP3A4 and CYP3A5 genes in 135 OS samples, including biopsy, surgery, bone adjacent to tumour (nonmalignant tissue), metastasis and lung adjacent to metastasis (nonmalignant tissue). As control, we used normal bone and lung tissues from patients with no malignant disease. We also investigated the modulation of CYP expression by chemotherapy drugs (cisplatin, doxorubicin and methotrexate) in OS cell lines (Saos-2, MG-63, KHOS, U2-OS and M-OS).

Results: The adjacent lung samples presented higher CYP1A2 gene expression than normal lung (p=0.0256). The biopsy samples presented lower CYP3A4 gene expression than normal bone (p=0.0314). The highest CYP1A2 gene expression in surgery samples and the highest CYP3A4 gene expression in adjacent bone were correlated with better event free-survival

(p=0.0244) and good response (p=0.0484), respectively. Moreover, the highest gene expression of CYP1A2, CYP3A4 and CYP3A5 were associated with toxicity events, such as infection, mucositis, fever, diarrhea, nephrotoxicity and hepatotoxicity. Furthermore, the chemotherapy drugs upregulated the CYP expression in OS cell lines.

Conclusion: CYP1A2 and CYP3A4 genes play a role in lung microenvironment to OS metastasis establishment and to primary OS tumorigenesis, respectively. The chemotherapy drugs upregulated CYPs expression in OS cell lines and their overexpression after chemotherapy were correlated with better treatment response in OS patients. Therefore, our findings suggested that CYP genes play an important role in primary and metastatic OS tumorigenesis, as well as treatment response.

P-0153 | The Role of Immunoscores in the Survival of Paediatric Osteosarcoma

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Background/Objectives: The role of the immune system and its interplay with tumour cells in osteosarcoma (OS) is poorly defined.

Design/Methods: We investigated the expression profile of 34 primary and metastatic paediatric OS. Data was compared to a customized body map of 852 samples and 27 healthy human tissues. Different gene sets were defined to estimate a multi-variate immunoscore system. A previously defined chemokine (CK) score, costimulatory (CS), and coinhibitory (CI) scores as well as an antigen presenting machinery (APM) and a T cell (TC) score. Expression data were normalized and background adjusted. An exploratory dataset was used to stratify the expression in patients with poor vs. good prognosis. Correlation analysis of survival data was performed.

Results: Genes upregulated in the APM score included CANX, B2M, PDIA3 and proteasome subunits MB1, δ , Z, and LMP10. HLA-I molecules A, B, C and G were upregulated while HLA-F was downregulated. For the CS score, higher expression of CD80, OX40, OX40L, CD40, CD30, CD30L, and lower expression of ICOS, ICOSLG, CD27, LIGHT, 4-1BBL, 4-1BB, DR3, GITR, GITRL, TIM1, TIM4 and SLAM contributed to a higher score and a higher survival rate. Higher expression of coinhibitory molecules CTLA4, PDL2, CD80, LAG3 contributed to a higher CI score. TC score included genes contributing to T-differentiation, migration and activation. Lower levels of CCR7, CD27, CD62L, CXCR3 contributed to higher TC score and higher survival.

A higher score of all five immunoscores was correlated with significantly higher survival rates (log rank P=0.0165, HR=3.86 with 95% CI=1.280 - 11.64).

Conclusion: The interplay between the immune system and OS reveals an important role of tumour immunoeediting and its contribution to patient survival and disease progression. The scores could be integrated into pathologic characterization of OS phenotype contributing to prognosis. The investigation of therapeutic and immunologic mechanisms underlying these phenotypes is underway.

BRAIN TUMOURS

P-0154 | The Shift from Delayed Radiotherapy to Localized Radiotherapy Strategy in Treatment of Infantile Medulloblastoma Challenging Experience from LMIC

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Background/Objectives: Medulloblastoma patients below 3 years had inferior survival rates due to several reasons, we aim to investigate the treatment end-results of medulloblastoma under 3years old and determine the factors affecting its prognosis.

Design/Methods: Twenty eight childrens below the age of 3 years were treated at Children's Cancer Hospital_Egypt during the period from July 2007 and Oct 2015. Gross total resection was performed in 19 children (67.8%), subtotal excision in 10 children (35.7%) and biopsy in one patient, twenty (71.4%) were non-metastatic, while 8(28.6%) metastatic M₁₋₃. Twelve (42.8%) children received infantile medulloblastoma chemotherapy protocol and localized posterior fossa irradiation, while the other 16(57%) delayed craniospinal radiotherapy protocol post chemotherapy. Eight metastatic children received craniospinal irradiation (CSI). Twelve of the M0 patients received posterior fossa (PF) irradiation, while the other 8 received CSI at age of 3 years.

Results: The 4 year OS for non-metastatic was 80±6.7% and 37.5.9 ± 13% for M+ children. The EFS for nonmetastatic was 58.4±8.3% and 37.4.0±11.8% respectively. The infantile chemotherapy protocol with localized radiotherapy in M0 patients led to 4-year OS of 78.6±7.9% compared to 62.5 ± 12.6% for delayed craniospinal radiotherapy for M0 patients. The OS for delayed CSI for M+ was 37.5. ± 13%. OS of GTR and less than GTR is 78.6 ± 8.2%, 62.5 ± 8.8% respectively. EFS for localized PF radiotherapy protocols are 83.3 + 7, and 37.5+ 12.3. EFS for delayed CSI M+ was 25+ 11.8. Two patients of the CSI group developed CNS relapse and other two patients had spinal relapse. No relapse in patients who received PF irradiation. Non of these detected differences were statistically significant.

Conclusion: Non metastatic status in Infantile Medulloblastoma carry out better OAS and EFS than metastatic category irrespective to the treatment protocol. Shift from delayed CSI

post chemotherapy to the localized PF protocol is unique experience that improved survival profile and tr decrease toxicity profile.

P-0155 | Nimotuzumab Therapy in Treatment of Paediatric Central Nervous System Tumors: Single Center Experience

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Background/Objectives: To evaluate the treatment results of patients with central nervous system (CNS) tumors treated with nimotuzumab.

Design/Methods: Medical files of patients diagnosed as CNS tumors between 2010 and 2015 were searched. Nimotuzumab was used alone or in combination with vinorelbine or other drugs. Nimotuzumab treatment schedule was 150 mg/m²/dose intravenously, every week in first 12 weeks, then every other week until tumour progression or end of two years.

Results: There were 33 patients treated with nimotuzumab. There were nine patients with pons glioma, eight patients with medulloblastoma, three patients with anaplastic ependymoma, three patients with glioblastoma multiforme, and three patients with primitive neuroectodermal tumour (PNET). Nimotuzumab was first line treatment in four patients, second line treatment in 12 patients, third line treatment in 14 patients, and fourth line treatment three patients. In 67% of patients nimotuzumab was combined with vinorelbine. Median duration of nimotuzumab treatment was 2.5 (0.75 – 18) months.

After initiation of nimotuzumab patients were followed median 8 (1 – 51) months. Four of the patients were with full remission (three patients with medulloblastoma, one patient with PNET), three patients had regression in tumour (one patient with anaplastic ependymoma, one patient with low grade glial tumour, one patient with gliomatosis cerebri), three patients had stable disease (one patient with anaplastic ependymoma, one patient with glioblastoma multiforme, one patient with pons glioma), and other patients had progression. Three year overall survival was 42.6%. Three year progression free survival after initiation of nimotuzumab treatment was 23%.

Conclusion: Relapsed or progressive high grade gliomas and pons gliomas have very poor prognosis with five year overall survival of less than 10%. We found that three year progression free survival rate was 23%. In patients with relapsed or progressive CNS tumors nimotuzumab may be a treatment option.

P-0156 | Clinical Experience in Treating Paediatric Infratentorial Ependymoma in a Single Institution Over Ten Years

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Background/Objectives: Infratentorial ependymoma has two clinically and molecularly distinct subgroups with varying prognosis. We aimed to evaluate our experience in treating these tumors.

Design/Methods: We reviewed charts of patients <18 years old at diagnosis of infratentorial ependymoma presented to King Hussein Cancer Center, Jordan between 2005-2014. Clinical characteristics, pathology and MRI scans were reviewed.

Results: We identified 22 patients (14 males), median age at diagnosis was 4 years (1.6-16 years). Main symptoms were increased ICP (86%), unsteady gait (55%), head tilt (27%) and squint (23%) with median duration of 5 weeks (0.5-12 weeks). They were twelve midline tumors and ten laterally located. Most tumors were large (73% had one dimension >5cm) and majority had hydrocephalus (91%). One tumour was M3. Half of cases underwent GTR/NTR and quarter needed shunts. Seven postsurgical morbidities (44%) were documented; four meningitis (one died, one severely disabled) and three neurological deficits (mutism, CN7/CN10 deficits).

Pathology was anaplastic in fifteen tumors (68%) and grade II in seven; however the grade was changed in 38% of the reviewed samples. Five patients received pre-radiation chemotherapy; two progressed and only one had 2nd surgery (STR). All patients received focal radiation (54-59.4Gy) except one CSI (M3). Eight recurrences (including M3) occurred (6 local, one spinal, one both). Four had re-surgery and five received re-irradiation (three CSI, one spinal, one stereotactic). Excluding one recently re-irradiated, all other relapsed patients died within median of six months (0.2-3.3years).

With median follow up of 3 years (0.9-8.2 years), 5year OS was 47%±14.7; significantly better in midline tumors (p=0.04). Laterally located ependymomas had 5 year OS 37.3%±19; no difference for tumour grade (p=0.69) or degree of resection (p=0.79). Midline ependymomas had 5 year OS 80%±13. This was 100% if GTR/NTR (p=0.02) or grade II (p=0.06); however number of patients was small.

Conclusion: Totally resected midline grade II ependymoma had excellent prognosis. More complete resections, better post-operative infection control and standardized salvage protocols would help improve our patients' survival.

P-0157 | Secondary Meningioma in Children with Cancer Treated with Cranial Irradiation

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Background/Objectives: Introduction: Secondary tumours are becoming increasingly prevalent in survivors of childhood cancer. Predisposing factors include chemotherapy, young age,

genetic predisposition, CNS and brain infiltration and intracranial irradiation. Meningiomas are rare in the paediatric and teenage and young adult population, but with increasing prevalence as a secondary tumour. The current study was conducted to review current literature in this area.

Design/Methods: The NHS Evidence Portal was used to search Medline, PubMed, CINAHL and PsychInfo, using clearly defined search terms, matched to the encyclopaedis of each search engine. Clearly defined exclusion criteria were utilised. Duplicates were removed with a final list of 37 articles.

Results: Results: Secondary meningioma was described in children treated for acute lymphoblastic leukaemia, primary brain tumours and metastatic CNS disease. Clinical presentation of secondary tumours included fatigue, seizures, hyperostosis, vomiting, visual disturbance and proptosis. Clear differences in the behaviour of radiation induced meningiomas are clearly described, including aggressiveness and recurrence. Increased risk of secondary meningioma in childhood cancer patients treated with growth hormone is described.

Conclusion: Conclusion: Many modern treatment protocols for childhood cancers have changed in recognition of significantly increased risk of secondary CNS following treatment (e.g. Acute Lymphoblastic Leukaemia - intrathecal and high dose methotrexate). With increasing length of survival in childhood cancer patients, it is imperative that long-term and longitudinal epidemiological studies are conducted alongside biological research to understand rare secondary tumours.

P-0158 | Assessment of Health Related Quality of Life (HRQOL) in Children and Young People with Meningioma

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Background/Objectives: Meningiomas are rare tumours in children, teenagers and young adults, accounting for less than 4% of primary brain tumours. The aim of this study was to review current literature reporting the disease in this population, focussing on the effects of the disease and its treatment on HRQoL, and assessment methodologies.

Design/Methods: The NHS Evidence Portal was used to search Medline, PubMed, CINAHL and PsychInfo, using clearly defined search terms, matched to the encyclopaedis of each search engine.

Results: Following application of exclusion criteria, duplicates and abstract review, 62 articles were included in the final literature review. The majority of studies described case reports, case series (largest 22 patients), cross sectional surveys and methodologies including case note review. Both qualitative and quantitative studies were conducted. HRQoL measures utilised included WHO QoL-100, Karnofsky Performance Scale, EORTC-QLQ-C30, with no description of validation within this population. Paediatric and TYA was often reported alongside adult, and often not distinguishable. No longitudinal studies were identified. Predominant treatment related effects on HRQoL included pain, fatigue, sleep disturbance and mood.

Conclusion: Meningioma is a rare disease in children and young people. It is imperative that paediatric data is identifiable when reported alongside adult patients. With the increasing use of novel treatments such as proton beam therapy, longitudinal research is essential, including the assessment HRQoL parameters (especially cognitive effects), and longterm late-effects follow-up.

P-0159 | Medulloblastoma: Relapse or Second Tumour

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Background/Objectives: Medulloblastoma, accounts for approximately 20 percent of all intracranial tumors in paediatric patients, and one-third of the posterior fossa. We report a relapse or second tumour after 39 years after treatment of childhood with medulloblastoma.

Design/Methods: 50 year old female patient, with a history of medulloblastoma at age 11, treated with surgery and radiotherapy in brain. She didn't present evidence of disease or complications until 2009 when she started to present internal disorders of balance and dysmetria, and increased the intracranial pressure. CT and MRI studies showed a tumour in posterior fossa, a biopsy was made and diagnosed medulloblastoma. A second surgery with complete resection was performed macroscopically, confirming the diagnosis of typical medulloblastoma. Started with standard chemotherapy treatment.

Results: Recurrence of medulloblastomas can occur in the site of the primary tumour or, in non-contiguous sites of the central nervous system. It occurs usually between 5 and 26 months of treatment of primitive tumour, and is relatively high. 50% lies in the posterior fossa, and 10% may present metastasis extracranial, being most common bone. In late relapse, it is necessary to do a biopsy or resection to confirm histology. As other entities such as a secondary tumour or necrosis of the brain related to the treatment cannot be distinguished clinically from a recurrence of the tumour. The indicated treatment is first surgery with complete resection, and then, radiotherapy and chemotherapy. In this case the radiotherapy wasn't indicated because she died it 39 years ago. After the surgery the chemotherapy included vincristine, cyclophosphamide, carboplatin, and etoposide. She died after 8 month treatment because of toxicity (sepsis).

Conclusion: The five-year survival rate of medulloblastoma is 50%. Most patients relapse during the first two years after being diagnosed. At present, there is no evidence that show a medulloblastoma after 39 years of the primitive.

P-0160 | Intracranial Metastatic Hemangiopericytoma in an Adolescent, A Case Report

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Background/Objectives: To report an adolescent with a rare tumour, hemangiopericytoma and metastatic disease.

Design/Methods: Hemangiopericytoma is a rare hypervascular tumour that accounts for less than 0.5% of all the Central Nervous System. It has two clinical types according to the location: intracranial and extracranial. The differential diagnosis of this rare tumour from other extracranial masses plays an important role in treatment planning. Here, we present an atypical clinical presentation of this rare tumour.

Results: A 21 year old patient, suffering from January 2013 a right lower limb peresthesia, with progression right hemiplegia. At the time of his hospitalization, a cranial computerized tomography showed a mass at the left parietal lobe. The patient underwent surgery twice with partial excision of the mass, which turned out to be a Hemangiopericytoma. He finished brain radiotherapy performed in Dec. 2013.

Control continues until January 2015, which begins with generalized arthralgia. In June 2015 in bone scan, multiple bone metastases is reported. The biopsy result was hemangiopericytoma metastases. The treatment temozolamide/bevacizumab and irradiation therapy. The patient is still alive in controls without evidence of disease progression.

Conclusion: The Hemangiopericytoma intracranial is an uncommon tumours that behave aggressively, they tend to relapse and cause distant metastases. The treatment are surgery plus radiotherapy and there is not evidence with the use of chemotherapy.

P-0161 | Treatment Outcome in Patients with Primary Central Nervous System Germ Cell Tumour: Clinical Experience from a Regional Cancer Centre in North India

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Background/Objectives: Primary intracranial germ cell tumour (GCT) is a rare entity and constitutes 2-3% of all paediatric brain tumours. We herein intend to report the clinical features and treatment outcome of patients with primary central nervous system (CNS) GCT treated at our institute.

Design/Methods: Clinical data was collected by retrospective chart review from 2006-12. Histopathology slides were reviewed and relevant immunohistochemistry stains were done. Overall survival (OS) was analyzed by Kaplan-Meier product-limit method.

Results: Twenty patients met the study criterion (male: female=7:3). Median age at presentation was 13 years (range 8-48 years). Tumour location was pineal in 10, suprasellar in 6, thalamic in 2, basal ganglion in 1 and spinal in 1 patient respectively. Leptomeningeal spread was noted in 1 patient at presentation. Surgical resection was gross-total in 7(35%), near-total in 2(10%), sub-total in 4(20%) and limited to biopsy in 6(30%) patients. Tumours were germinomatous, non-germinomatous and mixed GCT subtype in 17(85%), 2(10%) and 1(5%) patient respectively. Systemic chemotherapy (median 4 cycles) was given in 19(95%) patients. The common regimens used were BEP in 14(70%) and EP in 5(25%) patients respectively (B-Bleomycin;E-Etoposide;P-Cisplatin). Radiation therapy (40-50 Gray, median 42 Gray) was delivered in 17(85%) patients- local radiation in 6 and whole ventricular, whole brain and craniospinal irradiation followed by local boost in 5, 3 and 3 patients respectively. After a median follow-up of 23.13 months (mean-32.36 months), 17(85%) patients were in complete response and 3(15%) patients had progressive disease. Death and disease recurrence were noted in 4(20%) and 1 patient respectively. Median OS was not reached. The actuarial rate of OS at 2 and 3 years were respectively 82.6% and 74.4%.

Conclusion: Multimodality management comprising limited resection followed by platinum based chemotherapy (3-4 cycles) and radiotherapy (40-50 Gray) is a reasonable treatment strategy in patients with primary CNS GCT in a developing nation.

P-0162 | Targeting Primary Ciliogenesis in Atypical Teratoid/Rhabdoid Tumors

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Background/Objectives: Atypical teratoid/rhabdoid tumors (ATRT) are highly malignant CNS tumors commonly diagnosed in infants. Recently, comprehensive genomic studies elucidated three distinct molecular subtypes (TYR, MYC and SHH) of ATRT. Specifically, TYR-ATRT show overexpression of genes involved in ciliogenesis compared to other subtypes. As primary cilia have already been shown to play an important role in the initiation and progression of other tumour entities, we aimed to characterize the distribution of primary cilia in ATRT, and to target primary ciliogenesis therapeutically in these tumors with dismal prognosis.

Design/Methods: We performed immunofluorescence of primary cilia in ATRT cell lines (n=2) and primary tumour sections (n=13) using antibodies against pericentrin and acetylated tubulin staining the basal body and the axoneme of the primary cilium, respectively. The functional role of primary cilia in ATRT was investigated by siRNA-mediated knockdown of the ciliary proteins KIF3A and IFT88 and by pharmacological inhibition using Ciliobrevin D, a cytoplasmic dynein inhibitor, known to target primary ciliogenesis.

Results: We detected primary cilia in all ATRT cell lines and primary tumour sections investigated in this study using immunofluorescence. Notably, TYR-ATRT were highly ciliated (range 12-22%), while MYC-ATRT and SHH-ATRT showed a variable degree (range 4-29%) and a low proportion (range 2-6%) of cells with primary cilia, respectively. Knockdown of both KIF3A and IFT88 significantly reduced self-renewal capacity. Pharmacological inhibition of primary ciliogenesis phenocopied the results from the knockdown experiments and the inhibitory effect was specifically pronounced after induction of primary ciliogenesis through serum starvation in two ATRT models.

Conclusion: For a long time, primary cilia have been regarded as rudimentary organelles, while a crucial role for primary cilia in cancer initiation and progression is now emerging. Our results implicate primary cilia as a universal feature of ATRT and suggest primary ciliogenesis as a potential therapeutic target especially in TYR-ATRT.

P-0163 | Early Outcomes Following Focal Proton Therapy and Intensive Chemotherapy for Paediatric Atypical Teratoid Rhabdoid Tumour (ATRT)

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Background/Objectives: Central nervous system (CNS) atypical teratoid rhabdoid tumour (ATRT) carries a poor prognosis despite aggressive multimodality therapy. We report 18-month outcomes and toxicity with the use of multimodality therapy that includes proton therapy (PT).

Design/Methods: From 2009-2015, 19 children with CNS ATRT were treated with surgery, chemotherapy, and PT. Median age was 1.9 years (range, 0.7-15.4). Seven tumors were infratentorial and 12 supratentorial. Gross- or near-total resection was achieved in 14 and subtotal resection in 5. The median PT dose was 54CGE (range, 50.4-54). Systemic therapy regimens included ACNS0333 (n=4), Eu-Rhab (n=1), Dana-Farber protocol (n=5), and SJYC07 (n=9). Toxicities were prospectively recorded using CTCAEv4.0. Necrosis rates were assessed with Fisher's Exact Test and disease control with the Kaplan-Meier product limit method. A log-rank test statistic assessed significance between strata of prognostic factors.

Results: Median follow-up was 1.5 years (range, 0.2-6.2). Eighteen-month local control, progression-free survival, and overall survival were 91%, 49%, and 80%. Median time to progression was 0.8 years (range, 0.1-1.4). No association for progression-free or overall survival was found for age, sex, site, extent of resection, tumour size, or PT dose. One local failure occurred with simultaneous distant CNS failure. No radiation-related acute or subacute toxicities were observed. Four patients experienced grade 3 brain necrosis (1 cerebellar, 3 supratentorial) at median 0.7 years after PT (range, 0.6-1), the only serious late toxicity. Two children with necrosis were treated per ACNS0333 and 2 per Dana-Farber protocol. The actuarial rate of necrosis at 18 months was 29%. Two patients experienced complete resolution of symptoms, 1 partial resolution, and 1 has persistent deficits.

Conclusion: Combined PT and intensive chemotherapy for paediatric ATRT results in excellent local control at the cost of high rate of brain necrosis. Despite prolonged methotrexate-based chemotherapy, over half of children experience metastatic relapse following focal radiation.

P-0164 | Infants with Low Grade Gliomas (LGG) in One Center

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Background/Objectives: Infants constitute less than 10% of all children with LGG and are rarely studied as a separate group. Survival rates for children under 2 years of age published in the literature are lower than in older children. Aim -to present own experience in the management of children <1 year of age with LGG.

Design/Methods: Analysis of 31 patients, aged 1 day-11 months, median 6 months treated between 1998-2015. Analysis included: first symptoms, tumour location, pathology, treatment and outcome.

Results: Three patients had prenatally diagnosed tumors. The most frequent presenting symptoms were failure to thrive-9, seizures-9, nystagmus-9, vomiting-8, diencaphalic syndrome-5, increased head circumference-5, paresis-5, imbalance-5, strabismus-2, torticollis-1. Six children had infratentorial and 25 supratentorial tumour. Eight patients had desmoplastic infantile ganglioglioma/astrocytoma, 6-pilocytic astrocytoma, 3-ganglioglioma, 3-pilomyxoid astrocytoma, 1-oligoastrocytoma, 1-oligodendroglioma. Twelve patients underwent surgery alone (resection: total-8, subtotal-4), 7 patients-had partial tumour resection and chemotherapy, 2-tumour biopsy followed by chemotherapy and 1-received chemotherapy followed by partial resection. In 9 children with typical radiographic image of LGG chemotherapy was implemented without pathological confirmation. Two children underwent irradiation one at the age of 4 and the second patient-twice at 3 and 7.5 years of age due to disease progression. Twenty nine patients are alive 4 months to 16.5 years (median 3.3 years) from diagnosis. Two patients died one of disease the other of neuroinfection 2 months and 1.5 year from diagnosis respectively.

Conclusion: Survival rate at 3 years is 93% as in older population. Further follow up of infants with LGG is required to confirm the results.

P-0165 | An Atypical Progression of An Infant with Desmoplastic Infantile Astrocytoma

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Background/Objectives: Desmoplastic Infantile Astrocytoma (DIA) is a rare paediatric brain tumour, which is commonly seen between 1 and 24 months of age. Although the prognosis of these tumours are generally considered favorable after gross-total resection, rare cases with progression are also reported. We describe here a case of DIA with malignant transformation.

Design/Methods: A 5-months-old boy presented with convulsion. MRI of the brain showed a large partially contrast enhancing and cystic lesion in right frontal temporal parietal region.

Results: The patient underwent gross-total resection of the lesion. The pathology was found to be DIA. The histopathological evaluation revealed a high grade glial tumour with features of glioblastoma such as high mitotic activity and necrosis. A prominent component of the tumour was the desmoplastic reticulin-rich stroma, giving rise to the thought of a pre-existent DIA. The decision was made to do close follow-up of the patient due to atypical histologic features. Three months later, the baby came to the emergency room with lethargy. MRI showed tumour recurrence in the frontoparietal lobe with leptomeningeal involvement with no seeding in the spinal axis. Chemotherapy with vincristine and carboplatinum was started and the patient received chemo for 2 cycles. Follow-up MRI showed significant regression of the mass lesion. Two more cycles of chemo was planned. The patient presented with lethargy to the emergency room again 6 weeks later. MRI of the brain showed significant progression of the tumour with severe brainshift. The patient underwent subtotal resection of the tumour; because of cardiac instability, total resection of the tumour could not be performed. After surgery, cardiopulmonary functions deteriorated and the patient deceased several hours after surgery.

Conclusion: DIA, when histologically characterized with highly anaplastic features, the biological behavior of the tumour remains uncertain. More experience and molecular research is needed to develop treatment recommendations particularly for atypical DIA.

P-0166 | Pilot Study of a Surgery and Chemotherapy-Only Approach in the Upfront Therapy of Children with Wnt Positive Standard Risk Medulloblastoma

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Background/Objectives: Children with Wnt-positive medulloblastoma, which in historical cohorts represents between 10-15% of children with medulloblastoma, have an excellent prognosis when treated with radiotherapy followed by adjuvant chemotherapy. Various therapy reduction strategies are being proposed. The purpose of this study is to determine whether radiation therapy can be entirely omitted in newly diagnosed children with standard risk, Wnt positive medulloblastoma utilizing a chemotherapy-only approach.

Design/Methods: Following initial tumour resection, eligible subjects must have a gross-total resection, no evidence of metastatic tumour, and non-anaplastic histology. Wnt medulloblastoma is defined as beta-catenin nuclear reactivity by immunohistochemistry, monosomy 6 as determined by array CGH, and the absence of MYCN or MYC amplification as determined by fluorescent in-situ hybridization. A total of thirteen subjects can be enrolled.

Results: Five children have been screened to-date who met initial standard-risk criteria. 1/5 children met the protocol definition for Wnt-positive medulloblastoma with one child diagnosed with sonic hedgehog (SHH) medulloblastoma and three children with non-SHH/non-Wnt medulloblastoma. An additional 4 tumour specimens did not demonstrate nuclear beta-catenin reactivity and were not further evaluated for possible inclusion. The parents of the one eligible child elected not to enroll their child on the subsequent treatment arm.

Conclusion: As anticipated, frequency of Wnt-positive medulloblastoma is rare, resulting in slow accrual to the planned protocol therapy. The study is currently open in five centers. Updated accrual, rationale for the study design, and early outcomes of subjects enrolled on the trial will be detailed.

P-0167 | Timing to Radiotherapy in an Irish Cohort of Patients with Medulloblastoma/PNET

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Background/Objectives: We reviewed the Irish experience of paediatric medulloblastomas over an 8 year period to determine time to radiotherapy in our cohort.

Design/Methods: We performed a retrospective review of all paediatric patients with medulloblastoma/PNET diagnosed in the Republic of Ireland from 2007 to 2014.

Results: Fifty-three patients were diagnosed with Medulloblastoma / PNET during this time period: 40 patients were male (75%), 13 were female (25%), age range of 0.38 - 15.9 years.

Eighteen children (34%) did not have radiotherapy – all of whom were <4 years at diagnosis (range 0.38-3.95 years). Three (17%) received palliative-intent treatment relative to parental request. Of the remaining 15, all of whom had adjuvant chemotherapy, 8 (44%) are alive in follow up and 7(39%) have died.

Thirty-five children (66%) proceeded to have radiotherapy during treatment (range 16-83 days). Two had delayed radiotherapy as per chemotherapy protocol, 3 required radiotherapy following chemotherapy due to disease progression.

Of the remaining 30 children, 11(37%) proceeded to initial craniospinal radiotherapy within 42 days of surgical resection (early group), range 16-42 days. Of these, 9 (82%) are alive, 2 have died (18%). Nineteen children (63%) started their radiotherapy after 42 days (late group), range 43-83 days. Of these, 6 children had posterior fossa syndrome and 1 child had post-operative complications, which contributed to delays (range 45-83 days). The remaining 12 children proceeded to radiotherapy within 43-66 days post surgery, these delays were likely multifactorial. Of these 19 children, 10 (53%) are alive and 9 have died (47%). Overall survival

in the early and late groups, across the available follow-up period (range 19 to 77 months) is 81.8% and 57.9% respectively (p=0.21).

Conclusion: Challenges remain in relation to early initiation of radiotherapy treatment in our cohort. Early involvement of all multidisciplinary colleagues is important to expedite the surgical to radiotherapy journey, thereby promoting treatment efficacy.

P-0168 | Paediatric Low Grade Glioma with Complete vs Incomplete Resection

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Background/Objectives: Surgical resectability is the major prognostic factor in paediatric low grade gliomata. We reviewed outcomes following resection for Irish patients over a 10-year period.

Design/Methods: We performed a retrospective review of all paediatric patients diagnosed with low grade gliomata in the Republic of Ireland between 2005-2014. Children with optic pathway gliomata were excluded.

Results: One hundred and twelve children were diagnosed over a 10-year period (52 male (46%), 60 female (54%), Age range 0.23 – 15.87 years, Median 6.3 years).

One hundred and eleven children had surgical procedures performed while 1 child had a radiological diagnosis only. 14/111(13%) had biopsies alone. Sixteen (14%) had biopsies followed by resection, while 79(71%) had upfront resections. We were unable to determine the specific procedure in 2 children.

77/79 patients had upfront craniotomies. 40/77 (52%) had Gross Total Resection (GTR) confirmed by post-operative imaging. Of those with confirmed GTR (excluding patients with Neurofibromatosis Type 1), 3 patients (4%) relapsed; all within 15 months of GTR. Thirty-seven (96%) patients who had a GTR are disease free to date (median 47 months, range 15 – 127 months).

37/77 (48%) had incomplete resections. 20/37 (54%) have had disease progression. 9/20 (45%) had 1 initial neurosurgical intervention and are disease free in follow up. 5/20 had a second surgery; 3 of whom had subsequent chemotherapy and 1 had chemoradiotherapy for further progression.

5/20 received chemotherapy alone and 1 died following no additional treatment.

14/37 (38%) have stable disease with no evidence of progression to date. 3 patients (8%) have been lost to follow-up.

Conclusion: Recurrence following GTR is rare, but early if it happens. Disease progression in incomplete resections is more common. Scanning intervals can be increased after 2 years in those with confirmed GTR and alternative strategies including second-look surgery should be considered for those with incomplete resections.

P-0169 | Astrocytomas in Children: 10 Years Experience of a Single Institution

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Background/Objectives: Astrocytomas is the most common histological type of central nervous system tumors in children. Resection extent has been strongly associated with progression-free survival: patients undergoing gross total resection appear to have a substantially better prognosis than those undergoing incomplete resection. Histological features indicative of malignancy are clearly associated with a poor outcome.

Objectives: The aim of the study was to evaluate the epidemiology and the outcome of astrocytomas in children.

Design/Methods: Retrospective study of 65 children (28 girls and 37 boys) with astrocytomas, treated in the Pediatric Oncology Department -Institute of Oncology Bucharest between January 2004- December 2013.

Results: 39 patients-60% were under the age of 10 at diagnosis. Tumour location: supratentorial- 30 patients-46.1%, infratentorial 24 patients- 37% (from which 11 cases located at the posterior fossa), spinal cord 6 patients- 9.2%, optical pathway 5 patients-7.7%. Histological type: Low-grade astrocytomas 57 patients-87.7% with a predominance of pilocytic astrocytoma, high-grade astrocytomas 8 patients- 12.3%. Treatment: surgical resection was performed in 54 cases-83%: complete removal (42.6%), partial removal (57.4%). Chemotherapy was given in 55 patients-84.6%, 40 patients-62.5% were treated with radiotherapy; 8 patients received palliative anti-angiogenic metronomic therapy. The five-year overall survival rate was 70.8%. The five-year survival rate in pilocytic astrocytoma was 87%. The five-year survival rate was 70.8%. Survival rate according of the resection extent: 100% for complete removal versus 75% for partial removal.

Conclusion: 1. The most common location was supratentorial 2. The most common histological type was pilocytic astrocytoma. 3. Anti-angiogenic metronomic therapy could determine a long-term stable disease.

P-0170 | Slow Improvement in the Diagnosis of CNS Tumors in Children in the Last Decade

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Background/Objectives: Children with CNS tumors may present symptoms for a long time prior diagnosis which are ignored or misinterpreted. We have identified this problem studying our patients treated between 1997–2000. To improve this situation teaching courses on

symptomatology of CNS tumors for health professionals were conducted for 10 years. The aim of the study was to analyze what has changed during a decade in the diagnosis of childhood CNS tumors.

Design/Methods: 184 medical records of children with brain tumors treated between 2000-2005 were studied. More than 50% of tumors were infratentorial. Medulloblastoma was the most common followed by low and high grade glioma. 32 patients had brain stem tumour. Analysis included; type of first symptoms, time from symptoms onset and diagnosis, specialists involved and type of diagnostic procedures performed before final diagnosis. The results were compared to data from own study performed with the same methodology on patients treated between 1997-2000 (reference group –RG).

Results: Posterior fossa tumors had the shortest median diagnosis (1.7 months) and midbrain tumors the longest - 7.5 months in both groups. Appropriately oriented diagnosis was performed in 56% of patients as compared to 47% in the RG. Preliminary diagnosis of CNS tumour was made by 61% of paediatricians as compared to 24% in RG. The 30% of patients still have gastrologically oriented diagnosis. 54% of patients had final diagnosis in < 1 month, 20% in < 3 months, 19% from 4-12 months and in 7% the diagnosis took over 1 year, for the RG it was 50%, 25%, 16%, 9% respectively.

Conclusion: Some improvement is observed in the diagnosis of childhood CNS tumors which is owed to educational programs. Pediatricians had the greatest part in making the proper preliminary diagnosis and were the majority of participants of our program.

P-0171 | Gliomatosis Cerebri in Children

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Background/Objectives: Gliomatosis cerebri (GC) is an infrequent glial - astrocytic neoplasm. These lesions involve the brain diffusely. Usually a mass is not identified.

Design/Methods: We present children with GC from our hospitals, two patients had extensive evaluations. Their MRI findings and pathology studies are exposed.

An 11 years-old boy developed strabismus and diplopia. One month later presented ataxia, and seizures. MR showed hyperintensities of the white matter of the frontal and temporo-parietal left hemisphere, corpus callosum and parts of the right hemisphere. By MR spectroscopy, the choline:creatinine ratio was high. Pathology showed an infiltrating astrocytoma with increased cellularity and scattered atypia, Ki-67 5%, p53 and MIB1. PI3KC and IDH-mutations were found.

14 years-old female with headaches, nausea, emesis, decreased visual acuity followed by left sided proptosis and hypopituitarism. MRI on FLAIR and T2-weighted demonstrated infiltrative disease involving the left frontal lobe, right frontal lobe, bilateral temporal lobes, and mid brain. MR spectroscopy demonstrated increased choline and decreased NAA. Pathology disclosed diffuse astrocytic neoplasm consistent with gliomatosis cerebri, WHO grade III/IV, exhibited a proliferation index (MIB-1) of 10%.

Other three patients include an 8 years-old boy with seizures and nystagmus. MR and spectroscopy showed lesions in thalamus, medulla oblongata, temporal and frontal lobes. An 8 years-old girl with respiratory distress and coma with a Glasgow score of 8/15 arrived in critical condition after the diagnosis of gliomatosis cerebri was confirmed and treated elsewhere; and, a 12 y old boy with emesis and headaches, MR and spectroscopy confirmed GC.

Results: Treatment consisted on radiation therapy, temozolamide and/or palliative care. Median age of diagnosis was 10 years. Only one patient is alive with progressive disease. The survival time for the remaining patients ranged from 1,5 to 24 months.

Conclusion: GC carries a poor prognosis. Treatment options include radiation therapy, temozolamide, vincristine-carboplatin or lenalidomide. Adequate palliative care is warranted.

P-0172 | Analysis of a Friendly Panel for Molecular Classification of Medulloblastoma (MB) in WNT, SHH and Non-WNT/SHH Groups to Clinical Practice and Clinical Trials

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Background/Objectives: There are a virtual explosion of molecular data in recent years, which has established that MB is a heterogeneous disease composed of four distinct subgroups, WNT (Wingless), SHH (Sonic Hedgehog), group 3 and group 4.

Our goal is to validate 9 IHC biomarkers and two FISH probes panels according to recent published results in a Brazilian cohort of paediatric patients with confirmed diagnosis of MB.

Design/Methods: We retrospectively retrieved paraffin samples from 76 patients as well all clinical data for demographic, descriptive, overall and progression-free survival analysis using Stata 13.1 statistical software. Pathological evaluation was done in four steps: central review for confirmation of the diagnosis of MB, histological classification based on last edition of WHO for CNS Tumours, immunohistochemistry panel for beta-catenin, DKK1, GAB1, SFRP1, GLI-1, NPR3, KCNA1, YAP1 and GLI-3 and fluorescent in situ hybridization for c-MYC and N-myc.

Results: Median age was 8.83 years (range 0.2 - 23.23), 63% male, 82% non metastatic, 51% stratified as high risk, 56% performed gross total surgical resection, 78% chemotherapy and 64% radiotherapy. 52% of patients were alive and 48% was dead of disease progression. It was performed IHC and FISH in 46 samples. 21%, 34% and 45% was classified to group Wnt, SHH and non-Wnt/SHH. Median age was 8.54, 13.7 and 6.62 years respectively (p=0.013) which classic (89%), desmoplastic/MBEN (50%) and large cell/anaplastic (40%) types belong to Wnt, SHH and non-Wnt/SHH groups respectively. Molecular classification and recurrence was correlated with OS and PFS.

Conclusion: Only four IHC markers (beta-catenin, YAP1, GAB1 and GLI-3) and c-MYC FISH probe were effective for molecular classification of MB and highly correlated with demographics, recurrence and outcome. Large cell/ anaplastic type morphology and high mitotic index may be additional findings in non-Wnt/SHH group which predicts worse survival and be allocated to more aggressive therapy.

P-0173 | Decreased Expression of BATF2 is Significantly Associated with Poor Prognosis in Childhood Medulloblastoma

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Background/Objectives: Medulloblastoma (MB) is an embryonic central nervous system cancer, originated at cerebellum. It is the most common malignant solid tumour in childhood. Zebularine is a DNMT inhibitor that causes DNA demethylation and shows low toxicity. In our previous study, we found Zebularine exerts anticancer effects in MB (data in publication process), and among its effects we observed the overexpression of *Basic Leucine Zipper Transcription Factor, ATF-Like (BATF2)* gene. *BATF2* is downregulated in several tumors and correlated with poor prognosis, although its role in MB is still unknown. Hence, this study aimed to investigate *BATF2* expression in MB samples.

Design/Methods: To this, we investigated *BATF2* expression (qRT-PCR) in 46 consecutive samples of MB (TU), 4 MB cell lines (CL) (DAOY, ONS-76, UW402 and UW473) and 5 non-neoplastic cerebellum samples (NC). We also evaluated DNA methylation levels (Methyl-Collector Ultra) in 11 MB samples, in 5 NC and in the 4 CL.

Results: We found that *BATF2* expression was significantly reduced in the four MB cell lines (p=0.02) and in most TU samples when compared with NC tissues, however this difference was not significant. It was found to be significantly lower in patients with relapse/metastasis events (p=0.04) and in high risk MB (p=0.016). Furthermore, patients with lower *BATF2* expression showed a shorter survival than those with higher expression (p=0.003). Additionally, Zebularine treatment induced *BATF2* gene in DAOY cells and the methylation analysis revealed regions richly methylated in *BATF2* gene.

Conclusion: This study provides a better understanding regarding the mechanisms of tumorigenesis of MB through the elucidation of the role of this gene and consequently raises the possibility of development of a more effective and/or personalized therapies for these patients.

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P-0174 | Return of Genomic Results Relevant to Personalized Decision-Making in Brain Tumour Patients: Pilot Questionnaire Results

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Background/Objectives: The iCHANGE project is investigating genetic drivers and biomarkers of high grade gliomas (HGG) in young adults and children. Discerning patient opinions as to the acceptability of genetic testing at diagnosis to predict response to treatment is essential in predicting uptake in implementing a clinical test. Understanding attitudes to sharing these genetic results with family, roles of surrogate decision-makers, and acceptability of these serial biomarkers to predict HGG relapse is also needed.

Design/Methods: Baseline and Follow up questionnaires (one each for Adults with HGG, Surrogate-decision makers, and Parents of children with HGG) were developed using a review of the literature and questions from previously validated questionnaires. 31 item baseline and 22 item follow up questionnaires were piloted for individual question and overall content validity in each subgroup.

Results: Between June and August 2015, 7 adults with brain tumors, 5 surrogate decision-makers and 5 parents of children with brain tumour conducted a formal content validity (CV) assessment. All items, but one, in each questionnaire met a CV index of > 0.8 (Lynn (1986)). All questionnaires scored 1.0 for overall CVI. We report the combined results. All (n = 11) would likely accept a blood or tumour genetic test, for themselves or their child, that describes an effective chemotherapy strategy but also that no known effective therapy exists. Most would accept biomarker testing in follow up for themselves even with no known effective therapy (n = 10). In the event of death, most would be comfortable with sharing genetic research results with family members (6/10) before their death and all following.

Conclusion: Pilot results show excellent content validity index ratings. Respondents want genetic biomarker test results, even if it indicates that no chemotherapy would be effective for their tumour. Most are not concerned with sharing genetic research results with family.

P-0175 | Local NK Cell Immunotherapy for Medulloblastoma

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Background/Objectives: Medulloblastoma (MB) is the most common malignant brain tumour of childhood, usually located in the posterior fossa. Current therapies are toxic and not always curative that necessitates development of targeted immunotherapy. Interactions between NKG2D activating receptor on NK cells and its ligands (NKG2DL) on MB cells are essential for NK cell anti-tumour cytotoxicity. However, MB cells can evade NK cell immunosurveillance by downregulating NKG2DL. In this work, we have explored NK cell cytotoxicity against

MB cells *in vitro*, and the feasibility of a local therapy in an *in vivo* model. In addition, we have used Spironolactone, a drug capable of upregulating NKG2DL on tumour cells.

Design/Methods: *In vitro* Activated and Expanded NK (NKA) cells cytotoxicity against human MB cells was assayed by performing conventional 4-hour europium-TDA release assays using Daoy cell line as target. Daoy cells were treated with 56 μ M Spironolactone (an NKG2DL upregulator) or DMSO (vehicle) for 72h. For the *in vivo* model, Daoy cells expressing luciferase were orthotopically injected in the posterior fossa of NOD/scid IL2rgnull mice. One week after, mice were monitored and randomized. Mice were treated with an intracerebral injection of NKA cells along with daily i.p injections of IL-2 for 5 days, and i.p injections of Spironolactone twice a week for 2 weeks.

Results: *In vitro*, Spironolactone treatment enhanced NKG2DL expression on MB cells and NKA cells cytotoxicity. *In vivo*, mice treated with NKA cells and spironolactone showed lower tumour progression than control groups, however we did not observe an improvement on survival.

Conclusion: *In vitro*, Spironolactone avoids MB immune evasion from NK cells by upregulating NKG2DL. Local NKA cell treatment of MB along with Spironolactone treatment is feasible and delays tumour growth; however, the complexity of this model limits the positive impact on survival.

P-0176 | Management of Disseminated Low Grade Gliomas of Childhood (DLGG)- One Institution Experience

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Background/Objectives: Disseminated childhood low grade glioma at presentation as well as at progression/relapse is rare with incidence of approximately 2-5%. Data on pattern of dissemination, management and outcome in these rare entities are scarce and require further investigation.

Design/Methods: Aim: To present one-institutional experience in the management of children with disseminated low grade gliomas (DLGG).

Patients and methods: 7 pts: 2 girls and 5 boys aged 4yrs 4ms to 17yrs with DLGG treated between 1998 and 2015 were assessed. Analysis of primary tumour location, pattern of dissemination, tumour pathology, extent of surgery, treatment applied and outcome was performed.

Results: Three patients presented with primary tumour located in the hypothalamic-chiasmatic region, 1 in the third ventricle, 1 had spinal location, 1- multifocal disease with largest lesion in right frontal lobe and in one patient it was not possible to define the primary tumour. One patient underwent partial resection, remaining 6 had biopsy. One patient was diagnosed with pilomyxoid astrocytoma (grade II), 6 had pilocytic astrocytoma (grade I). Four patients presented with neuraxis dissemination and one- with multifocal disease at diagnosis, in 2 patients neuraxis dissemination was detected at tumour progression/relapse.

All patients received low grade glioma chemotherapy protocols. Six patients had tumour progression: two were treated with LGG chemotherapy protocols and radiotherapy, 1 pt received HGG chemotherapy protocol and radiotherapy, three were treated with other chemotherapy protocols.

Six patients achieved stabilization of the disease, 1 experienced multiple relapses.

Six pts are alive 3ms, 20ms, 4yrs 8ms, 9yrs 2ms, 9yrs 3ms and 10yrs 2ms from diagnosis.

One patient died of progressive disease 8yrs 5ms from diagnosis.

Conclusion: DLGG is a rare presentation among low grade glioma of childhood with no well-established treatment standards. However disease progression is more common in this group of patients, responses to LGG chemotherapy protocols as well as long-term survival are achievable.

P-0177 | Discovery of a Novel BRAF Fusion in a Case of Pleomorphic Xanthoastrocytoma

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Background/Objectives: Pleomorphic xanthoastrocytoma (PXA) is a low grade glioma of children and young adults. BRAF V600E mutation is found in most PXA's, and successful treatment of recurrent PXA with the BRAF inhibitor vemurafenib has been described. We report a case of PXA harboring not BRAF V600E mutation, but instead a novel TMEM->BRAF fusion.

Design/Methods: A 10 year old female presenting with seizures underwent resection of a temporal lobe lesion, reported as PXA with anaplastic features. She had local recurrence 6 months later, prompting re-resection. She had further tumour progression, refractory to irradiation. Whole exome sequencing was performed on DNA from frozen tumour tissue (second surgery) and blood, using the SureSelect Human All Exon V6 exome capture reagents, and Illumina sequencing on a HiSeq. In addition, transcriptome sequencing using the Illumina Stranded RNAseq kit was performed on tumour RNA (second surgery). Following alignment, tumour specific sequence variants were detected using NextGene (Softgenetics, State College PA). RNAseq data were analyzed using TopHat, and rejected reads were evaluated for fusions using FusionMap.

Results: Immunohistochemical stain for BRAF V600E was negative in both specimens. No germline mutations were identified. Tumour copy number changes identified included gain of chromosome 7, loss of 13, and loss of heterozygosity of 9p. Transcriptome sequencing

detected a novel TMEM106B->BRAF fusion on chromosome 7, involving exons 1-3 (or 1-4) of TMEM106B fused to exons 8-18 of BRAF.

Conclusion: The TMEM106B->BRAF fusion in our case results in replacement of the N-terminal regulatory domain of BRAF with the N-terminal region of TMEM106B, while leaving the kinase domain of BRAF intact. This fusion is expected to result in activation of BRAF signaling, but will not be targeted by BRAF inhibitors. The response of PXA and other tumors harboring BRAF fusions to agents such as MEK inhibitors (*e.g.* selumetinib) is currently under investigation.

P-0178 | Modulation of the CTNNB1 (B-CATENIN) by the Aurora Kinases Inhibitor AMG900 in Paediatric Medulloblastoma Cell Lines

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Background/Objectives: Medulloblastoma (MB) is the most common malignant brain tumour in childhood. Tumour formation/progression has been associated to dysregulation of signaling pathways such as Wingless (Wnt). Cell cycle proteins Aurora-kinase (A, B and C) have been widely studied since they were found overexpressed in many cancers, including MB. Recent studies have shown that there is an association between Wnt pathway and Aurora kinase proteins. However such association remains to be addressed in MB. The aim was evaluate Wnt pathway modulation by Aurora kinases inhibitor AMG900 in paediatric medulloblastoma cell lines.

Design/Methods: Conventional PCR, sequencing, qRT-PCR, transient transfection, clonogenic assay, Western Blot and cell cycle assays.

Results: UW402, UW473 and ONS-76 cell lines did not present mutations in exon 3 and exon 15 of CTNNB1 (β -catenin) and APC genes, respectively. Moreover, there is not a significant expression of CTNNB1 as well as its target genes in these cell lines, confirming that they did not have Wnt pathway activated. After CTNNB1 transient transfection there was an increased expression of CTNNB1 gene and its target genes *Cyclin-D1* and *C-Myc* in the cell lines. CTNNB1 transfection also leads to a reduction in the number of colonies in UW473 and ONS-76 cell lines. Additionally, there was an increase in Aurora A and B proteins in UW473 cell line, but not in ONS-76 cell line. After treatment with AMG 900, a pan Aurora kinases inhibitor, there was a decrease in protein expression of β -catenin, Aurora A and B in both cell lines (UW473 and ONS-76). Transfection did not change the cellular percentile in G2/M in UW402 and UW473. In ONS-76 there was a significant increase in G2/M, and the treatment with AMG900 potentiated this block only in this cell line.

Conclusion: These results suggest that there may be some relation between Aurora kinases proteins and Wnt pathway in MB.

P-0179 | Profound Hearing Loss in Posterior Fossa Low Grade Gliomas Excluding Chemotherapy or Radiation Therapy as Cause

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Background/Objectives: Hearing assessment for hearing loss is well-known to children with low grade gliomas (LGG) receiving ototoxic chemotherapies or radiation therapy (RT). However, hearing loss in children with posterior fossa (PF) LGG may be missed in patients undergoing surgery alone and may exist prior to giving ototoxic chemotherapy or RT.

Design/Methods: We retrospectively reviewed 206 patients with PF LGG at our institution for hearing loss. Inclusion criteria was hearing loss with surgery alone or existing prior to follow-up chemotherapy and/or RT at tumour recurrence. We excluded hearing loss after chemotherapy or RT.

Results: Thirteen patients (6.3%) of PF LGG (70% male; 30% female; median [range] age 4.8=[0.6- 14] years) had profound unilateral hearing loss and met inclusion criteria. Median time from tumour diagnosis to hearing exam was 0.3 (0-13.6) years. Median age of hearing loss was 6.9 (0.6-24.6) years. Two patients had unilateral hearing loss before tumour diagnosis and 11 patients had hearing loss median 3 (2 days-13.6 years) months after surgery. 46% patients had hearing loss with surgery alone and 54% had hearing loss prior to chemotherapy or RT given at tumour recurrence. Tumour types were pilocytic astrocytoma (9), ganglioglioma (2), gangliocytoma (1), and LGG not otherwise specified (1). 92% had no involvement of internal auditory canal (IAC) and one patient had tumour abutting IAC.

Conclusion: Hearing loss is a risk in children with PF LGG (not involving the IAC) treated with surgery alone or prior to chemotherapy and RT at tumour recurrence. Hearing testing should be warranted in PF LGG treated with surgery alone and prior to chemotherapy and RT. We recommend hearing assessments before and after surgery in PF LGG even if tumour does not invade IAC.

P-0180 | Neurofibromatosis type 1 and Low Grade Glioma, 10 years Single Center Experience

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Background/Objectives: Neurofibromatosis type 1 (NF 1) is one of the most common autosomal dominant inherited tumour predisposition in our population. The most serious complication of the individuals with neurofibromatosis type 1 are malignant tumors of the CNS. In

about 15% of patients mostly up to 5 years of age tumors that are commonly associated with the disorder include glioma of the optic pathway.

Design/Methods: The aim of our study was to perform 10 years retrospective analysis of our patients with Neurofibromatosis type 1 and Low grade glioma (LGG) in term of treatment, toxicity and survival. Our cohort of patients was treated according protocol SIOP LGG/GPOH a SIOP- LGG 2004 at single center in Bratislava, Slovakia. Patients were treated in period January 1/2006 -12/ 2015. We have analyzed the cohort of 33 patients with NF1 and LGG, 17 boys/16 girls, with age 8 - 132 months, median 45 months.

Results: In 32 children with NF1 glioma of the optic pathway had developed, in 1 patient there was LGG - pilocytic astrocytoma WHO gr. I in basal ganglia area. Treatment was indicated in case of radiological or clinical progression. Chemotherapy received 12 patients, in 21 children there was no treatment applied and they have regular follow up. In our cohort 96.9% of children are alive, median of follow up 32 months. Patient with LGG of basal ganglia had recurrent progression and died.

Conclusion: The presence of NF1 generally is associated with more indolent disease, reflected in longer times to disease progression and higher rates of PFS and OS. According the published data children with NF1 and LGG of glioma of the optic pathway have better 3-years PFS (67.5% vs those without NF 1 54.9%), 3-years OS is 89.1%. In our small cohort, the outcome is in concordance with published data.

P-0181 | Low Grade Gliomas in Morocco

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Background/Objectives: In an effort to standardize care in Morocco, the Moroccan Society of Pediatric Haematology and Oncology created on 2010 a national PBT working group. This group initiated a data collection system and developed treatment guidelines for the more common paediatric brain tumors based.

We report the clinical and therapeutic data collected about Low Grade Gliomas LGGs, the most frequent PBT.

Design/Methods: We retrospectively reviewed the charts of all the patients referred to the Moroccan paediatric oncology units for LGGs from 2010 to 2015. We studied demographic data, clinical presentation, diagnosis workup, treatment plan and follow up. Two institutions participated to the study.

Results: Forty six LGGs cases were registered. Most of them were female (27 cases). The median age of diagnosis was 6.5 years old range 7 months to 15.5 years old. Median duration of symptoms was 6 months and 6 cases more than 2 years. There was a wide range of symptoms: ophthalmologic symptoms, cephalaea, and school difficulties. The main location was fossa posterior in 23 cases and optic pathway in 11 cases (3 cases had café au lait spots). In two cases the tumour size was 8 cm. Histology was available in 21 cases and 9 were pilocytic. Data about treatment plan were available in 40 cases. Nine patients had surgery (2 complete and 7 partial) and 8 had a stereotaxic biopsy. 23 had chemotherapy mainly combination of carboplatine /vincristine and 3 cases of radiosurgery.

Data about follow up were available for 38 patients; 12 abandoned 4 died, 2 in progression 29 are alive in stable disease or complete remission.

Conclusion: This report stress an important recruitment bias. Early diagnosis, efficient data collection system, multidisciplinary approach and communication can improve the prognosis of LGG in Morocco. Results will be updated during the upcoming meeting.

P-0182 | A Single Center Experience of a Treatment for Medulloblastoma

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Background/Objectives: To evaluate clinical characteristics and treatment outcome of medulloblastoma cases treated in our center.

Design/Methods: Between 1988-2016, paediatric patients with medulloblastoma were reviewed retrospectively. Clinical characteristics, details of surgery, chemotherapy and radiotherapy were reviewed, and overall (OS), event free survival (EFS) rates were analyzed.

Results: Fortyfour percent of 1009 malignant childhood tumors excluding leukaemia was CNS tumors in our center. Medulloblastoma (n:60) constituted 6% of the paediatric cancer cases. Fiftytwo patients were eligible out of 60. The median age at diagnosis was 6 years, M/F:1,5. The median duration of complaints was one month. Complaints were vomiting and headache (85%), ataxia (68%), visual disturbance (47%), neurological deficits (32%), behavioral changes (6%), motor deficits (6%). Spinal seeding rate was 29%. Gross total resection had been performed in 63% of cases. Eightyfive percent of cases had hydrocephalus and 32% of them was required ventriculoperitoneal shunt surgery. Histopathologic examination revealed classic-MB (%71), nodular desmoplastic-MB (%17), anaplastic-MB (%10). Chang staging system was used. Sixty percent of cases was in high risk group. Craniospinal radiotherapy was performed in 77% of patients. Chemotherapy was given in 56% of cases. Different chemotherapy protocols have been used over the years. Vincristine, Carboplatin/Cisplatin, Etoposide, Ifosfamide combinations have been used. VCR+CCNU were used in 3 patients. Median follow-up time was 10 months (1 month-23 years), 5, 10, and 5-years EFS was 52%. Relapse, refractory disease, progression were occurred in 10 patients. 5,10 and 5-years OS was 73%. Nineteen patients died, 84% of them died with progression. Two cases died in early postoperative period, and one patient died with treatment toxicity. Secondary malignancy occurred in one patient.

Conclusion: Gross total tumour resection was aimed, and risk stratification based treatment protocols were performed in our center. Administered chemotherapy protocols were different. The survival rates of our patients were acceptable. Analysis of medulloblastoma biology couldn't be done.

P-0183 | Dysembryoplastic Neuroepithelial Tumour of Childhood: EGE University Experience

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Background/Objectives: Dysembryoplastic neuroectodermal (DNET) tumors are benign glial-neuronal tumors that are rarely seen in children. They are mostly located in cerebral hemispheres. Patients usually present with seizures. Some of the patients have refractory epilepsy. In this retrospective study, we aimed to investigate the characteristics of the cases with DNET followed-up by our institution.

Design/Methods: Fourteen cases with DNET diagnosed and treated between January 2005 and February 2016 were retrospectively analyzed. The demographic characteristics of the patients, symptoms, tumour location, histopathology, surgical and prognostic findings and survival rates were evaluated.

Results: The demographic characteristics of the patients were as follows: male / female ratio of 14 patients was 4/12, and the mean age is 10 (from 5 to 17.5 years). All patients were admitted with the complaint of seizure. Most of these seizures were partial seizures. Two patients presented with headache, vomiting, balance disorders, while one had numbness in his left arm. All cases had been followed-up by adult or paediatric neurology units due to seizures before they were diagnosed. They had experienced seizures in an average of 21.4 months under antiepileptic treatment.

According to the MRI findings, tumour locations were temporal lobe in 9 (64.2%) patients, and occipital in 4 (28.5%) patients, while 1 in the frontal lobe.

Temporal lobectomy was performed by neurosurgeons for all the cases with temporally localized tumors, whereas near-total or total tumour removal was performed in the cases with frontal and occipital located ones. Only 2 of the cases relapsed in the follow-up (6 months and 11 years). Both of these relapses were in primary lesion area.

Conclusion: Dysembryoplastic neuroepithelial tumour must be considered in the differential diagnosis of resistant seizures and temporally localized tumors. Patients are provided with full recovery after surgery in majority of them and their seizures end.

P-0184 | A Multicenter Evaluation of Nimotuzumab Containing Regimens for Paediatric Diffuse Intrinsic Pontine Gliomas

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Background/Objectives: Overexpression of epidermal growth factor receptor (EGFR) is detected in some paediatric brain tumors including diffuse intrinsic pontine gliomas (DIPGs). Nimotuzumab is an (EGFR) IgG1 antibody that targets DIPG. DIPGs have a dismal prognosis.

Design/Methods: DIPG patients receiving nimotuzumab containing regimens in three centers were evaluated. After 2012, nimotuzumab was administered during progressive disease (PD) after radiotherapy (RT) + Temozolomide (TMZ). After 2012, nimotuzumab, 150mg/m²/dose once a week for 12 weeks, was also used as primary treatment with TMZ/vinorelbine during RT, and then biweekly until PD. PD patients using nimotuzumab + TMZ, switched to nimotuzumab+vinorelbine.

Results: Nimotuzumab was used in 30 children (12 PD, 18 primary diagnosis). In 12 PD patients, 4 had significant clinical improvement for 18, 8, 8 and 8 months; all are dead of disease (DOD). The other 6 PD progressed under nimotuzumab treatment after a median of 2 (1-4) months and are DOD. One PD patient is alive for 70 months. One PD patient refused further treatment. In 18 patients who received Nimotuzumab primarily, 11 remained stable for a median of 6 (3-21) months; 1 patient is AWD for 10 months; others are DOD after a median of 11(8-35) months. 7 primary Nimotuzumab receivers deteriorated under RT and died at a median of 4 (3-8) months. The overall survival at 1 year for all (n=30) is 37.9% with a median follow-up of 11.5 months (3-70 mo.). The progression free survival at 1 year and 2 year are 36% and 16%, respectively. In 18 patients who were under Nimotuzumab treatment since diagnosis; 1-year overall survival is 27.5% with a median survival of 10 months (3-35mo.).

Conclusion: Nimotuzumab±TMZ was well tolerated with no major adverse effect. Although the survival rate is higher than historical controls with only RT, it is still poor. Its efficacy has to be tested in larger series.

P-0185 | Sleep Problems in Children following a Brain Tumour Diagnosis. Surveillance in a Tertiary Paediatric Neuro-Oncology Centre

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Background/Objectives: Children and young adults treated for brain tumours may be at risk of sleep problems. Tumours localised to the hypothalamus may cause hypocretinergic neuronal dysfunction and secondary narcolepsy, with impairment to quality of life.

We aim to assess prevalence of excessive daytime sleepiness (EDS) specifically, and sleep disorders more generally, in children with brain tumours. Secondary aims are to assess predictors of sleep problems, including tumour location and treatment.

Design/Methods: Parents of children with brain tumours, attending neuro-oncology follow-up clinic in a tertiary paediatric neuro-oncology centre, completed the Child's Sleep Habits Questionnaire (CSHQ) and Epworth Sleepiness Scale (ESS). Where appropriate, children also completed the ESS. Standardised scoring criteria were applied. Data on tumour histology, location and treatment was collected.

Results: We collected data from 24 children (15 male) aged 5 to 17 years (median age 12.3 years), with a median time of 2.82 years since diagnosis (range 2 months to 12.9 years). Tumour locations included posterior fossa (n=10), cerebral hemisphere (n=7), sellar/suprasellar (n=2) or other (n=5). Treatment included neurosurgery (n=19), chemotherapy (n=6) radiotherapy (n=7) or no treatment (n=4).

CSHQ scores indicated risk of sleep disorders in 62.5% (15/24). Based on child ESS responses, 26.3% (5/19) reported EDS. Sleep problems and EDS were reported in both children treated for sellar/suprasellar tumours. Sixty-three percent (12/19) of children who had neurosurgery recorded a potential sleep disorder compared to 28.6% (2/7) of patients who received neurosurgery and radiotherapy and/or chemotherapy.

Fifty percent (11/22) of parents reported a change in their child's night-time sleep. 'Worrying about things' post-treatment, a possible factor for sleep disruption, was reported in 68.2% (15/22).

Conclusion: Our study shows that sleep disorders are common and a proportion of children experience EDS. Recruitment continues to further explore the relationship between sleep disorders, treatment and tumour location.

P-0186 | Use of Endocrinological and Neurological Medication among 5-Year Survivors of Young Onset Brain Tumors in Finland

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Background/Objectives: The burden of late-effects for survivors of young onset brain tumour (BT) needs more careful evaluation. Our aim was to assess the need for endocrinological and neurological medication among this specific group.

Design/Methods: We identified 5-year survivors diagnosed at the age of 0-24 years between 1988 and 2004 from the Finnish Cancer Registry (N=602). Data on endocrinological and neurological drug purchases were collected from the Social Insurance Institution of Finland.

Results: At 5 year survival the most commonly purchased drugs had been: antiepileptics (44.8%), systemic hydrocortisone (18.3%), female sex hormones (17.6%), thyroid hormones (11.2%), and growth hormone (10.0%). The survivors showed an increased HR for a need for new types of drugs still 5 years after diagnosis. Thyroid hormones (HR 10.6, 95% CI 5.1, 21.4), estrogens (HR 8.0, 95% CI 2.1, 25.7), and antiepileptics (HR 6.3, 95% CI 3.4, 11.2) were bought with high frequencies. Irradiation increased the hazard for drug-purchases other than antiepileptics. Cumulative incidence of purchases of estrogens or androgens increased still 15 years after diagnosis. The cumulative incidence of purchasing thyroid hormones and antiepileptics showed continuous increase for the youngest group, whereas survivors diagnosed at 15-24 years of age reached stable level before 15 years from diagnosis.

Conclusion: The need for new medication continued more than a decade after BT diagnosis. Especially the need for new thyroid or sex hormone medication among survivors of childhood BT may emerge long after diagnosis.

P-0187 | Proton Therapy in Irish Paediatric Oncology – A Review of Toxicities

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Background/Objectives: To: (1) produce a descriptive study of Irish children referred abroad for proton therapy (PT), and (2) to discuss toxicities attributable to PT observed in these patients.

Design/Methods: A retrospective review of all children referred for PT before October 2015 was performed.

Results: Seventeen children treated in Ireland have been referred abroad for PT to date, with following diagnoses: rhabdomyosarcoma (4), craniopharyngioma (3), ependymoma (6), meningioma (1), pilocytic astrocytoma (1), germinoma (1) and ATRT (1). Two patients suffered relapse of their disease while the remaining 15 are currently alive with complete response.

Four(24%) of our patients have encountered PT-related adverse effects. A 6 year old (yo) with periorbital rhabdomyosarcoma developed orbital asymmetry due to scar tissue formation. A 2yo with a posterior fossa ependymoma developed brainstem and cerebellar radiation necrosis requiring hyperbaric oxygen and corticosteroid treatment. The patient has persistent neurological sequelae, including the ongoing requirement for nocturnal continuous positive airway pressure ventilation. A 4yo developed isolated growth hormone deficiency following PT to a

cerebellopontine angle clear cell meningioma. A 5yo female with a craniopharyngioma developed significant hypothalamic syndrome and panhypopituitarism and suffered subsequent transient ischaemic attacks as a result of extensive radiation-induced vasculopathy of the Circle of Willis.

Conclusion: At present no PT facility exists in Ireland and patients are referred abroad on the basis that the physical properties of protons allow a better sparing of normal tissues, with consequent reduction of acute and late toxicities. While planning studies have clearly demonstrated superior conformality and reduced risk to normal tissues, the level of published evidence supporting superiority over conventional treatment remains low. In recent years, particular concerns have arisen regarding unexpected toxicity seen with PT in children with brain tumours as well as uncertainties regarding the relative biological effectiveness of protons. Although PT is likely here to stay, the results of present and future studies are needed to shape its future application.

P-0188 | Treatment Results of Embryonal Brain Tumors and Anaplastic Ependymoma in Infants

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Background/Objectives: Treatment results of infants with embryonal brain tumors and anaplastic ependymoma in high risk group are not satisfactory.

The aim of this study was to estimate progression-free survival (PFS) in infants treated on MTX-OPEC (vincristine, methotrexate, cisplatin, cyclophosphamide, etoposide) – based chemotherapy regimen with or without followed by high-dose chemotherapy (HDCT) with autologous stem cell transplantation.

Design/Methods: From 2008 to 2015 years 47 infants with de novo non-desmoplastic, non-MBEN variants of medulloblastoma – MB (15), supratentorial primitive neuroectodermal tumour – sPNET (9) and atypical teratoid rhabdoid tumour – sATRT (10), anaplastic ependymoma – AE (13) were included in trial. Average risk group (ARG) was defined as: MB and AE with ROM0; high risk group (HRG) as: M+, R1, LCA MB, C-MYC amplification MB, sPNET, sATRT. Induction chemotherapy – 2 MTX-OPEC cycles. Radiation therapy: posterior fossa – 23.4Gy, local radiation therapy to the tumour bed – up to 54Gy – for MB and AE; CSI 10Gy as a part of conditioning regimen – for 4 sPNET and sATRT. Consolidation chemotherapy: 2 cycles MTX-OPEC and maintenance chemotherapy – for all MB, AE, for 11 sATRT, sPNET; HDCT topotecan, melphalan or thiophosphamide, carboplatin for 8 sATRT, sPNET.

Results: Thirteen infants were included in ARG, 34 – in HRG. R0 status was revealed in 34% patients, R1 in 66%, M0 in 72.4%, M+ in 27.6%.

In ARG PFS was 62.5 ± 9.4% (MB), 83.3 ± 15.2% (AE); for HRG: PFS was 37.5 ± 17.1% (MB), 42.9 ± 17% (AE), 0% (sATRT), 25.9 ± 12% (sPNET) with a median follow-up 34.6 ± 9.2 months (MB), 59.1 ± 8.2 (AE), 8.3 ± 1.6 (sATRT), 23.9 ± 9.5 (sPNET). Four events were revealed in ARG, 25 – in HRG. Treatment related mortality was 4.2%.

Conclusion: We have achieved good therapeutic effect only in infants with anaplastic ependymoma in ARG.

P-0189 | Treatment Results of Non-Desmoplastic, Non-MBEN Medulloblastoma Variants in Infants According to MTX-OPEC - Based Chemotherapy Program

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Background/Objectives: The aim of this study was to estimate event-free survival (EFS) and progression-free survival (PFS) in infants treated on MTX-OPEC (vincristine, methotrexate, cisplatin, cyclophosphamide, etoposide) – based chemotherapy regimen.

Design/Methods: From 2008 to 2014 fifteen infants with de novo non-desmoplastic, non-MBEN variants of medulloblastoma were included in trial. Male/female ratio was 8/7. Median age – 26 ± 2 months. Average risk group (ARG) was defined as: ROM0, non-LCA; high risk group (HRG) as: M+, R1, LCA, C-MYC/N-MYC amplifications. Infants of ARG and HRG underwent induction chemotherapy (2 cycles MTX-OPEC), radiation therapy (posterior fossa – 23.4Gy, to the tumour bed – up to 54Gy, daily fraction 1.8 Gy), consolidation chemotherapy (2 cycles MTX-OPEC) and maintenance chemotherapy.

Results: Seven infants were included in ARG, 8 – in HRG. R0 status was revealed in 7 patients (46.7%), R1 – in 8 (53.3%), M0 – in 11 (73.3%), M+ – in 4 (26.7%), ROM0 – in 7 (46.7%), R1M0 – in 4 (26.7%), R1M+ – in 4 (26.7%), LCA histological variant – in 2 cases (13.3%), C-MYC amplification – in 1 case, iso17q (Group 3) in 2 patients.

In ARG PFS was 62.5 ± 9.4%, EFS was 53.6 ± 20%; for HRG: EFS was 37.5 ± 17.1%, PFS was 42.9 ± 18.7%, 7 patients (4 with ROM0, 3 with R1M0) alive at the present time without evidence of disease with a median follow-up 34.6 ± 9.2 months. Three events were revealed

in ARG, 5 – in HRG. Events were presented by: progression after radiation therapy in 1 case, during maintenance therapy – in 4 cases, early relapse in 1 case. Treatment related mortality was 13.3% (2 children) due to septic complication in 1 and acute cardiac failure in 1.

Conclusion: MTX-OPEC – based chemotherapy program showed unsatisfactory results for infants with non-desmoplastic, non-MBEN medulloblastoma variants.

P-0190 | Treatment Results of Anaplastic Ependymoma in Infants According to MTX-OPEC - Based Chemotherapy Program

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Background/Objectives: At the present time results of some international infant's protocols for treatment of anaplastic ependymoma were published. Results of treatment anaplastic ependymoma in high-risk group were not satisfactory. The aim of this study was to estimate event-free survival (EFS) and progression-free survival (PFS) in infants treated on MTX-OPEC (vincristine, methotrexate, cisplatin, cyclophosphamide, etoposide) – based chemotherapy regimen.

Design/Methods: From 2008 to 2014 thirteen infants with de novo anaplastic ependymoma were included in trial. Male/female ratio was 1.6/1 (8/5). Median age – 20.7 ± 2.7 months. Average risk group (ARG) was defined as: R0M0; high risk group (HRG) as: M+, R1. Infants of ARG and HRG underwent induction chemotherapy (2 cycles MTX-OPEC), radiation therapy (posterior fossa - 23.4Gy, local radiation therapy to the tumour bed – up to 54Gy, daily fraction 1.8 Gy), consolidation chemotherapy (2 cycles MTX-OPEC) and maintenance chemotherapy.

Results: Six infants were included in ARG, 7 – in HRG. R0 status was revealed in 6 patients (46.2%), R1 – in 7 (53.8%), M0 – in 12 (92.3%), M+ – in 1 (7.7%), R0M0 – in 6 (46.2%), R1M0 – in 6 (85.8%), R1M+ – in 1 (14.2%). In ARG EFS, PFS was 83.3 ± 15.2%; for HRG: EFS, PFS was 42.9 ± 18.1%, 8 patients alive at the present time without evidence of disease with a median follow-up 59.1 ± 8.2 months. One event was revealed in ARG, 4 – in HRG. Events were presented by: late relapses in all cases, local relapses in 3. Treatment related mortality was not observed.

Conclusion: MTX-OPEC – based chemotherapy program showed good therapeutic effect for infants with anaplastic ependymoma in ARG.

P-0191 | Bicentric Retrospective Observational Study on the use of Anti-Epileptic Drugs in Children with Brain Tumors

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Background/Objectives: Seizures are described in up to 30% of the children with primary brain tumors (PBT). There are no official guidelines on the use of anti-epileptic drugs (AED) in this population. Some might result in deleterious drug interactions, in particular with chemotherapies. There is a general agreement for the use of levetiracetam (LEV) and valproic acid (VPA) for the treatment of PBT-related seizures in adult patients, because of their suspected antineoplastic properties.

Design/Methods: The goal of this observational retrospective study was to describe the population of children with PBT-related seizures treated at the University Hospital and at the Oscar Lambret comprehensive cancer Center of Lille, France, between January 2000 and December 2014. We collected data concerning seizure occurrence and AED management.

Results: Among 521 patients, 156 (30%) had had at least one seizure. Risk factors for seizures before diagnosis of PBT were supratentorial ($p < 0.001$) and low-grade tumors ($p < 0.001$). Risk factors for seizures after diagnosis of PBT were high-grade tumors (HR: 2.0 (1.2-3.1), $p = 0.004$), incomplete tumour-resection (HR: 3.3 (1.8-6.0), $p < 0.001$), tumour relapse (HR: 6.3 (3.7-10.8), $p < 0.001$) or metastatic tumour at diagnosis (HR: 2.3 (1.4-3.9), $p = 0.001$). At least one AED was prescribed in 111 children, with a total number of 206 AED-prescriptions collected. The most commonly AED prescribed were LEV (25%), VPA (25%) and carbamazepine (17%). The rate of LEV-use increased after 2010, while VPA-use decreased. Concomitant use of AED with chemotherapy was described in 29 children, without any change in the AED, even if it had enzyme-inducing properties. There was no major AED-related side effect described during PBT-treatment.

Conclusion: LEV and VAL should be regarded as first line treatment in children with PBT presenting with seizures. Lack of studies should not undermine the necessity of international guidelines to harmonize AED-use in this population.

P-0192 | Radiation Therapy for 72 Children with Intracranial Germinoma

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Background/Objectives: To evaluate the treatment outcome of radiotherapy in children with intracranial germinoma.

Design/Methods: From Jan.1996 to Aug.2013, there were 133 patients with intracranial germinoma who were treated by radiotherapy in our department. Of them, there are 72 children (age ≤ 14 years old). 16 patients were pathologically verified germinoma and others were clinically diagnosed by diagnostic radiotherapy and clinical signs. The median age at diagnosis was 13

years old (range, 4–14 years). There were 48 patients with localized germinoma, 18 patients with bifocal disease and others with disseminated disease. Radiotherapy used linear accelerator, conventional RT for 56 patients, 3D-CRT for 2 patients and IMRT for 14 patients. Treatment field included local field, whole ventricular irradiation with a boost, whole brain radiotherapy with a boost and craniospinal irradiation (CSI) with a boost. RT dose to the primary site ranged from 29Gy to 52Gy (median, 45Gy) and the prophylactic dose to the whole ventricular, whole brain and spine cord ranged from 17.8Gy to 36Gy (median, 25Gy). 9 patients were treated by chemoradiation therapy. The median follow-up time was 66months (range, 6–222months).

Results: The 5-year overall survival and relapse-free survival for 72 children with intracranial germinoma were 91.6% and 75%. Relapse was noted in 11 patients. There are 5 of 41 patients with localized germinoma omitting spinal irradiation recurrence in the periphery of the ventricle and no spinal cord failure. There are 2 of 12 patients with bifocal disease omitting spinal irradiation metastasized to spinal and 3 of them appeared intracranial failure. Only one of 19 patients with CSI happened recurrence. No treatment failure happened in chemoradiation group, 3D-CRT and IMRT groups.

Conclusion: Radiotherapy for intracranial germinoma resulted in excellent treatment outcome. Omitting spinal irradiation was feasible for germinoma with localized disease, but CSI was still recommend for multifocal disease. 3DCRT and IMRT technique were recommended for the treatment.

P-0193 | Brain Metastases in Paediatric Patients with Extracranial Solid Primary Cancer: 30-Years Experience

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Background/Objectives: Brain metastases (BrM) are frequent in adult cancer patients (50% of all brain tumours); but rare in children (1-10%). We present a serie of cases of BrM in children and adolescents diagnosed and treated of solid non brain tumours in a referral hospital.

Design/Methods: A retrospective study of paediatric metastatic neoplasms to the central nervous system (CNS) treated in a 30-year period (1985-2015) in patients less than 18 years of age. We evaluated their frequency, histological subtypes, sites of origin and staging at initial cancer diagnosis, clinical and radiological findings of BrM, treatment, and outcome.

Results: 973 tumour cases: hematological 36%, CNS 22.5%, non brain solid tumors 41.5%. Of the latter group, nine (2%) had BrM: neuroblastomas (4/110, 3.6%), renal tumours (2/44; 4.5%), soft tissue sarcomas (1/78; 1.3%), bone sarcomas (1/54; 1.9%) and retinoblastoma (1/13; 7.7%). Average age at diagnosis of the primary cancer was 5 years (range 1-10) and BrM 7 (2-14). Female/male: 6/3. 55.5% had distant metastases, synchronously in 22%. The rest were diagnosed in their evolution, with a median of 30 months after first diagnosis (13-68). Clinical presentation: vomiting +/- headache (55.5%), seizure and/or altered level of consciousness (33.5%), visual impairment (11%). All were diagnosed by image (5 CT, 4 MRI), and three confirmed histologically. Most were supratentorial (90%) and 55.5% solitary. Lansky medium scale: 30 (10-50), despite which were treated 90% (4 chemotherapy, 2 radiotherapy and chemotherapy, 2 surgery and chemotherapy). All died with a median overall and disease-free survival after cancer diagnosis of 29 and 8.5 months, respectively, and median survival of 2.5 months after CNS metastases diagnosis (0-9).

Conclusion: BrM in paediatric extracranial solid tumours are rare. The most common tumors with CNS metastases are of kidney/adrenal origin, predominantly neuroblastomas. The most frequent clinical manifestation is headache, and supratentorial location. The prognosis is dismal, despite aggressive therapy.

P-0194 | Temozolomide and Valproic Acid in Combination with Vinorelbine for the Treatment of Paediatric High-Grade Gliomas: Preliminary Analysis of a Study Protocol

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Background/Objectives: The prognosis for children with high-grade gliomas (HGGs): anaplastic astrocytoma, AA; glioblastoma multiforme, GBM) remains poor despite aggressive surgical resection and, in older children, radiotherapy.

Design/Methods: Our proposal for paediatric HGG was a chemoradiotherapy protocol developed by EORTC/NCIC for adults (Neurology, 2011), with Vinorelbine (20 mg/sqm iv weekly during radiotherapy, and 30 mg/sqm iv bi-weekly in the adjuvant phase). Moreover, the adjuvant phase was prolonged to 12 months.

Results: We treated 15 paediatric patients. Twelve (80%) have completed treatment at the time of analysis. The median age was 10 years (range 6-24). Five (33%) patients had a GBM, and 10 (67%) had an AA. We have considered 12 (80%) supratentorial (5, 42% in hemispheres and 7, 58% in diencephalon) and 3 (20%) infratentorial (2, 67% in brainstem and 1, 33% in cerebellum) tumors. Surgery was performed in 13 (86.7%) patients. It was radical without residual in 5 (38.4%) cases. Six patients (40%) had a disease progression during the adjuvant phase. About these patients, five (84%) have received a second line treatment, and 2 (33%) a subsequent third line treatment.

There are no significant differences in Progression-Free Survival (PFS) (not reached, NR vs 9.05 months, $p = 0.28$) and Overall Survival (OS) (NR vs 14.3 months, $p = 0.29$) between AA and GBM, with a favorable trend for AA. There are no significant differences also for primary tumour site, and for surgery in PFS and OS.

Patients who experienced disease progression during the adjuvant phase had a significant worse survival (12.1 months vs NR, $p = 0.0009$). After progression, none of these patients has obtained a disease control with subsequent treatment lines.

Conclusion: In paediatric HGG, a disease progression which occurs during an induction treatment represents a negative prognostic factor for survival. This identifies a subgroup of patients with a marked chemoresistance despite of treatment lines.

P-0195 | Evaluating Intensity Modulated Proton Therapy Relative to Passive Scattering Proton Therapy for Increased Vertebral Column Sparing in CSI of in Growing Paediatric Patients

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Background/Objectives: To demonstrate the feasibility of delivering vertebral body sparing (VBS) versus whole vertebral body (WVB) craniospinal irradiation (CSI) with intensity modulated proton therapy (IMPT) in growing children treated for medulloblastoma. VBS techniques may decrease adverse effects in patients' spine growth.

Design/Methods: Medulloblastoma patients, treated with CSI passive scattering (PS) proton radiation therapy (PRT) were selected and three additional IMPT plans were generated for the spinal part of the irradiation for each patient. This resulted in four plans with the following beam arrangements: (a) single posterior-anterior (PA) PS field covering the WVB (PS-PA plan), (b) single PA IMPT field covering the WVB (IMPT-PA plan), (c) single PA IMPT field including only the thecal sac in the target volume (IMPT-PA2 plan) and (d) two posterior-oblique (35°, 35°) IMPT fields including only the thecal sac in the target volume (IMPT2 plan). For all cases, a prescription dose of 23.4Gy(RBE) was assumed to 95% of the spinal canal. Dose, LET and variable-RBE-weighted dose distributions were calculated for all plans using the TOPAS Monte Carlo system.

Results: Both VBS techniques spared efficiently the anterior vertebral bodies (AVB), even when accounting for the higher LET values and variable RBE. V10Gy(RBE) decreased from 100% for the WVB techniques to 72-90% for the cervical, 38.3-45% for the thoracic and 28.1-33.3% for the lumbar, and V20Gy(RBE) decreased from 99.6-100% to 15.4-17.4% for the cervical, 17.6-18.8% for the thoracic and 10.5-12.6% for the lumbar AVB when VBS techniques were applied.

Conclusion: Advanced proton techniques may sufficiently reduce the dose to the vertebral body and allow for vertebral column growth for children with CNS tumors requiring CSI. This even holds if variable RBE values are considered. This technique should be explored in pre-clinical or clinical trials. A clinical trial is planned starting with the lumbar +/- thoracic spine VBS.

P-0196 | Modulation of AKT, CTNNB1, GLI1, KDM6A, KDM6B, NOTCH2, PTCH1 and Tert Genes Expression in Medulloblastoma Cell Lines Exposed to Drug Treatment

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Background/Objectives: Medulloblastoma (MB) is a malignant neuroepithelial embryonal tumour of cerebellum. This study aim to investigate the cytotoxicity of valproic acid (VA) and cisplatin (CDDP), and their role in viability and gene expression in MB cell lines (DAOY and D283MED).

Design/Methods: Treatments of DAOY and D283MED cells were distributed in three groups: (1) VA single, (2) CDDP single, and (3) VA combined with CDDP, during 24h, 48h and 72h. Untreated cells were the control for the assays. Cell viability was measured by Presto Blue assay; qPCR was performed to quantify gene expression.

Results: DAOY and D283MED showed different behaviors when submitted to the three treatments proposed. CDDP treatment was more effective reducing cell viability than VA single or combined in DAOY (p<0.0001). Otherwise, VA and CDDP combined treatment was more effective reducing cell viability than single treatments in D283MED (p<0.0001). We observed higher *KDM6B* gene expression in DAOY cells treated with CDDP, for 24h, compared to untreated cells (p<0.0001). In 48h, *AKT*, *KDM6B*, *GLI1* and *TERT* genes expression increased in the three groups of treatments (p<0.0001). In 72h of treatment, *GLI1* and *KDM6B* genes expression decreased in the three groups of treatments (p<0.0001 and p=0.0300, respectively). In general, cells submitted to single treatments (groups 1 and 2) showed higher gene expression levels than combined (group 3) in the first 24h. However, in 48h, the combined treatment group reached high expression levels, and the maintenance of these levels was more prolonged than observed in the groups 1 and 2.

Conclusion: Expression modulation of genes involved in tumorigenesis process was dependent of drug treatment, and its importance in relation to treatment response must be clarified. This study suggests that a new strategy of drug regimen, combining CDDP and VA, as observed for D283MED cell line, will possibly leads to clinical advantages over classical CDDP-based therapy.

P-0197 | Distribution of TERT Alternative Splicing Variants in Paediatric Brain Tumors

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Background/Objectives: The mechanism of telomerase regulation remains unclear, but has been suggested that *TERT* is regulated by alternative splicing. Besides the full-length (FL) transcript, alternatively spliced variants have been described within the reversetranscriptase domain of *TERT* including, minus alpha (α^-), minus beta (β^-), and minusalpha beta ($\alpha\beta^-$). Medulloblastoma (MB) and Ependymoma (EP) are two of more frequent brain tumors of childhood. We investigated and described the principal *TERT* transcripts; FL, α^- , β^- and $\alpha\beta^-$ and whether or not the presence of these isoforms could be associated to clinicopathological characteristics and survival of paediatric EP e MB.

Design/Methods: We selected 58 MB and 43 EP samples. *TERT* alternative splicing variants were amplified by nested PCR and the amplified products were electrophoresed on 2% agarose gel.

Results: In general, around 5% of the samples of each group of tumors exhibited exclusively FL variant. *TERT* variants with deletion, exclusively or combined, were detected in 70% of MB and 39% of EP tumors. 27% of MB and 60% of EP samples did not show any of the patterns. We did not observed significant association between *TERT* splicing variants and clinicopathological characteristics of MB e EP tumors.

Conclusion: Since FL pattern is the only associated with reverse transcriptase activity, our results suggest that the association of *TERT* mRNA expression to clinicopathological characteristics of patients must be analyzed with caution. Further investigations will help to elucidate the complex mechanism involving alternativesplicing of *TERT* gene and the function of deleted variants in paediatric brain tumors tumorigenesis.

P-0198 | Retrospective Review of Iranian Cases with Central Nervous System Tumors: The Fundamental Search for Designing Future Plans

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Background/Objectives: There is an interest in Iran in improving the outcome of children with brain tumors. To achieve this, we must understand the current situation in Iran, so an extensive review of Iranian literature on brain tumors was performed.

Design/Methods: A literature review of the articles published in English or Persian languages from 1990 to Dec 2016 was performed using Scopus, Web of Science, PubMed, Google advanced search, and Google scholarship search engines. The following Mesh term headings were used: "central nervous system tumors" OR "brain OR spine OR spinal OR CNS" AND "tumour OR tumors OR neoplasm*" OR "medulloblastoma*" OR "glioma*" OR "astrocytoma*" OR "germ cell OR germinoma*" OR "embryonal brain tumors OR peripheral neuroectodermal OR PNET OR atypical rhabdoid teratoid OR ATRT OR choroid plexus tumors OR ependymoma*" AND "child OR children OR childhood OR paediatric OR adolescent". The findings were combined with the word "Iran" to execute the searches. Only papers discussing primary brain tumors in Iran were included in the final analysis.

Results: We found 76 papers (72 in English, 4 in Persian) that fit the search criteria: 47 studies were excluded because they discussed unrelated topics such as metastatic and secondary brain tumors. The 29 studies (26 in English, 3 in Persian) included discussed adults (n=3), children (n=13), or both (n=13). The total number of patients included in these studies was 9300 (range, 1 to 3434/study). The range of 5-year overall survival rates in these studies was 8.7% to 68.5%.

Conclusion: Some limitations exist in the early diagnosis and management of Iranian paediatric brain tumors. We believe that this study will help guide future efforts in Iran to improve outcome for children and adults with brain tumors.

P-0199 | Transient Magnetic Resonance Imaging Changes in Paediatric Patients with Central Nervous System Tumors Treated Radiation and High Dose Chemotherapy with Stem-Cell Rescue

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Background/Objectives: Radiation and high dose chemotherapy (HDC) with autologous stem-cell rescue (ASCR) used in the treatment of paediatric central nervous system (CNS) tumors can result in imaging changes similar to tumour progression. Study objective was to review transient MRI changes versus true progression during and immediately after treatment.

Design/Methods: Retrospective review of radiologic and clinical outcomes of paediatric CNS tumors treated with photon radiation and HDC with ASCR from 2000 to 2014.

Results: Our study included 23 patients (15 male; 8 female). Median age at diagnosis was 7.3 years (range: 1.1-21.9 years). Tumour types included primitive neuroectodermal tumour (n=11), medulloblastoma (n=9), and atypical teratoid/rhabdoid tumour (n=3). Eighteen patients received radiation and carboplatin/thiotepa with ASCR. Five patients received radiation and vincristine/cyclophosphamide/cisplatin with ASCR. Median follow-up time was 3.7 years (range: 0.6-14.7 years). Among patients who received carboplatin/thiotepa, enhancement and/or T2 signal changes were noted in 50% (n=9) either during or immediately after treatment [median: 3 months; range: 1-5 months from first stem cell transplant (SCT)]. Six (33%) of these patients had progressive disease while 3 (17%) patients had resolution/improvement in 1.38-5.98 months. Among patients who received vincristine/cyclophosphamide/cisplatin 60% (n=3) had T2 signal changes and/or enhancement changes on MRI brain/spine during treatment (1.5-1.8 months from first SCT). All 3 patients had resolution/improvement on imaging over time. In both treatment groups, transient changes were parenchymal and/or leptomeningeal. Patients

with transient changes were asymptomatic while 50% of patients with progressive disease had clinical symptoms coinciding with onset of imaging changes. Median follow-up time for patients with transient lesions was 2.5 years (range: 1.3–14 years). Two patients developed recurrent disease 1.6 and 2.1 years later.

Conclusion: Transient parenchymal and leptomeningeal MRI changes mimicking tumour progression/recurrence can occur during and/or immediately after HDC with ASCR. Patients with progressive disease may be clinically symptomatic compared to patients with transient lesions. Since such radiologic findings can pose a diagnostic dilemma and impact treatment course, awareness of these changes may help guide appropriate management.

P-0200 | A Comprehensive Molecular Biochemical Profile of Paediatric Medulloblastoma Brain Tumours in a South African Context

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Background/Objectives: Medulloblastoma (MB) is the most common malignant brain tumour in children with a high mortality and survivors often neurologically disabled. There are currently no reliable data of brain tumours in children in South Africa and the absence of this data restricts our understanding of the burden of childhood brain tumours in South African children and our involvement in international trials of novel therapies and protocols of treatment. One area in which Africa in general have not kept pace with international trends has been the recognition of molecular characterisation of MB and its potential implications for treatment. MB can now be classified into 4 main subgroups each of which correlates with prognosis which opens the way for an exciting era of targeted treatment according to subtype.

Design/Methods: Molecular profiles of MB were generated from a retrospective cohort using techniques involving FFPE tumour gene expression measured by Nanostring nCounter gene expression panel and confirmation by a select immunohistochemistry panel.

Results: The epidemiology relating to MB subtype is shown here, for the first time in an African cohort. There is a 25% incidence of the WNT, 30% of SHH, 30% Group3 and 15% Group 4 subtypes respectively in this cohort. The demographics show an equal spread between male and female patients with MB, and an average age of 5.7 years at diagnosis.

Conclusion: We are demonstrating the first molecular data of MB subtype in a South Africa cohort, with the incidence and representation of subtypes in agreement with international cohorts of similar age ranges. There is however a differing sex ratio as other studies have suggested more representation of this disease in male patients whereas we have seen an equal representation. The disease subtypes looks similar in local cohorts with the slight overrepresentation of younger patients and no striking male over-representation.

P-0201 | Astroblastoma Without Disease Recurrence at 1 Year Following Gross Total Resection Alone: A Case Report

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Background/Objectives: Astroblastoma is a rare tumour classified by the WHO as a high-grade glial neoplasm, however, recent review suggests that following gross total resection cure may be achieved with no significant benefit from adjuvant therapies. The following is the case of a patient diagnosed with astroblastoma without disease recurrence at 1 year after diagnosis following gross total resection alone.

Design/Methods: Case Report

Results: A 6-year-old girl presented with first-time seizure complicated by prolonged left face, arm and leg paralysis. MRI scan showed a right parietal lesion measuring 2.5cm × 1.8cm × 1.5cm. A gross total resection was achieved and confirmed on post-operative MRI scan. MRI total spine and CSF remained negative for metastases. Pathology was initially thought to be consistent with ependymoma given significant cellularity. However, on pathological review by Children's Hospital of Pittsburgh, St. Jude Children's Research Hospital and Johns Hopkins Hospital, the tumour was consistent with WHO Grade II astroblastoma given the presence of epithelioid perivascular formations typical of astroblastoma. Despite the unusually cellular nature of the tumour, mitoses were widely scattered and MIB-1 rate was low in addition to low proliferation index confirmed on Ki67 and PHH3 immunostain. Vimentin and BRAF were strongly positive. EWSR1 FISH negative for translocation. Given her diagnosis of astroblastoma and recent reports in literature of increased survival advantage with gross total resection alone without further therapies she has undergone no further treatment. She continues to be followed 1 year after the time of diagnosis and resection with MRI every 3 months. She has had no recurrence of her disease.

Conclusion: This case addresses concerns surrounding optimal treatment in cases of astroblastoma given the rarity of this intracranial neoplasm and supports that gross total resection without adjuvant treatment may be indicated and may prevent tumour recurrence.

P-0202 | Thinking Outside the Shunt - Sterile CSF Malabsorption in Pilocytic Astrocytomas: Case Series and Review of Literature

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Background/Objectives: Ventriculoperitoneal (VP) shunt insertion is the most common cerebrospinal fluid (CSF) diversionary procedure used for the treatment of chronic hydrocephalus.

Sterile CSF ascites is a rare complication of VP shunt insertion. This can arise from either an overproduction of CSF or inadequate filtration of CSF at the level of the peritoneum. By either mechanism, the development of CSF ascites requires an intact VP shunt.

Design/Methods: The authors discuss two paediatric cases diagnosed with suprasellar pilocytic astrocytomas treated with platinum-based chemotherapy, who subsequently developed sterile CSF ascites. We review the literature with regards to CSF malabsorption, and discuss it as a contributing factor to shunt malfunction.

Results: Conversion of the VP shunt to a VA shunt, lead to a complete resolution of the ascites and the patients were discharged home.

Conclusion: CSF malabsorption with resultant ascites is a rare complication of VP shunting with many etiologies. There appears to be an association between optic pathway gliomas and the development of CSF. In the cases presented in this manuscript, two common predisposing factors included the use of platinum based chemotherapeutic agents, as well as the specific neuro-pathology. Detailed analysis of our understanding of tumour dynamics in this patient group is important in establishing future therapeutic strategies.

P-0203 | High-Throughput Drug Screening in Primary Brain Tumour Cultures for Individualized Therapies

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Background/Objectives: Drug screening in primary brain tumour cultures entails compelling opportunities to elucidate tumour biology and to provide novel strategies for personalized therapy in neuro-oncological patient care. Especially, in the situation of therapy-resistant relapses, this approach may prove highly attractive to suggest treatment alternatives in clinical cases, where successful therapeutic interventions are lacking.

Design/Methods: We developed a protocol to reliably establish primary brain tumour cultures from samples generated during neurosurgical tumour resection in a fast and affordable manner. By means of 1536-well microplates, which are usually employed in industrial ultra-high-throughput screening (UHTS) approaches, the required total number of cells was drastically reduced. Drug screening was then performed using a clinical inhibitor library (n=199) comprising established chemotherapeutic agents and novel anti-cancer compounds currently in phase III and IV studies.

Results: We were able to generate at least primary cultures from each tumour, if not cell lines. Assay miniaturization emerged as a crucial step in platform development due to limited cell numbers or stability of primary cultures in some cases. All patient samples (n=5) could be successfully screened in less than a month after the initial surgery was conducted revealing reliable dose-response data for almost all inhibitors. These drug screening profiles were compared to a panel of normal control cell lines (n=3) consisting of neural stem cells and astrocytes. Consequently, we identified exceptional responses by overlaying the individual drug response profiles with profiles generated using other primary brain tumour cultures as well as established cell lines (n=21), and by comparing distinct histopathological entities with each other.

Conclusion: In all, we have established a UHTS pipeline for primary cultures investigating 199 clinical inhibitors at once. Continuous accumulation of drug response data will enable us to identify exceptional drug response patterns for individualized therapeutic approaches and to suggest novel agents for future clinical trials in high-risk patient cohorts.

P-0204 | Low Grade Glioma (LGG) Located in the Spinal Cord. Successes and Pitfalls of the Treatment

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Background/Objectives: Spinal cord LGG constitute approximately 3,5% of all LGG locations. No specific therapeutic guidelines are available for this specific LGG site. The aim of the study was to analyze childhood spinal cord LGG.

Design/Methods: 28 patients treated between 2004–2015 were analyzed for: sex, age, symptoms, pathology, treatment and outcome.

Results: There were 20 boys and 8 girls, aged 10 months–17 years, median 4.5 years. Paresis, scoliosis and pain were the most common symptoms. Pathology revealed Pilocytic astrocytoma in 21, Piloxyoid astrocytoma in 4, LGG NOS in 3 patients. In 5 patients total or subtotal resections was performed, in 17 partial resection, in 6 biopsy were performed. In 13 pts neurological improvement was observed, in 7 – deterioration, the rest remained stable. 13 patients had no further treatment. 15 received chemotherapy: 7 following surgical treatment, 8 at tumour progression. 12 patients started with LGG protocol, 3 with VLB. In 10 patients stabilization, in 5 minimal tumour regression were observed. All patients are alive with median follow-up 3 years 8 months. 5 yr and 10 yr EFS are 52,1%, 27,7, respectively. 10 patients are walking without paresis, 9 with paresis, 2 have scoliosis, 6 pts use wheelchair, 1 is paralyzed.

Conclusion: Spinal cord LGG have a good prognosis. Surgery improves neurological outcome, but radical resections are not mandated to achieve that. Some patients with tumour residual may not require further treatment, but at tumour progression chemotherapy is the residual of choice. Quality of life should be the priority in choosing surgical strategy.

P-0205 | 15-Year- Medulloblastoma Standard Risk Experience in the Service of Oncology "Hospital Ricardo Gutierrez"-Argentina

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Background/Objectives: Report the epidemiological characteristics and overall survival (OS) of patients (p) with standard risk medulloblastoma (SRM). To compare the results with our previous studies.

Design/Methods: A retrospective, descriptive study of patients with medulloblastoma over 3 years with localized tumors and complete resection, classic histology admitted in our institution from January 2000 up to June 2015. These patients were treated with radiotherapy and chemotherapy (similar schemes used internationally like CCG9892 / A9961 and ACNS0331 COG trials).

Results: Fifty three p were admitted with medulloblastoma over 3 years. Twenty five with SRM. Twenty one p were evaluable. Median age was 9 years (r: 3-14). The male / female ratio was 3.4 / 1. The most common symptoms were: vomits (68%), headaches (68%) and ataxia (24%). OS was 71% and EFS 66% at 2 years.

Patients treated with CCG9892 / A9961 similar chemotherapy schemes: 11p, 8p still alive and 3p died due to progression. OS 72% Patients treated with ACNS0331 COG similar chemotherapy schemes: 10p, 7p still alive. Two patients died because of toxicity and 1p for second neoplasm. OS 70%.

The most frequent sites of relapse were spinal cord (57%) and posterior fossa (28%).

All progressed/relapsed patients received second line treatment with high doses of cyclophosphamide/ temozolomide alone or combined with irinotecan and bevacizumab. One of them treated with temozolomide/irinotecan/bevacizumab is alive 14 months from relapse, with stable disease and good quality of life.

Conclusion: We achieved better 2 years EFS and OS than our previous reports. These results are similar to international data. In future evaluations it would be important to describe toxicities profiles and sequelae.

P-0206 | Memmat - A Phase II Study of Metronomic and Targeted Anti-Angiogenesis Therapy for Children with Recurrent/Progressive Medulloblastoma

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Background/Objectives: Patients with recurrent medulloblastoma have a poor prognosis, irrespective of therapy used, including surgery, conventional chemotherapy, re-irradiation, and high-dose chemotherapy. An alternative approach is an antiangiogenic metronomic combination therapy that inhibits multiple pro-angiogenic pathways targeting non-overlapping aspects of neovascularization and exerting its effect on the microenvironment to overcome treatment resistance.

Design/Methods: We present an international phase II study intended to include 40 patients with recurrent or progressive medulloblastoma who will be treated with a metronomic antiangiogenic regimen. Treatment consists of bevacizumab infusion every two weeks, continuous oral celecoxib, thalidomide, and fenofibrate, with alternating 21-day cycles of low-dose cyclophosphamide and etoposide, and alternating intraventricular therapy with etoposide and liposomal cytarabine. The primary endpoint is the response rate 6 months after start of antiangiogenic treatment. Secondary endpoints are overall survival (OS), progression free survival (PFS), toxicity, quality of life, performance status, and prognostic factors.

Results: The first patient was enrolled in April 2014, study completion is expected in 2020. To date, 8 patients aged 9-15 years (mean age 10 years) were enrolled. Six of the patients had first recurrence, while two had third recurrence. No major unexpected toxicities and no treatment related deaths were reported. To date, all patients are still alive, with a mean follow-up time of 14.5 months.

Conclusion: The preliminary results suggest that the MEMMAT regimen has promising clinical activity and is reasonably tolerated in children with recurrent medulloblastoma.

P-0207 | Endocrine Late Effects in Paediatric Brain Tumour Survivors

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Background/Objectives: To evaluate endocrine late effects in childhood brain tumour survivors.

Design/Methods: A population-based cross-sectional study; fifty-two (69%) out of 75 invited brain tumour survivors diagnosed at younger than 17 years of age between 1983-1997 and treated in Tampere University Hospital, Finland, were examined at a mean age of 14.2 (range 3.8-28.7) years after a mean follow-up time of 7.5 (1.5-15.1) years. Twenty-nine (56%) were treated by surgery only. Twenty (38%) had received cranial irradiation and 17 (33%) chemother-

apy; 14 (27%) both radiotherapy and chemotherapy. Laboratory tests included serum estradiol in female and testosterone in male patients, for both sexes serum follicle-stimulating hormone, luteinizing hormone, prolactin, cortisol, insulin-like growth factor (IGF-1), thyroid-stimulating hormone and free thyroxine.

Results: Thirteen patients (25%) received hormone substitution, nine (17%) more than one. Ten (19%) received thyroxine. New cases of thyroid dysfunction were not found. Twelve (23%) had growth hormone deficiency (GHD) and four of them received GH treatment. Based on IGF-1 measurements new GHD cases were not found. One (2%) received treatment because of sexual precocity. Six (12%) had hypogonadism and received sex hormone replacement. In addition two had high gonadotropin levels, so altogether eight of 36 pubertal/postpubertal patients (22%) had sex hormone deficiency. Seven (13%) had hyperprolactinemia. One female had a child. Four (8%) received glucocorticoid and one of them also mineralocorticoid treatment. Hypocortisolism appeared in six (12%). Three (6%) had diabetes insipidus and desmopressin treatment. Altogether 22 (42%) had one or more above mentioned endocrine abnormalities. Hormonal abnormalities were statistically significantly associated with tumour location in sellar/parasellar region, radiotherapy and/or chemotherapy.

Conclusion: Almost half of the survivors had endocrine late effects. GHD, hypothyreosis and hypogonadism were the most common endocrine late effects. Undiagnosed hypogonadism, hypocortisolism and hyperprolactinemia appeared. These findings underscore the importance of careful follow-up.

P-0208 | Posterior Fossa Brain Tumors in Children: Clarification and Added Value of Multimodal MRI. A Report from the Goce, Grand Ouest Oncology Study Group for Children

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Background/Objectives: Over the last few decades, the care of children with brain tumors benefited from major advances partly thanks to the development of new imaging techniques.

Design/Methods: A review of literature was based on 71 studies investigating paediatric cerebral tumors and multimodality techniques in RMN. We also performed a retrospective review of the MR imaging initial presentation of 68 children (with a mean age of 7 years old) and compared it to the literature.

Results: Our population was quite similar to that represented in the literature. Although conventional MRI is essential for diagnosis of typical aspects of tumour, nonspecific imaging of posterior fossa tumors was not rare and, for these cases, multimodality techniques improved diagnostic accuracy. ADC (Apparent diffusion coefficient) value seemed to reliably provide medulloblastomas diagnosis. A quantitative rCBVmax (relative cerebral blood volume) threshold of 1.38 has a high negative predictive value for excluding high-grade neoplasms. But there was a significant variability in rCBV values reported for each tumour type. MR spectroscopy with TE (echo time) of 35ms and TE of 135ms is also a helpful tool to distinguish the four most frequent posterior fossa tumors in children.

Conclusion: Out of these findings, we produced a practical MR flow chart for differentiating types of posterior fossa tumors in children, and a MR standard protocol to improve diagnostic accuracy in preoperative paediatric patients, standardize practice guidelines, and simplify patient management.

P-0209 | Epidemiology and Survival Pattern of Paediatric Low Grade Glioma: A Perspective from Middle Income Country

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Background/Objectives: To review demographic data, clinical presentation, treatment and outcome of children with low grade glioma (LGG) treated at tertiary centre in Malaysia.

Design/Methods: A retrospective analysis was performed on all paediatric patients diagnosed with LGG at University Malaya Medical Centre between 2001 and 2014.

Results: There were 20 children, aged 1.0 to 16.0 years (median 5.75) including 1 with neurofibromatosis type 1. Visual impairment, vomiting and ataxia were the common presenting symptoms. Median duration of symptoms was 8 weeks (range: 1-52). Fifteen tumours were WHO grade I (75%) and 5 were WHO grade II including 2 diffuse fibrillary astrocytomas, 2 pilomyxoid astrocytomas and 1 ganglioglioma. The commonest sites were optic pathway hypothalamic region (50%), posterior fossa (20%), pons (10%), spine (10%), thalamus (5%) and pineal gland (5%). Twelve patients underwent a primary surgery in the form of partial, subtotal or gross total resection, and the remaining 8 patients had a biopsy. Five of them were remained in stable disease with primary surgery alone. Four patients achieved stable disease with primary surgery and chemotherapy (vincristine, carboplatin). Second surgery was performed in 3 patients for recurrence; 2 of them required chemotherapy (vincristine, carboplatin, etoposide) with radiotherapy and 1 patient was treated with chemotherapy alone (vincristine, carboplatin). Three patients, who had a biopsy at diagnosis, underwent second surgery for disease progression after chemotherapy (vincristine, carboplatin, etoposide). In addition, one patient with post-biopsy was only observed after second surgery. One family refused treatment after biopsy and another patient abandoned treatment while on chemotherapy. Two patients succumbed post-biopsy secondary to progressive disease. The estimated 5-year overall survival rate was 88% (SE ±8.1%) and 5-year progression-free survival rate was 49.7% (SE ±15%).

Conclusion: Although LGG has been considered as an indolent tumour that is rarely progressive, 35% of patients in our cohort experienced disease recurrence and progression.

P-0210 | Brain Stem Glioma Registry: Pilot Program

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Background/Objectives: Brain stem gliomas are a heterogeneous group of tumors with poor outcome in childhood. This disease affects patients between 5 and 9 years old and usually have no effective treatment. Medical attention is given by radiotherapists, paediatric oncologists, adult oncologists, neurosurgeons or sometimes by paediatricians. In Mexico there is a lack of systematic registry of oncologic patients treated. Our first aim was to make a pilot study in order to establish a statistic page where different paediatric oncologists from different hospitals in Mexico City could register their cases.

Design/Methods: Inclusion criteria was only age less than 18 years old and the presence by magnetic resonance image of a brainstem tumour. We considered eighteen years of follow up. We carried out a retrospective and descriptive study including 5 hospitals.

Results: Three institutions were public: Instituto Nacional de Pediatría (58), Medical Center 20 de Noviembre (20), Hospital Juárez de México (10) and two were private: Hospital Angeles del Pedregal(2) and Hospital Médica Sur(2). Forty-five percent were female, age range was from 4 to 6 years. Main symptoms were ataxia in 63% of cases, hydrocephalus in 54%. Overall survival was 68% at 5 years of follow up and 62% up to 15 years.

Conclusion: This study has several bias as memory, quality of imaging, interpretation results and various treatments. At a first approach, we can observe better survival than the one registered in literature probably because of histology. This is the first national effort to establish the number of cases with brain stem gliomas in a period of time in order to establish a prospective registry with more valid information.

P-0211 | Managing Progressive Low Grade Glioma in Children - 15 Year Experience from a Single Centre in the UK

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Background/Objectives: Paediatric low grade gliomas (LGG) are associated with excellent outcome. However, a subset of patients develop recurrent or progressive disease (PD). We present our experience in managing children with progressive LGG.

Design/Methods: A retrospective study in children with LGG diagnosed between 2000 and 2015 who developed PD. Demographics, histopathology, treatment and follow-up data were analysed. Conventional statistics was used and survival rates calculated by Kaplan-Meier method.

Results: Twenty four of 104 children (23.1%) diagnosed with LGG developed PD. Median age at diagnosis was 6.5 (1.4-15) years. Tissue diagnosis was available in 22 patients (91%), 16 (72%) had WHO Grade I tumours (14/16 had pilocytic astrocytoma). Cerebellum and hypothalamus (29% each) were most common sites of disease. 15 patients (62%) underwent surgical resection at diagnosis (gross in 1, near-total in 6 and subtotal in 8), whereas 7 (29%) were treated non-surgically. Two patients were kept under observation only. Median time to progression was 20 (4-74) months.

On progression, 10/24 patients (41%) underwent surgery, including 3 who received adjuvant treatment. Nine (37%) were treated non-surgically (5 - chemotherapy, 4 - radiotherapy) while observational approach was used in 5 (20%). Fourteen (58%) patients experienced further progression, 4 (17%) of whom later died. Median time to death was 53 (35-120) months. Progression free survival (PFS) at 5 and 10 years following initial progression were 39±12.3% and 15.6±9.9%. Overall survival at 5 and 10 years were 83.1±9.0% and 71.2±13.4% respectively.

At last follow-up 14/20 survivors had stable disease but 19 had long-term neurological sequelae. Poor compliance to follow-up appointments was seen in 8/20.

Conclusion: Nearly a quarter of patients developed progressive disease with dismal outcome relating to residual neuro-disability, quality of life and low further PFS. More studies relating to progressive/recurrent LGG are warranted to predict the natural history of disease and develop effective treatment, rehabilitation and follow-up strategies.

P-0212 | Gliomas of Optical Pathway - Indications for Oncology Treatment and its Outcome, Experience of a Single Oncology Center During Period of 5 Years

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Background/Objectives: Optical pathway gliomas typically appear in early childhood and manifest the strongest growth during the first 3-5 years of life. They are low grade gliomas, and constitute 5% of all brain tumors in children. In Croatia we have 2-3 newly diagnosed patients diagnosed annually in Croatia.

Design/Methods: Optical pathway gliomas are well differentiated and histologically a very heterogeneous group of tumors that are of glial origin (astrocytic, oligodendrocyte) – according to World Health Organization they are grades I or II.

By localization, optical nerve glioma can be divided into gliomas of chiasm, optic tract and optic radiation. They are often infiltrated to adjacent structures (the hypothalamus, temporal lobe).

In connection with neurofibromatosis type 1 there are about 50% of all patients with optical pathway gliomas and show specific clinical course. Given the indolent nature of these tumors, patients are subsequently controlled by neurologist, ophthalmologist and neuroimaging procedures.

Results: In this paper we present 11 patients who were controlled in the Children's Hospital Zagreb during the five-year period (2010 to 2014). We have displayed different indications that warrant oncology treatment and also the course of the disease for each patient.

Conclusion: Particular importance is focused on patients with neurofibromatosis where there is the possibility of metachronous tumors as well as constraints in the implementation of chemotherapy and radiotherapy.

P-0213 | Systematic Review of Health-Related Quality of Life in Paediatric Brain Tumour Survivors

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Background/Objectives: Pediatric brain tumour survivors (PBTs) are at high risk for numerous late effects including decreased health-related quality-of-life (HRQL). However, research findings have been inconsistent and are complicated by issues of heterogeneity, sample size, and widely varying measurement strategies. Our aim was to summarize studies describing HRQL in PBTs.

Design/Methods: A literature search using online databases EMBASE, MEDLINE, and PsychINFO identified relevant peer-reviewed articles published within the past 10 years. Original studies were included if they described outcomes for PBTs diagnosed between infancy and 18 years using a quantitative measure of HRQL. Potential bias was evaluated with an adapted score [0-30] based on established assessment tools; papers were classified as having low [27-30], moderate [21-26] or high [0-20] risk of bias. Inter-rater reliability of abstracted data and agreement of bias-risk were determined by Cohen's kappa statistics and intraclass correlation coefficients (ICCs), respectively.

Results: The search strategy identified 525 unique abstracts for screening; 144 papers were retrieved for further review based on inclusion criteria. Data from 68 unique articles were abstracted by two independent raters. Inter-rater reliability was moderate (k=0.61). ICC for agreement of bias-risk was 0.74. Of these, n=8 (11.8%) were classified as Low Risk of Bias, while n=43 (63.2%) and n=17 (25%) were classified as Moderate and High Risk, respectively. Studies varied in design, sample size, conceptualization and operationalization of HRQL. Papers described 35 different HRQL tools. The Pediatric Quality of Life Inventory (PedsQL) was the most commonly cited tool (n=21), followed by the Health Utilities Index (n=15). Of those comparing PBTs to control groups such as peers, siblings or survivors of other cancers (n=36), 86% reported that survivors experienced significantly lower HRQL, while 11% found no difference.

Conclusion: Most studies suggest that PBTs are at increased risk of experiencing poor HRQL, even when compared to other cancer survivors.

P-0214 | Retrospective Analysis of Prognostic Factors in Children with Medulloblastomas Under 5 Years Old

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Background/Objectives: Prognostic-factors-based stratification in children under 5 yo with MB can probably allow to individualize conventional treatment.

Design/Methods: We retrospectively analyzed the data of 86 pts, who were treated or have follow-up (f-u) information and are observed in Rogachev's Center and other hospitals of Russia from 1993 till January 2016. The ratio of boys to girls was 1, 5:1. 5 pts were <12 months (m), 43 (50%) - 12-36 m, 38 - 36-60 m (med 21 m). Total tumour resection was in 31 pts, incomplete resection in 49 pts, biopsy - 3, unknown - 3. 43 pts (50%) had classic MB, 21 pts - desmoplastic, 7 pts - large cell/anaplastic, 1 pt - MBEN, MB NOS - 14 pts. SHH was 10 pts, group 3 - 5 pts, C-MYC amplification - 2 pts. M0 was in 30 pts, M1 - 15, M2 - 4, M3 - 25, M4 - 1, Mx - 11. R0M0 - 14 pts. HIT SKK regimen was in 90%. RT response was in 91.5% pts. PD was in 34 pts. 64 pts (74.4%) of 86 are alive; 83% of pts finished therapy.

Results: The 5-y OS was 0,42±0,06 (median f-u time 39,5 m, 2-271 m), the 5-y PFS was 0,60±0,05 (median 27,5 m, 2-235 m). PFS in boys/girls - 0,70/0,49 (p=0,13). Age PFS: 0,2 (<12 m), 0,52 (12-36 m), 0,78 (>36 m) (p=0,03); M-stage PFS: M0/M1/M3=0,62/0,59/0,53 (p=0,25), M2/M4 - 0; histology PFS: classic/desmoplastic/MBNOS/anaplastic=0,70/0,55/0,58/0,29 (p=0,15); volume of resection: 0,53 (R+)/0,66 (R0), p=0,28. OS SHH pts was 0,8, Group 3 - 0,25 (p=0,69). OS in SHH pts without RT was 0,33, with RT - 0,75 (p=0,29).

Conclusion: Adverse prognosis factors were age under 12 months, large cell/anaplastic histological variant, M-stage, residual tumour, absence of RT in SHH group. For further strategy treatment verification additional studies are needed.

P-0215 | Pharmacological Modulation of Blood-Brain Barrier Improves the Therapeutic Efficacy of Doxorubicin and Temozolomide in An Orthoptic Model of Human Glioblastoma

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Background/Objectives: Doxorubicin (Dox) is one of the best-studied drugs for high grade gliomas in preclinical models. In vitro and in vivo studies suggested that prolonged exposure to Dox had a strong anti-neoplastic activity against human gliomas. Morphine is able to alter the neuronal and glial microenvironment, leading to the stroke of the Blood-Brain Barrier (BBB) and enhancing the access of molecules normally unable to cross it, as Dox.

We have developed a xenograft mice model of human glioblastoma in order to verify the effectiveness of Dox and the common anti-glioblastoma agent, temozolomide (TMZ) alone or in association with morphine.

Design/Methods: Foxn1 mice were injected with U87MG-luc cells in the left lobe of the brain and treated with Dox (5mg/kg and 2.5mg/kg, weekly) or TMZ (1.77mg/kg, weekly) with or without morphine (10mg/kg, weekly). Intracranial tumour growth was quantified by Bioluminescence Imaging (BLI).

Results: The data showed that only Dox 5mg/kg determined a significant regression of BLI in a xenograft mouse model of brain glioma while the lower dose of 2.5 mg/kg was not effective. The average BLI for Dox 5mg/kg was 5-fold lower than that measured for Dox 2.5mg/kg (P=0.0238) and morphine 10mg/kg (P=0.0098) and 8-fold lower than vehicle (P=0.0012). The average BLI for Dox 2.5mg/kg plus morphine was 5-fold lower than Dox 2.5mg/kg alone (P=0.0053) and 8-fold lower than vehicle (P=0.0004). TMZ showed an amplified effect in combination with morphine. In this condition is 2.5 fold lower than average BLI measured for the administration of TMZ without morphine. These results demonstrated that there is a higher effectiveness of TMZ in combination with morphine on tumour regression in this GBM model.

Conclusion: The present findings emphasized that molecules as morphine are able to interfere with molecules normally unable to cross the BBB as DOX and common antineoplastic agents as TMZ.

P-0216 | Pharmacokinetic Profile of High-Dose Methotrexate in Children Aged Less Than 12 Months Affected by Brain Tumour

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Background/Objectives: Methotrexate (MTX) is an important drugs for the treatment of aggressive brain tumors, and in particular its use with high doses for its ability to reach therapeutic concentration and adequate action time in the brain parenchyma. In paediatric brain tumour patients there are few data on pharmacokinetics of high-dose MTX.

The purpose of this retrospective mono-centric analysis was to collect data on MTX doses and plasma levels at different times after drug infusion in infants aged less than 12 months treated for aggressive brain tumors.

Design/Methods: Infants aged less or equal than 12 months with newly diagnosed of brain tumors were eligible. MTX was the first course of a multi-drug treatment plan. The infant protocol for CNS tumors provided the administration of MTX at the dose of 8g/m² or 250mg/kg intravenously, in a 6-hours infusion. Drug levels in the patients' blood were checked after 24, 48, and 72 hours from the beginning of the infusion. At these checkpoints MTX levels should be lower than 10, 1, and 0.2 μM/L respectively.

Results: The median weight was 5,63 kg (range 3,12-9,0). The median steady-state MTX concentration at the end of 6-hr infusion was 486 μM/L (range 227-790). In these early infants, altered drug elimination was associated to a weight of less than 4 kg (p: 0.0179). Moreover, a systemic clearance lower than 2,5 L/h/m² at the end of the 6-hours MTX infusion could predict a delayed elimination in the following hours (p: 0.0179). Age, sex, steady-state MTX concentration at the end of the 6-hours infusion had not a significant correlation with delayed drug elimination.

Conclusion: Our analysis confirms that a dose adjustment in infants treated with high-dose MTX is required. A weight-based dose adjustment may not be sufficient in infants weighing less than 4 kg.

P-0217 | Intracranial Germinoma in Caucasian Brothers with Autism Spectrum Disorder: Report of Two Cases in a Family

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Background/Objectives: Intracranial germinoma is a rare form of paediatric brain tumour in Caucasians and no familial cases have been reported in the Western world.

Design/Methods: This is a Retrospective Case Report.

Results: We report the first Caucasian siblings with intracranial germinoma, both were also autistic. The first case was a 14 year old autistic male presented with progressive left sided dystonia. MRI brain revealed a right basal ganglia mass. He underwent a subtotal resection,

and histology was consistent with intracranial germinoma. Three months following his diagnosis, his 12-year-old brother presented with history of behavioral changes, decreased activity and upward gaze palsy. Brain MRI revealed a pineal mass, which was confirmed to be an intracranial germinoma by biopsy. He was also autistic, and was found to have hydrocephalus at 11 months of age, status post VP shunt. Both brothers received chemotherapy including carboplatin and etoposide followed by whole ventricular irradiation with a boost to the tumour bed. While there have been no significant improvement in their autistic symptoms following treatment, both brothers are doing well from the oncology perspective three years off treatment. There was no family history of autism, brain tumour or other cancer, no consanguinity, and there are no other sibling in the family.

Conclusion: Intracranial germinoma is rare in the Western world, but 5-8 fold more common in Japan and other East Asian countries. Significant enrichment of germline variants in JMJD1C was recently reported among Japanese intracranial germ cell tumour (IGTC) patients. We feel that concurrent autism and germinoma in the Caucasian brothers we describe are likely due to some to-be-identified genetic factors, instead of a random occurrence. Genetic analysis for both brothers and their parents are in process. We hope the results might shed light in further understanding the biology of this rare disease.

P-0218 | Analysis of Molecular Pathways by Rnaseq Following GDF15 Knockdown in Paediatric and Adult Glioblastoma Cell Lines

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Background/Objectives: Glioblastoma (GBM) is the most common and malignant primary brain tumors. GBM displays high heterogeneity with complex genetic alterations, characterized by resistance to traditional treatments. Among the genetic changes, our group observed a high *GDF15* expression in primary GBM samples and cell-lines. The *GDF15* is a growth factor that in normal physiological conditions is poorly expressed, but in cases of inflammation and malignancies your expression is increased. This study aimed to analyze molecular pathways by RNAseq after *GDF15* knockdown in pediatric (KNS42) and adult (U343) cell-lines of GBM.

Design/Methods: RNA sequencing was performed in sequencer HiSeq 2500 (Illumina). The counting of sequenced transcripts was analyzed after filtering quality of sequential basis, recording the known gene transcripts aligned in the gh19 through DSeq2 program. With the data obtained by RNAseq was conducted the analysis of Fold change (Fc), comparing the gene counts of the silenced cell lines with control cell lines. To determine the genes that have differential expression, it has been considered the Fc±2. For bioinformatics analyses, DAVID was used for GeneOntology enrichment analysis. Ingenuity Pathway Analysis was used to build a biological network based on gene-gene interactions contained in its database.

Results: Some common pathways were altered in both GBM cell-lines, however while most pathways had upregulated genes in the cell line U343, KNS42 had downregulated genes. The main pathways modified in both cell lines were STAT3, PTEN, PI3K/AKT, JAK/Stat and ERK/MAPK. In addition to these molecular pathways, there are others that have been modified specifically for each cell line. In U343, these pathways were Wnt, TGF-β, NFK-B, and others. For KNS42 the pathways altered were p38 MAPK, Notch, HIF1α, and others. Most of these pathways were described as influencing GBM tumorigenesis.

Conclusion: This study showed that *GDF15* knockdown promoted different molecular pathways expression between cell lines of paediatric and adult GBM.

P-0219 | Differential miRNA Expression in Medulloblastomas, Fetal and Non-Fetal Non-Neoplastic Cerebellum. Identification of Potential Prognostic Markers

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Background/Objectives: Medulloblastoma (MB) is the most common CNS malignant solid tumour in children. Several factors contribute to the development and progression of this disease, among them the regulation of gene expression by microRNAs (miRNAs). The aim of the study was to evaluate the profile of differentially expressed miRNAs in MB and non-neoplastic cerebellum samples, correlate their expression levels with patients' clinical features, and identify potential prognostic markers.

Design/Methods: Fifteen miRNAs were selected based on data obtained from a large-scale gene expression analysis using 24 medulloblastoma samples at diagnosis and 2 non-neoplastic human cerebellum controls by the Human miRNA Microarray Kit (V3, 8 × 15K, Agilent). The expression analysis of the microRNA selected was performed by RT-qPCR, analyzing 51 MB samples at diagnosis, 10 non-neoplastic fetal and 7 non-fetal cerebellum samples. The comparison between miRNA expression and clinical and biological features was performed by Mann-Whitney test and event-free survival analysis (EFS) and overall survival (OS) by Kaplan-Meier and log-rank test.

Results: The miRNAs miR-329, -383, -433, -485-3p, -485-5p, -491-5p, -512-3p, -539-5p were downregulated in tumors when compared to fetal and non-fetal cerebellum; miR-31-5p was downregulated and miR-199a-5p was upregulated in tumors when compared to non-fetal cerebellum; miR-202-3p and miR-650 were downregulated in tumors when compared to fetal cerebellum (P<0.05). In addition, miR-211-5p was downregulated and miR-512-3p was

upregulated in patients with a lower EFS and OS ($P < 0.05$). The expression of miR-211-5p was an independent prognostic factor for EFS when analyzed by Cox regression model ($P < 0.05$).

Conclusion: Differential pattern of expression of miRNAs was observed in MB when compared with fetal and non-fetal non-neoplastic cerebellum. The present data suggests also that some miRNAs could be biomarker for this disease. Further studies need to be conducted to investigate the role of these miRNAs in the progression of this tumour.

P-0220 | Revision of the RCPCH Clinical Guidance on Brain Tumour Diagnosis Using Current Evidence and the Next Focus for HeadSmart: Be Brain Tumour Aware Campaign (www.headsmart.org.uk)

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Background/Objectives: HeadSmart: Be Brain tumour aware (www.headsmart.org.uk) launched in 2011 to amplify RCPCH endorsed guidance on brain tumour diagnosis in children. Under "NHS Evidence" requirements five yearly evidence review is required. The aim was to identify new evidence in the literature and analyse HeadSmart data to update the clinical guidance and identify focus for the next phase.

Design/Methods: Medline, Pubmed and Embase databases were systematically searched from 2005-2015. Data on signs/symptoms of all paediatric brain tumours were recorded. Effect size and pooled proportions were calculated. Subgroup analysis by age, location and system was also performed.

Results: 25,104 abstracts were identified. 1003 papers were reviewed in full; 152 met the inclusion criteria, describing the signs/symptoms in 8712 children. The symptom profile remains unchanged from previous review. Increasing head circumference is newly identified as the commonest clinical sign in the under 3 age group. Symptom stratification by systems showed clusters of symptoms in gastroenterology, ophthalmology, endocrinology, psychiatry, neurology, ENT and respiratory systems. HeadSmart cohort data analysis shows children with low grade glioma, optic pathway glioma, craniopharyngiomas have the longest TDI (median of 11.9, 10.4, 15.1 weeks respectively), as do the adolescent age group (median 12.1 weeks compared to 6 weeks in 0-5 and 8 weeks in 5-11 ($p < 0.001$)). Based on this analysis, we have developed a speciality professional awareness poster, highlighting the symptoms that may present to each speciality and the likely location of brain tumour.

Conclusion: Increasing head circumference and unexplained weight change will be incorporated into the new guidance after a consensus process. The system based stratification allows targeted guidance to subspecialists who may not consider a brain tumour diagnosis.

P-0221 | Optic Nerve Glioma- Appropriate Follow up

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Background/Objectives: We reviewed the imaging of all patients with optic nerve glioma in our department over the last 15 years in order to determine the frequency of MR Imaging and surveillance which puts significant burden on our imaging department where MRI access is limited especially under general anaesthesia.

Design/Methods: n/a.

Results: Forty patients ranging between 2 months and 16 years were imaged over the last 15 years. One of the patients had 27 MR Imaging under anaesthesia over a span of 11 years, averaging 2.45 MR Imaging in one year. We tried to identify a subgroup of patients that may justifiably need imaging over time. We found out that the initial imaging characteristics of the tumour and ongoing clinical symptoms may be the main determinants to consider.

Conclusion: Optic nerve glioma is an indolent tumour and may require frequent surveillance over time. We found out that majority of the patients did not need to have surveillance imaging and that the initial imaging characteristic of the tumour and ongoing clinical symptoms may be the two main determinants for further imaging.

P-0222 | Tandem High-dose Chemotherapy with TTC/MEC Regimens in Paediatric Brain Tumour

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Background/Objectives: This study aims to evaluate the outcome of high-dose chemotherapy (HDC) and autologous stem cell transplantation (ASCT) with Topotecan-thiotepa-carboplatin (TTC) and melphalan-etoposide-carboplatin (MEC) regimens in paediatric brain tumour.

Design/Methods: We retrospectively analyzed the data of 33 patients with brain tumour who underwent HDC at Seoul National University Children's Hospital between 2010 and 2014. TTC (topotecan 2mg/m² on days -8, -7, -6, -5 and -4, thiotepa 300mg/m² on days -8, -7, and -6, and carboplatin on days -5, -4, and -3) and MEC (melphalan 140mg/m² on day -7 and 70mg/m² on day -6, etoposide 200mg/m² and carboplatin 350mg/m² on days -8, -7, -6 and -5) regimens were used for the first and second HDC, respectively.

Results: There were 16 medulloblastoma (MBL), 10 primitive neuroectodermal tumors of central nervous system, 4 atypical teratoid/rhabdoid tumors, 2 choroid plexus carcinoma and 1 pineoblastoma. Eleven patients younger than 3 years of age were eligible for HDC to avoid radiotherapy. Eight patients with high risk MBL (presence of metastasis and/or postoperative residual tumour >1.5 cm²), 8 patients with other high risk brain tumour, and 6 patients with recurrent brain tumour were enrolled. Eighteen of the 33 patients underwent single HDC. The event-free survival (EFS) of all patients was 63.4% at a median follow-up with 24.2 months from the first ASCT. The EFS in patients younger than 3 years of age, high risk MBL, other

high risk and relapsed tumour was 72.7%, 70.0%, 77.8%, and 20.0%, respectively. Treatment related mortality occurred in 4 patients. Six patients relapsed after the first ASCT, and 1 patient relapsed after the second ASCT.

Conclusion: This result showed that tandem HDC with TTC/MEC regimens was feasible in paediatric brain tumour. However, survival rates with recurrent brain tumour were low in spite of HDC. Long term follow up was needed to elucidate the late adverse effects.

P-0223 | Renal Function Assessment in Children Treated for Central Nervous System Malignancies

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Background/Objectives: The aim of the study was to evaluate renal function in children previously treated for CNS malignancy, and to assess the usefulness of the following nephrotoxicity markers: cystatin C (CYS C), beta-2-microglobulin (B2MG) and neutrophil gelatinase-associated lipocalin (NGAL) in this patient population.

Design/Methods: We analysed data on 38 children previously treated for CNS tumour. Mean age at evaluation was 14.2 years (range 2.1-22 years). The mean follow-up time after the completion of chemotherapy was 3.2 years (range 0.16-6.5 years). Laboratory studies evaluating glomerular filtration were referred to the results of new markers of nephrotoxicity: cystatin C, B2MG, NGAL. Tubular function was estimated by the calculating the ratio of the renal reabsorption of phosphate (TRP) and renal tubular threshold for phosphate (T_{mp}/GFR).

Results: Subclinical chronic kidney disease (GFR 90-60 ml/min/1.73m²) was found in 22 patients (57.8%), while renal insufficiency (GFR <60 ml/min/1.73m²) was found in 6 children (15.7%). It has been demonstrated statistically significant negative correlation between the eGFR and cystatin C concentration ($p < 0.0001$), and eGFR and beta-2-microglobulin concentration ($p < 0.016$). Conversely, there was no correlation between eGFR and NGAL. Children with chronic kidney disease had significantly higher levels of Cystatin C (1500.21 ng/mL vs 992.64 ng/mL) and B2M (2.06 mg/L vs 1.23 mg/L), as compared to the remaining subjects. NGAL levels were comparable in both subgroups (18.91 ng/mL vs 18.94 ng/mL). 13 children (34%) developed drug-induced tubulopathy. Cystatin C and B2M levels showed a strong positive correlation with TRP and T_{mp}/GFR ($p < 0.001$). There was no such correlation between NGAL and TRP ($p = 0.714$) or NGAL and T_{mp}/GFR ($p = 0.762$).

Conclusion: Children treated for CNS tumours often develop drug-induced chronic renal disease, involving the glomeruli and/or renal tubules. Cystatin C and beta-2-microglobulin can serve as effective markers of late drug-induced nephrotoxicity, which is not true for NGAL.

P-0224 | Adolescents with Low Grade Glioma- Experience from One Center

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Background/Objectives: Adolescent LGG accounts for about 5.5% of all LGG in children.

Design/Methods: Analysis of LGG in adolescents. Among 1183 children with LGG treated between 1998-2014 139 (11.7%) were adolescents. Analysis included: age, sex, tumour location, LGG subtype, treatment, outcome.

Results: Median age was 16.5 years. Most common location was supratentorial 63%. 3 patients had disseminated disease. 62% underwent complete, 15.8% subtotal/partial resections, 20.9% biopsy. One patient had radiological diagnosis only. There were 106 patients with astrocytoma I, 32 patients with astrocytoma II. 121 patients were managed with clinical and radiological follow-up in our center until 18 years of age. After that they were referred to adult's centers and were lost to follow-up. Eighteen patients at some point in time received further treatment in our department. Among them 14 tumors were supratentorial and 1 infratentorial, 3 had disseminated disease. Most patients had pilocytic astrocytoma (66.6%). All patients had primary partial resection or biopsy. Treatment included chemotherapy (10) radiotherapy (1), both methods (7) patients. In 11 patients chemotherapy was administered at the time of diagnosis. The rest of the patients were treated at tumour progression (7pts). Median time to progression was 8 months. Out of 18 patients 17 are alive with median follow-up 9.5 years. Five yr EFS and OS is 60%, 94% respectively.

Conclusion: Adolescents with LGG seem to have favorable outcome. Since their current status is unknown evaluation of their long term prognosis is not possible. Cooperation with adult's care centers is necessary.

P-0225 | Paediatric Atypical Teratoid/Rhabdoid Tumour Treated by Proton Beam Therapy: Initial Experience at the West German Proton Therapy Center Essen

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Background/Objectives: Atypical teratoid/rhabdoid tumour (AT/RT) of infancy and childhood is a unique histologic entity with an extremely aggressive natural history. Following multimodality treatment more than 50% of patients suffer swift disease recurrence and death owing to tumour progression with median survival estimated at 6 months to a year. Proton beam therapy (PT) allows for optimal dose distributions, with the added benefit of no exit dose. Hence, here we report prospective data on early outcomes and acute toxicities in treatment of AT/RT treated at the West German Proton Therapy Center Essen (WPE).

Design/Methods: Fourteen patients (9 male) were treated from November 2013 to November 2015 at WPE. The median age at diagnosis was 1.3 years (range, 0 months to 7.5 years). Single dose of 1.8 Gy were used to deliver 30-33 fractions. Patients received a median radiation dose of 54 Gy. All patients received focal irradiation to the brain with one patient receiving also craniospinal irradiation. All patients had been treated on the basis of EU-RHAB registry's recommendations and were registered on the registry (KiProReg) at the institution. Side-effects were classified according to CTCAE V4.0.

Results: Median FU time was 13.2 months (range, 4.3-25.4 months). Five patients developed disease progression (systemic progression (n=4), local recurrence (n=1)), 3 of them deceased due to systemic progression. Only mild acute skin toxicity was a common finding among the patients during treatment (Grade 1-2). Further mild toxicity observed was fever (n=3). Five patients presented with Grade 3 and 1 patient with Grade 4 haemotoxicity most likely due to concomitant or previous chemotherapy. Thus far, no higher grade early late toxicity was noted in the FU periods, especially no radionecrosis.

Conclusion: PT was feasible and well tolerated in children with AT/RT. Considering the generally poor survival, these early data are promising. Additional follow-up and larger patient cohorts are necessary.

P-0226 | Brain Tumors in Children Diagnosed and Treated at Hospital Infantil Teleton De Oncologia, A Paediatric Oncologic-Devoted Hospital in Mexico: the First Two Year of Experience

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Background/Objectives: Background: Brain tumors constitute the most common paediatric solid tumour and they are the third most frequent diagnosis (9.4%) after leukaemia and lymphoma. Hospital Infantil Teleton de Oncologia (HITO) started its operation in December, 2013, as the first paediatric oncologic hospital in Mexico.

Objective: To know the epidemiology and characteristics of patients admitted to HITO with brain tumour diagnosis.

Design/Methods: Methods: This is a descriptive and observational study. Medical records of children admitted to HITO with the diagnosis of a brain tumour between December, 2013-January, 2016 were reviewed. Variables: Age, gender, histopathologic diagnosis, tumour grade, topography, treatment schema, follow-up status and time of progression-free survival were recorded.

Results: Results: We found 22 cases of brain tumour. Average age at diagnosis was 8 years; 54% corresponded to male gender. About histopathologic diagnosis the most frequent was low-grade gliomas (41%) followed by embryonal tumors (27.3%), high-grade gliomas and ependymoma (13.6% each). Surgery: 66% of patients had a gross-total or near-total resection. Average follow-up time is 11.8 months (rank 1-25 months). Currently 78% of patients are in treatment and follow-up; 5.8% showed progressive disease. Mortality is 22%.

Conclusion: CONCLUSION: The findings and characteristics of children with brain tumors in HITO are similar to the published in international reports. HITO is following the protocols sponsored by COG, unlike other national institutions. Currently, we are doing cytogenetic and molecular analysis of tumour tissue, and cellular-proliferation index, that allow us to get relevant information for treatment.

P-0227 | Awake Craniotomy for Tumour Resection in a Paediatric Patient with a Multidisciplinary Approach. A Case-report from a Paediatric Oncologic Hospital in Mexico

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Background/Objectives: Background: Craniotomy for resection in awoken patient is required for tumors involving eloquent areas in cerebral cortex: sensory-motor, memory and/or language cortex. The goal is perform real-time evaluation, to avoid damage on this areas. This is seldom performed in children, because there is little experience but is difficult to reach. Complications, such as airway obstruction, hypoxemia or seizures can occur. Therefore, a multidisciplinary and well-trained team involving anesthesiologists and psychologists is required for pre-surgical conditioning of the child and management for anxiety and/or fear at surgery.

Objective: To demonstrate the feasibility and importance for accounting with multidisciplinary, well-trained team to perform complex procedures such as craniotomy/resection in awoken child with brain tumour.

Design/Methods: We report a male 11 year-old, with a 14-months clinical course, starting with behavioral abnormalities and a complex-partial seizures. 2 months afterwards, intermittent headache, nausea and vomiting appeared. Ten months later he was taken for medical evaluation. MRI revealed an intrinsic right-parietal tumour behind primary sensory-motor cortex. At surgery, he was awoken for resection, and clinical evaluation for sensory-motor and language functioning was performed.

Results: Results: Gross-total resection was achieved with an awake technique in a successful anesthetic and surgical procedures. Histologic diagnosis was pleomorphic xanthoastrocytoma

(WHO grade II). Six weeks after resection, the child was intact for neuro-psychological performance.

Conclusion: A multidisciplinary, well-trained team that works in a coordinated fashion, is necessary to achieve optimal results in performance of complex procedures required for treatment of children with brain tumors. These teams must have experience in management of potentially harmful situations occurring in these procedures

P-0228 | The Clinicopathological Feature of 92 Cases of Paediatric Embryonal Tumors of the Central Nervous System

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Background/Objectives: Embryonal tumors of the central nervous system (CNS) are a group of small round cell malignant tumors which are highly malignant, invasive and may display divergent degrees of differentiation. For better understanding the characteristics and providing the basis for diagnosis and treatment of paediatric CNS embryonal tumors, we retrospectively evaluated the clinical and pathological characteristics of this group of tumors.

Design/Methods: We retrospectively analyzed 92 patients younger than age 16 years with pathologically confirmed paediatric embryonic tumors in Xinhua Hospital affiliated to Shanghai Jiaotong University School of Medicine between July 2012 and July 2015. All patients were diagnosed according to the 2007 WHO classification of CNS tumour.

Results: Among the 92 cases, 60 were male and 32 were female (male to female ratio were 1.88:1) and 32 (34.78%) of the patients were under 3 years old. For the histological types, 57 (62.00%) cases were medulloblastoma, 20 (21.74%) cases were atypical teratoid/rhabdoid tumour (AT/RT) and 15 (16.30%) cases were primitive neuroectodermal tumour (PNET). For the lesion site, 87 tumors were located in intracranial site and 5 tumors were located in spinal canal. Infratentorial and supratentorial tumors account for 72.83% (67 cases) and 22.22% (20 cases) respectively.

Conclusion: The study showed that medulloblastoma is the most common histological type of paediatric embryonal tumors of CNS with a male preponderance. With the growth of age, the number of AT/RT and PNET were gradually decreased. However, medulloblastoma is more common in patients aged 3 to 5 years old, but the number of medulloblastoma is gradually decreased over the age of 5.

P-0229 | Paediatric Diffuse Intrinsic Pontine Glioma Patients. Experience from a Single Center

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Background/Objectives: Brain stem tumors account for 12.2% of all paediatric brain tumors. Eighty percent are diffuse intrinsic pontine gliomas (DIPG). The objective of this study is to describe epidemiological characteristics of patients with DIPG and compare outcome of different therapeutic approaches.

Design/Methods: Retrospective and descriptive study. We evaluate patients with DIPG treated at Oncology Unit of Hospital de Niños Ricardo Gutierrez from January 1995 to December 2015.

Results: Sixty patients (p) were admitted. Five exophytic tumour were excluded and 10p without appropriate follow up. Forty five patients were assessable. Histological diagnosis in 2p (4.4%) (low grade astrocytoma). Median age at diagnostic: 8.27 years (r 3.1-18.1). Male / Female ratio: 0.8. All patients received radiotherapy (RDT), except for 1p due to critical clinical state. Radiotherapy was given with concomitant chemotherapy (QMT) in 33p (73%): Temozolomide: 12p (36%), Nimotuzumab: 6p (18%), Nimotuzumab with Vinorelbine: 6p (18%), Nimotuzumab after progression with Temozolomide: 9p (27%). Median time of follow up: 12.9 months (r0.8-145m). Forty two patients (93.3%) died, 41p after tumour progression and 1p because of chemotherapy toxicity. Median time of overall survival (OS): 13.16m (r0.8-146.7m) and progression free survival (PFS): 11.8m (r0.8-146.7m). OS of all patients was 6.7% and PFS 4.4%. Outcome of different treatment groups: RDT without QMT: PFS 0%, median time free from progression (MTFP) 5.78 m; RDT + Temozolomide: PFS 0%, MTFP 7.33m; RDT + Nimotuzumab: PFS 0%, MTFP 9.79m; RDT + Nimotuzumab + Vinorelbine: PFS 16.7%, MTFP 8.69m; RDT + Temozolomide + Nimotuzumab: PFS 0%, MTFP 13.9m.

Conclusion: Although these conclusions lack statistical significance because low number of patients, we found better outcome results in the group that received RDT with concomitant QMT. MTFP was longer in patients treated with Nimotuzumab and PFS was better in the group that received combined treatment with Vinorelbine.

P-0230 | Malignant Childhood Central Nervous System Tumors: Retrospective Analysis of 60 Patients

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Background/Objectives: Malignant Central Nervous System (CNS) Tumors, are the most common solid tumors in children, accounting for 25% of all paediatric cancers. Despite recent improvement in survival in malignant CNS tumors of childhood, deaths from CNS tumors are the second leading cause of death under 20 years of age. In order to identify our institutional experience with malignant CNS tumors of childhood, we retrospectively evaluated clinical, radiologic and histopathologic findings and other factors affecting survival.

Design/Methods: The files of patients with malignant CNS tumors diagnosed between December 2012 and 2015 were retrospectively analyzed for symptoms at diagnosis, predisposing

disease existence, tumour localization, surgical procedure, chemotherapy and radiotherapy details and outcome.

Results: There were 60 patients with a median age of 8 years (range 10 month-17 years). The most common symptoms at diagnosis were headache and vomiting. Nineteen tumors were supratentorial, two were spinal, and 39 of them were infratentorial tumors. Histopathologic diagnosis was medulloblastoma in 21, astrocytoma in 19, ependymoma in 6, glioblastoma multiforme in 4, brain stem glioma in 3, primitive neuroectodermal tumour in 2, optic glioma in 2, and glioneuronal tumour in 2 patients. There were 3 Neurofibromatosis type 1 disease and 2 secondary malignancy in our patients. Eight patients died in a follow-up time of 1-36 months.

Conclusion: Appropriate and prompt multidisciplinary approach is the most important factor influencing survival in malignant CNS tumors in children. However, despite optimum management, improvement in survival rates are inferior compared to other solid tumors in children. Other factors should be identified for better understanding of biology of malignant CNS tumors and novel treatment target molecules should be discovered for improving survival in children with malignant CNS tumors.

P-0231 | Chinese Children with Medulloblastoma

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Background/Objectives: To investigate the clinical characteristic correlations of children with medulloblastoma (MB).

Design/Methods: We retrospectively analyzed the correlations amongst MB histopathological subtype, age at diagnosis, gender, primary tumour locations (including the fourth ventricle, the cerebellar vermis, both fourth ventricle and cerebellar vermis involved, both fourth ventricle and the other parts of central nervous system involved, both cerebellar vermis and the other parts of central nervous system involved, only the other parts of central nervous system involved), relapsed tumour and relapsed tumour locations (including brain, spinal cord, both brain and spinal cord, the primary tumour location) in 83 children who were diagnosed MB by histopathology subtypes from February 2012 to April 2015.

Results: Among the eighty-three cases (53 males and 30 females), which included younger than 3 years old 14 patients (nine males and five females) and older than 3 years old 69 patients (44 males and 25 females); 28 relapsed (19 males and nine females) and 55 non-relapsed cases (34 males and 21 females). The median age was 80.2 (13.1-184.7) months at diagnosis. There were 48.2% (40/83) was classic medulloblastoma (CMB) (less than three years old 2 cases), 24.1% (20/83) was desmoplastic/nodular medulloblastoma (DMB) (less than three years old 6 cases), 12.05% (10/83) was large cell/anaplastic medulloblastoma (LC/AMB) (less than three years old 1 cases), 3.6% (3/83) was extensive nodular medulloblastoma (MBEN) (less than three years old 1 cases), and 12.05% (10/83) (less than three years old 3 cases) was mixed subtypes. The relationships between age at diagnosis and histopathological subtypes, gender and primary tumour locations were statistically significance (chi-square test, $P < 0.05$) conducted by SPSS 22.0 statistical software.

Conclusion: The incidence of boys with MB is higher than girls'. There are some relations between age at diagnosis and the histopathological subtype distributions, gender and the primary tumour locations.

CHILDHOOD CANCER INTERNATIONAL (CCI)

P-0232 | Status Analysis of the Genes MYCN, MDM2 and TP53 and Protein Expression of MDM2, P53 and PRB in Patients with Retinoblastoma Underwent Enucleation

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Background/Objectives: The study of the cell cycle and its control mechanisms in retinoblastoma has identified potential therapeutic targets. The relationship between genes *RBI*, *TP53*, *MDM2* and *MYCN* in the initiation and development of retinoblastoma are well established. We propose to study the status of the *MDM2*, *NMYC* and *TP53* genes and the protein expression of MDM2, p53 and pRb in patients with retinoblastoma admitted over a period of seventeen years in the A.C. Camargo Cancer Center Hospital.

Design/Methods: Four hundred and sixty nine patients were admitted from 01/01/1986 to 12/31/2003. Two hundred and twenty-five patients were evaluated. The status of the genes was analyzed by FISH and protein expression by immunohistochemistry.

Results: The MDM2 expression was evaluated in 67.1% and p53 in 64.9%; there was 8% of *MYCN* amplification. There was a significant statistical difference in the probability of 5y-OS with the protein expression of MDM2 in intraocular cases (up to 30% - 5y OS: 98.6%; >30% - 5y OS: 94%; $p = 0.037$) and in the cases without optic nerve infiltration (up to 30% - 5y OS: 100%; >30% - 5y OS: 93.5%; $p = 0.02$). There was a significant statistical difference in the probability of survival after 5 years with the protein expression of p53 in intraocular tumors (up to 20% - 5y OS: 97.5%; greater than 20% - 5y OS: 85.5%; $p = 0.002$), in bilateral tumors (up to 20% - 5y OS: 96.2%; >20% - 5y OS: 75%; $p = 0.006$) and cases without choroidal infiltration (up to 20% - 5y OS: 97.3%; >20% - 5y OS: 81.8%; $p = 0.004$).

Conclusion: The protein expression of MDM2 and p53 have demonstrated differences in 5y-OS subgroups of patients and especially those without optic nerve infiltration (MDM2) and without choroidal infiltration (p53).

P-0233 | Incidence of Childhood Cancer in Costa Rica, 1999 – 2013, in an International Perspective

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Background/Objectives: Higher childhood cancer incidence rates, particularly for leukaemia, are reported from high-income countries versus lower income countries. However, estimating childhood cancer incidence globally is hampered by lack of reliable data from developing countries, including for Latin America. Costa Rica is one of the few developing countries with a longer-term nationwide population-based cancer registry, enabling to study high quality incidence data on childhood cancer.

Design/Methods: Data on incident cancers in children aged under 15 reported to the National Cancer Registry of Costa Rica between 1999 and 2013 were analysed by diagnostic group, age, gender, and geographical region at diagnosis.

Results: For the 15-year period a total of 2,419 children with cancer was reported, resulting in an overall age-standardised incidence rate (ASR) of 140.4/million. The male-to-female ratio was 1.2. The highest age-specific rate was observed in children aged 0-4 years (172.6/million). Most frequent cancer types were leukaemias (39.3%), malignant central nervous system tumours (13.6%) and lymphomas (11.8%). With an ASR of 57.1/million the observed leukaemia rate was among the highest in the world. Low rates in international comparison were observed for some solid tumours including sympathetic nervous system tumours (ASR 4.0/million), renal tumours (ASR 5.7/million) and soft tissue sarcomas (ASR 5.9/million). Most childhood cancer cases were resident in San José, the capital city of Costa Rica (34.4%).

Conclusion: Childhood cancer incidence patterns in Costa Rica were similar to those reported from high-income countries. Further research is recommended to explore which factors may drive the high leukaemia rate as well as the low rates observed for some solid tumours. Our data suggests applying caution when interpreting geographical variation, as this example of a developing country with established paediatric oncology and a well-functioning cancer registry showed little differences to childhood cancer incidence patterns in high-income countries.

P-0234 | Socio-Demographic Features in Patients with Cancer with Diagnosis Delay in the National Paediatrics Institute

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Background/Objectives: Background. A delay in diagnostic of patients with cancer impacts in the prognostic of the disease elevating the economic, social and psychology costs of the patients.

Objective: Describe the social-demographic and clinical characteristics of patients diagnosed with cancer since January 2015 in the Oncology Service of the NPI.

Design/Methods: Methods: A transversal prospective study was made using an opportune diagnostic poll applied on the oncology service to 170 patients.

Results: Results: 49.1% are women, 50.9% are men. 78.8% are from an urban development, whereas 21.3% from a rural. The responsible person of the patient 25% are single mothers, 70% are both parents, 2.5% other person. 60% have low income level, 33.1% a medium level and 6.3% a high level. 49.6% is the first child of the family, 26.9% is the second. 15.6% the third and 6.3% the fourth. 46.3% their house is provided, 35.8% they owned their house, and 16.5% paid rent. 92.9% went to see a doctor of which 90% went to an allopathic medical consultation, and 10% to a traditional. The first physician they visited was a general practitioner in 58.9% of the cases, 41.4% a Pediatrics and 12.5% a specialist. 25.6% went the next day they felt sick, 12.6% until 7 days later and 9.4% until 15 days later. 65.1% received treatment, 37.1% gave antibiotics, 25.9% NSAIDs. 12.4% of the doctors thought they had an infection of the upper air way and 19.6% another type of infection. 22.6% suspected of a malignant pathology. 60.1% where solid tumors and 39.9% hematologic. The median of diagnostic delayed is 139.1 days (1-1567). 23.96 days patients go to the physician after the beginning of the symptoms (0-365).

Conclusion: There is a delay in diagnostic in patients who finally are diagnosed with cancer in NPI. These results may have an influence in health politics.

P-0235 | Systematic Review of Strategies to Avert Treatment Abandonment in Childhood Cancer

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Background/Objectives: Treatment abandonment (TxA) is a significant contributor to treatment failure in global paediatric oncology. Awareness regarding magnitude and determinants of TxA has increased, less is known about how to effectively address it. This study primarily aimed to systematically review strategies to reduce TxA in childhood cancer and, anticipating a publication scarcity, secondarily aimed to review and learn from strategies geared towards reducing the burden of similar phenomena in childhood HIV and tuberculosis globally.

Design/Methods: Studies were identified in PubMed, EMBASE and CAB Abstract and included if they reported on strategies to address TxA in childhood cancer, HIV, or tuberculosis, from Jan-1995 to Sept-2015, and documented a post-implementation outcome. A comprehensive list of search terms was used. Two reviewers extracted and classified the interventions into illustrative domains.

Results: Of 5,665 studies retrieved, 104 met inclusion criteria; cancer (15 citations), tuberculosis (32), and HIV (57). Most (11) documented experience in childhood cancer was very recent (published 2013-2015). Strategies documenting a reduction of TxA in childhood cancer included: counseling (8 citations), subsidized/free medication (7), tracking defaulted patients (6), international collaboration (4) and training of health care workers (4). Decreases in TxA ranging from 8% to 78% (median 23%) and increases in survival ranging from 11 to 60% (median 18%) were reported. Additional strategies, reporting positive effect in HIV or tuberculosis, included: DOTS (24), intake medication reminders (9), locally adapted protocols, (11) and developing a satellite center (7).

Conclusion: Reports of concrete and effective strategies to address TxA in childhood cancer are emerging. However, more studies that validate these strategies while addressing sustainability, scalability, and applicability across regions and cultures are warranted. Effective strategies to increase compliance in childhood tuberculosis and HIV (particularly with oral medications) should also be considered and may prove valuable for improving treatment effectiveness of childhood cancer globally.

P-0236 | Road Blocks to Early Presentation for Children with Cancer in Tanzania – A Report from Upendo Ward

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Background: One third of children who present to Upendo Children's cancer ward have disease too advanced to treat. This study explores the reasons why to identify potential solutions which may improve survival.

Methods: Carers of children admitted to Upendo ward in February 2016 were interviewed in Kiswahili using a formal structured questionnaire. The answers were analysed using a simple excel programme.

Results: 74 interviews were conducted. The informants were mothers (73%), fathers (15%) with others representing 12%. Prior to presenting to Upendo ward between 1 and 9 (median 3) separate health advice efforts were reported per child. From symptom recognition to first health-seeking visit the mean delay was 1.4 months. On average, time from first effort to arriving on Upendo Ward was 5.6 months. Definitive treatment began a mean of 0.2 months from presenting to Upendo ward. Combined delays from first symptoms to definitive treatment totaled an average delay of 7.2 months. 65% of respondents confirmed that their first health-seeking visit was to a hospital. All but two children attended a hospital by their second effort. Cancer was not mentioned to 60% of carers. 40% of families were asked to pay for services costing on average 200Euros. 10% of children were never formally referred to cancer services. For the remainder it took on average 3 contacts before referral.

Discussion: This study highlights the fact that most families of children with cancer identify and act quickly when their child is unwell. Hospitals are accessed early but cancer awareness is low at most of these facilities and referral times are unacceptably delayed. Costs, distance, clinical acumen and national referral systems all contribute to delays.

Conclusion: Early warning sign campaigns targeting clinicians and a national fast track referral system should be introduced to improve early detection and cancer cure rates in Tanzania.

P-0237 | Study of the Effects of Childhood Cancer on Parents and Survivors: A Study on Some Survivors from the University Teaching Hospital, Port Harcourt, Nigeria

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Background/Objectives: The paediatric oncology unit of University of Port Harcourt Teaching Hospital, Port Harcourt receives a lot of children suffering from various types of cancers. Most often than not they present late, out of ignorance or dearth of information on the disease to parents/guardians of these children and wards. This is also a huge hindrance to effective treatment regime even when the prognosis is good. One of the challenges that caregivers face is the abandonment of treatment only for the parents and patients to return at the terminal stage of the disease. Some success have been recorded in parents and patients who followed through in this two-year study without abandoning treatment.

Design/Methods: Studies were carried out under the following areas: Economic Status, Religious beliefs, social stigma, family relationship (nuclear and extended), sibling reactions, awareness & Education, Health Care delivery system / treatment in the hospital, follow up by UPTH and other charity organisations/NGOs. A cohort of 14 patients who were admitted during the commencement of the study at various times in the year (2014) were recorded and a follow up chart was kept for each patient. Periodic checks were also carried out on each child while at home at the end of each chemotherapy/radiotherapy sessions.

Results: Before the end of the two-year study, five patients out of the fourteen died while receiving chemotherapy, four abandoned treatment when they saw signs of improvement in their condition only to return several months after the cancer had metastasized. Three patients followed through with their treatment and have gone into remission. Two patients had ALL and one patient had retinoblastoma.

Conclusion: It was discovered that involving the patients improved their positive disposition to treatment. Late presentation and denial of the sickness led to the poor survival of most the patients.

P-0238 | The Global Acute Leukaemia Network: Providing New Insight into Childhood Acute Lymphoblastic Leukaemia

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Background/Objectives: In high income countries acute lymphoblastic leukaemia (ALL) is the most commonly diagnosed cancer in children under the age of 15, with 5-year survival generally exceeding 85%. Although incidence rates are suggested to be lower in economically developing countries, there is a paucity of reliable data relating to global variations in incidence/survival. Capturing such data is challenging since cancer registries only cover 20% of the world's population, and a high proportion of cases in developing countries are thought to never reach a clinical facility. With a view to providing insight we established the Global Acute Leukaemia Network (GALnet), a platform to further understanding of ALL, and a framework to support disease burden in resources limited countries.

Design/Methods: GALnet is housed within the International Agency for Research in Cancer, bringing together clinicians, biologists and epidemiologists from all over the world, in particular those from low and middle income countries, and linking directly to hospitals and clinical facilities.

Results: GALnet currently comprises 19 countries, including 11 developing countries, selected to provide global representation, with the option to include new centres as projects evolve. Significant variations in demographics of children in GALnet centres have been observed, particularly, in relation to the proportion of boys, and age at diagnosis. With respect to the later whilst some centres reported a paucity of cases under 1 year of age, others found that 10% of all diagnoses occur in this age group (average being 4%). In addition, the proportion of leukaemia cases that are ALL ranged from 50% to 90%, averaging approximately 70% across all centres.

Conclusion: GALnet provides diverse global coverage with respect to economic development (low-, middle-, and high-income countries) and ethnicity and is an ideal platform for future investigations of childhood leukaemia. Moreover, it provides the infrastructure to extend investigations to other childhood cancers.

P-0239 | Improving Childhood Cancer Care in South Africa through Advocacy and Alliances

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Background/Objectives: Many of the challenges the cancer communities face are complex, or at such a scale, that individual organizations cannot tackle them alone. By bringing together different competencies and resources many issues can be resolved quicker. Collaboration through networks and alliances is essential to achieve success. The real impact can only be achieved if there is a collaborative mindset and an understanding of how different sectors think and operate.

Design/Methods: An assessment was made of the current position of childhood cancer in South Africa and CHOC partnered with several alliances, networks and the National Department of Health. Stakeholder meetings were attended, ensuring that childhood cancer issues are addressed and form part of the national strategy and policy environment.

Results: By serving on several alliances and networks deficiencies in the system and potential solutions, are identified ensuring that childhood cancer has a voice in SA. Through collaboration with the South African Childhood Cancer Study Group CHOC has an influence on the availability and accessibility of childhood cancer data in SA. Partnerships documents with mind-linked organizations have been signed to protect and grow the partnerships and collaboration. CHOC became the leader of childhood cancer in SA and a recognized voice amongst Government and Civil Society.

Conclusion: While it is essential to remain part of ongoing collaboration, challenges needs to be addressed so that partnerships do not under-perform or fail. Joint multi-sector efforts can make a difference to create permanent change in childhood cancer.

P-0240 | Ugam-Childhood Cancer Survivors Support Group of Indian Cancer Society-An Ambassador for Relay for Life Movement in India

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Background/Objectives: "Relay for life" (RFL) is a signature volunteer driven event of the American Cancer Society (ACS) which is now being conducted across globe in 26 countries including India. It brings together community to **Celebrate** (strength of survivors), **Remember** (loved ones lost to disease), **Fight back** (scourge of cancer).

To train and empower Ugam-Childhood Cancer Survivor Support Group functioning under aegis of Indian Cancer Society (ICS) as ambassador for RFL movement.

To emphasize role of young cancer survivors in promotion of cancer awareness through RFL.

Design/Methods: An expatriate student of Ecole Mondiale World School, who had participated in RFL in U.S.A, initiated first RFL in India as a project assignment in 2012.

He invited Ugam members to participate in the event and to start the relay with the Survivors lap. Survivors shared their experiences and life stories in the event. This event initiated dialogue between ACS & ICS for collaboration and culminated in licensing of ICS as nodal agency for RFL in India in 2014.

Results: Seven RFL events have been conducted by ICS from Jan 2014 – March 2016 in collaboration with Ecole Mondiale world School, Oberoi international School & Rural Social organization. Ugam members have been trained by ACS Global RFL team to work as volunteers for RFL. Ugam members have participated in all RFL as ambassador & strength of survivors in India.

Conclusion: RFL moment in India since 2012 spearheaded by ICS & Ugam has contributed constructively in bringing cancer awareness & increased participation from various organizations. The funds raised by RFL are channelized by ICS in helping Patients taking treatment for Cancer and for improving quality of life of Survivors of Cancer.

P-0241 | Dublin Multi-Disciplinary Long Term Follow Up Care for Survivors of Childhood & Adolescent Cancer - Bridging the Gap

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Background/Objectives: Children's cancer care in Ireland includes comprehensive counselling and medical support. This is replaced with a more limited care regime when survivors reach age 18. But chemo/radio therapies acting on immature tissues do have long-term effects. Some survivors experience medical, cognitive and psychological problems, all need life-long monitoring. Ireland as yet lacks a system for Long-Term Follow-Up Care (LTFUC) for survivors.

Our voluntary organisation, a registered charity, was founded in 2014 by two parents of survivors in co-operation with a cancer researcher.

Objectives: Recognize survivors as a group; Promote coordinated LTFUC; Gain recognition of the medical & psycho-social challenges resulting from the childhood cancer experience & treatments - and to establish provision of services to address survivors needs.

Design/Methods: Actions: Host a series of survivor meetings nationwide; Link with Drop-in/Care Centres; Create newsletter, website, Facebook page to communicate news and relevant national/international events; Participate in research on appropriate care models.

Survivor Meetings: One of our organisations most important activities is interactive meetings with survivors to discuss their issues at first hand; 'Should I tell my boss?'; 'my medical appointments are scattered over times and places', 'I need a medical card'. Volunteers to carry out the work of CC4L will be recruited at CC4L meetings

Membership is open to all, especially survivors and parents.

Results: Based on our discussions, we support the appointment of a Clinical Nurse-Specialist/Advance Nurse Practitioner to coordinate LTFUC for survivors of childhood and adolescent cancers. We have established an Advisory Panel of survivors plus medical/nursing and health service professionals to help us achieve these aims - our inaugural meeting will take place in Dublin in April 2016.

Conclusion: We are a new organization. We are encouraged by the support of medical professionals and especially of survivors and their families whose experiences we share. As one of our advisors said: 'Start small, but start!'

P-0242 | The Impact of Therapeutic Recreation Programming on A Child with Serious Illness

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Background/Objectives: Barretstown in Co Kildare, Ireland has been developing and delivering a suite of therapeutic recreation programmes to children and families from Europe affected by serious illness since 1994. The aim of this presentation is to describe the model of therapeutic recreation we use at Barretstown, how we implement it into residential camp programming and also to share some of the feedback we have received over the years.

Design/Methods: The paper uses practitioner reflection and literature review to consider the nature, content and potential impact of the model of therapeutic recreation used in Barretstown.

Results: Barretstown's unique model of therapeutic recreation is taken from elements of a number of disciplines including; occupational therapy, psychology, recreational therapy, adventure based counselling and education. At its simplest therapeutic recreation is all about giving control back to campers. Barretstown offers a child centred programme designed to meet the individual needs of each child/family member. The goal is to ensure that individuals gain, or regain, skills and an understanding of their own abilities that can enable them to make informed choices in other aspects of their lives. The loss of control that many children and their families experience as a result of a serious illness can gradually erode confidence, diminish self-esteem, body image and coping skills.

Conclusion: By using therapeutic recreation we have the ability to empower and encourage each individual to step out of their comfort zone and begin to re-build their confidence, trust and self-esteem and discover something new about themselves and their ability. Through careful guidance and encouragement from staff and each other, they learn to challenge themselves, to try something new in a safe, fun and supportive environment. These challenges are met with success as Therapeutic Recreation is experiential learning through fun.

P-0243 | Lund Vietnam Childhood Cancer Program (LVCCP) 2008-2016

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Background/Objectives: In 2007 paediatricians from Lund, Sweden visited the National Hospital for Pediatrics in Hanoi (NHP) to discuss the initiation of support of treatment for childhood cancer in Vietnam. The visit led to the formation of LVCCP, a National Program for treatment of Childhood Cancer in Vietnam.

In 2008 Pediatric oncology at NHP had six paediatric oncologists, 15 nurses and a ward with 40 beds. The paediatric oncologists had trained in USA, Russia, Australia or France. The oncology ward had 350 new patients per year, mainly with leukaemia or solid tumors. Children with CNS tumors were not treated there.

Design/Methods: The activities of LVCCP have focused on leukaemia and malignant solid tumors, especially surgery, radiology and pathology. The work eventually included nine major hospitals in Vietnam: three in Hanoi, four in Ho Chi Minh City, one in Hue and one in Da Nang.

Weekly Tumour Board meetings and informal on-call systems, for bone marrow aspirations and biopsies, have been established in NHP and are essential for the work. Young doctors, trained through LVCCP for 6 months in full-time courses in paediatric oncology, now work with childhood cancer in provincial hospitals.

Results: A first Vietnamese National meeting on Pediatric Oncology was held in Hanoi in 2008, and the 8th meeting in November 2015. These meetings, with 70-100 participants, have become natural meeting grounds for paediatric oncology doctors and nurses from all of Vietnam.

LVCCP has funded Vietnamese doctors' participation in national and international conferences, as well as national training courses. The Vietnamese Society of Pediatric Haematology and Oncology was established in 2010.

Conclusion: The success of this program was accomplished through the dedicated work of Vietnamese medical staff and their cooperation with professionals from LVCCP. It would not have been possible without the generous grant of 4.5 million Euros from IKEA Foundation.

P-0244 | The SIOP Africa/PODC Collaborative Wilms Tumour Project: Principles and Methods with A Focus on Data Collection and Follow Up

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Background/Objectives: The Collaborative Wilms Tumour Africa Project is implementing a SIOP PODC adapted treatment guideline as a prospective clinical trial in eight centres in sub-Saharan Africa. These are in Malawi, Cameroon, Ghana, Zimbabwe and Ethiopia. All centres obtained local IRB approval. The project is funded by World Child Cancer and SIOP. Challenges at each centre include priority setting, data collection and long term follow up.

Design/Methods: Local clinicians assess the feasibility of interventions, giving priority to those with the maximum expected impact on the long term outcome. A case record form (CRF) with a limited amount of data was developed with participating clinicians during a three-day workshop. We only collect data which are essential to answer the predefined clinical questions. Local patient registration is recorded in writing on the CRF. CRFs are sent to a central database, and entered into SPSS. At each centre a specific person is responsible for completing the CRF. On admission detailed patient contact details are documented, including landmarks nearby the patients' home, local schools, a map and mobile phone number(s) to facilitate follow up. Funding is available to pay for transport to the hospital and for active follow up when needed.

Results: Patient enrolment started in 2014. We have enrolled 128 patients. Data capture is over 90% complete for almost all data fields. Currently only three patients are lost to long term follow up. The short term outcome has improved significantly in comparison with our baseline data, and 66% of patients were alive after completing treatment.

Conclusion: Pragmatic and feasible solutions combined with dedication, long term funding and a good team spirit have overcome many local treatment challenges in the participating centres in sub-Saharan Africa.

P-0245 | Potential for Improving the Quality of Care of Children with Central Nervous System Tumors (CNS) in Low- to Middle Income Countries (LMIC) in Central/South America

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Background/Objectives: Improving cure and quality of survival among children with CNS tumors in LMIC is one of the most difficult challenges in global oncology. Pediatric neuro-oncology requires a multidisciplinary approach not often available in LMIC.

Design/Methods: Partnerships have been developed between Nationwide Children's Hospital (NCH) and the Ohio State University (OSU), St. Jude Children's Research Hospital, Toronto SickKidsHospital and several colleagues at institutions throughout Central and South America, including Argentina, Brazil, Colombia, Costa Rica, Dominican Republic, Guatemala, Haiti, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, and Uruguay. These collaborations have included (a) establishment of weekly real-time neuro-oncology tumour boards (through St. Jude's Cure4Kids.org) at which patient clinical, neuropathological and neuroradiological materials are reviewed, and treatment plans discussed and formulated, (b) development of formal "twinning" programs between institutions in Sao Paulo, Brazil, and Bogota, Colombia, (c) joint conduct of paediatric neuro-oncology conferences, the first of which was held in Sao Paulo, Brazil in 2015, (d) initiation of training programs for junior faculty from Central/South America at NCH, (e) development of standardized treatment protocols in Spanish for major paediatric brain tumour types, and (f) active participation in the neuro-oncology meeting at AHOPCA 2016.

Results: Since initiation of this program in late 2014 at NCH, 51 teleconferences have been held including 72 colleagues from 14 Central/South American countries, ultimately reviewing 87 patients. Two visiting faculty from Central/South America have undertaken observerships in paediatric neuro-oncology of up to 3 months duration at NCH (from Brazil and Colombia) and

3 are planned over the next year. Additional “twinning” relationships are under development between NCH/OSU with other institutions in Colombia and El Salvador.

Conclusion: An imperative is the development of assessment criteria that will determine the impact of the above relationships upon the survival and quality of survival of children with primary CNS tumors in Central and South America.

P-0246 | **CanCare4Living: Filling the Gap for Survivors in Ireland**

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Introduction

Children's cancer care in Ireland includes comprehensive counselling and medical support. This is replaced with a more limited care regime when survivors reach age 18. But chemo and radio therapies acting on immature tissues do have long-term effects. Some survivors experience medical, cognitive and psychological problems, all need life-long monitoring. Ireland as yet lacks a system for Long-Term Follow-Up Care (LTFUC) for survivors.

CanCare4Living (CC4L) was founded in 2014 by two parents of survivors – Patricia McColgan and Garry Owens, with a cancer researcher – Dr Julianne Byrne. CC4L registered as a charity in 2016.

An important CC4L activity is interactive meetings with survivors to discuss their issues at first hand: ‘Should I tell my boss?’; ‘my medical appointments are scattered over times and places’, ‘I need a medical card’. The sessions will extend beyond Dublin as resources permit.

Aims and Objectives of CC4L currently: Recognize survivors as a group; Promote coordinated LTFUC; Participate in research on appropriate care models; Promote LTFUC recognition of psycho-social problems related to childhood cancer, including poor self-esteem, low energy/achievement, difficulties with educators, employers and state bodies.

Aims & Objectives, near term: Support the appointment of a Clinical Nurse-Specialist to coordinate LTFUC; Extend survivor meetings beyond Dublin; Link with Drop-in/Care Centers; Create a newsletter, website, Facebook page to communicate news and relevant national and international events.

Membership is open to all, especially survivors and parents. Volunteers to carry out the work of CC4L will be recruited at CC4L meetings. An **Advisory Panel** of medical/nursing and health service professionals has been set up with the first meeting in April 2016.

Conclusion: CC4L is a new organization. We are encouraged by the support of medical professionals and especially of survivors and their families whose experiences we share. CC4L echoes the advice of an advisor: ‘Start small, but start!’

P-0247 | **The Miracle of Inner Strength**

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Background/Objectives: Medication for children with cancer needs a longer time than any other kind sickness. They very easily get bored, frustrated, anger, sensitive, disappointed, and many others. Therefore they need to be supported and given the right caring. And I, as a survivor cancer of Leukimia ALL, want to share my experiences and motivate them to become a stronger person. My name is Frida Prameswarini, I am now 20 years old. I was 5 months old when I got my Leukimia. Although I did not feel the pain as other children cancer patients during medical treatment, I got the effect when I was at primary school. I often got sick and was absent from school. Lots of children at school looked down on me as a weak person. They treat me differently. My parents is a member of YOAI, the Indonesian Childhood Cancer Foundation has so many knowledge on how to overcome children with cancer. So later I join the Cancer Buster Community (CBC), a community under the Indonesian Childhood Cancer Foundation's umbrella.

Design/Methods: Through the “Recovery Programs” of the Indonesian Childhood Cancer Foundation (YOAI), a program which is designed specifically for CBC such as upgrading, creativity, collaboration, problem solving, communications, management, and late effect of medication. This program is supported by the doctors, psychologists, nutritionists, and motivator trainers. We got these experiences through survivor cancer camp. My strength is at the late effect of medication.

Results: I was able to give and share with patients of children with cancer to have a strong self confidence and motivate themselves of how to overcome their problems.

Conclusion: It proves that the miracle of inner strength help children with cancer become a stronger person. They are able to show their capabilities such as creative, outgoing, flexible, and have lots of ideas.

P-0248 | **Letters to the World: A Heartfelt Message from Children Battling Cancer**

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Background/Objectives: Cancer can strike anyone, anywhere and anytime. Unfortunately, children are no exception. At such a young age, they are tossed into a world filled with unceasing hospital trips and countless cycles of chemotherapy. Yet, they remain as cheerful and happy. Moved by what she witnessed at *Rumah Anyo*, a temporary home for children with cancer, Helena Arnetta Puteri, a 16 year old, was inspired to write a book entitled, “Letters to the World”.

Design/Methods: The title, “Letters to the World”, signifies the message we are able to attain from these children. It was their joy and spirit in fighting cancer that further empowered Helena to pour their stories into a book. Realizing the situation of childhood cancer in Indonesia, this book aims to raise the awareness of childhood cancer by featuring numerous facts and

symptoms as well. For the past few months, Helena has visited *Rumah Anyo* and spent a lot of time with them, whilst writing this biographical book, which she wrote, photographed and designed herself.

Results: The funds obtained from the sales of this book, a total of Rp. 40.000.000, has been donated to the Indonesian Anyo Foundation for their movement entitled “1000 Ophthalmoscope Movement”, which aims to distribute ophthalmoscopes to 1000 community health centers throughout Indonesia. With a strong belief that the children, too, should feel an impact of Helena's project, the funds were also used to grant their wishes and bring them joy.

Conclusion: Writing this book has been a life-changing journey and the experience of a lifetime. It has inspired Helena to pursue a career as a paediatric oncologist hoping to inspire others and most importantly, to take part and bring a change in lives of these children. Helena truly hopes that “Letters to the World” could make a difference, just as this book has changed her life.

P-0249 | **Germ Cell Tumors of Children and Adolescents**

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Background/Objectives: The germ cell tumors represent a variety of tumours very heterogeneous on histologic, clinical and epidemiological, represent only 3% of childhood cancers. They have two peak frequency one in childhood and the other in the peripubertal period, with a predominance of nonseminomatous tumors. Through this work we studied characteristics epidemiological, clinical and therapeutic of germ cell tumors of childhood and adolescence.

Design/Methods: The present study is a retrospective study of the epidemiological profile of the germ cell tumors in children and adolescents at the level of Department of Medical Oncology Centre Pierre and Marie Curie, on a sample of 33 cases over the period of 2008 a2015. Among the cases studied 42% were male and 57% female. At the level of the sample there was 2 frequency peaks one to 3 years and the other at 11 ans. la location ovarian predominant was that the testicular location; the histological type most common is teratomas then vetelline tumors. Almost all children have undergone a resection surgery complete then adjuvant chemotherapy.

The reason for consultation depends on the location: abdominal pain, big stock exchange, HIC syndrome, retention or constipation, the alphaFP is high in 36% of cases, metastases were found in 02 cases only.

Results: Remission rates have been obtained in 81%, progressions after treatment well leads in 4 cases, a case of insuffisance renal and one case of deafness which forced us to stop turntables salts. There were 6 deaths.

Conclusion: the germ cell tumours are chemosensitive including Platinum salts. The surgery is important and must be both wound and conservative, their prognosis is excellent despite rare cases of recurrence after chemotherapy and refractory forms treatment where the prognosis is pejorative.

P-0250 | **The Nasopharyngeal Cancer in Children: Epidemiologic Aspect and Scalable**

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Background/Objectives: Malignant neoplasm of nasopharynx are mainly represented by the nasopharyngeal carcinoma (NPC) which is a tumour of epithelial origin. The most common historical-clinical entity is undifferentiated type nasopharyngeal carcinoma, the most common Carcinoma of the child who has a particular geographical distribution: Algeria - MAGHREB, the relationship EBV-nasopharyngeal carcinoma is highlighted.

Through this work we studied the epidemiological, clinical and therapeutic characteristics.

Design/Methods: This work consists of a retrospective study of the epidemiological profile of the nasopharyngeal carcinoma in childhood at the level of Department of Medical Oncology Centre Pierre and Marie Curie, on a sample of 43 cases a period of 2009 a2015.

Among the studied cases of nasopharyngeal cancer, 65% were male and 32% of female. We were 9 deaths due to such cancer among which 11.6% were boys and 9.3% of the girls. At the level of the sample, the average age of children with nasopharyngeal carcinoma was 12 ± 3 years. Almost all children have received neoadjuvant chemotherapy and radio-concomitant chemotherapy, the frequency of locally advanced stages was 25.58% for girls and 37.2% for boys.

Results: Rates of remission have been obtained; 23% among girls and 55.8% among boys, progressions well led post-treatment: 11.6% among girls and 13.95% among boys. There were deaths: 9.3% girls and 11.6% boys.

Conclusion: The nasopharyngeal carcinoma is frequent in Algeria, it is Lymphophilic and has a high metastatic potential.

It characterized by its Radiocurable and its chemosensitivity, but the diagnostic delay exposes local and systemic dissemination.

P-0251 | **Factors Associated with Abandonment of Care among Paediatric Oncology Patients in Tanzania**

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Background/Objectives: The majority of new paediatric cancer diagnoses are made in resource poor countries where survival rates range from 5-25%, compared with 80% in high-resource countries. At Bugando Medical Centre (BMC), one of the two cancer treatment centers

in Tanzania, the overall survival among paediatric cancer patients is 20%. However, over 40% of patients abandon treatment, significantly impacting outcomes.

The current study evaluated the factors contributing to abandonment of care, with the objective to guide future interventions to improve paediatric oncology outcomes in the region.

Design/Methods: Study design is a retrospective review of recorded hospital admissions and clinic visits to the oncology ward at BMC from January 2010–December 2014. 185 files were available for review. Abandonment of care was defined as not presenting for scheduled treatment for more than four weeks from the scheduled date.

Results: In total, 60% of the patients were male (n=111), and the average age was 7 years old. The most common recorded diagnoses were Burkitt lymphoma (n=31), followed by Wilms tumour (n=25), retinoblastoma (n=24), non-Hodgkin lymphoma (n=24) and acute lymphoblastic leukaemia (n=23). Most patients (92%, n=171) received at least one chemotherapy treatment. However, 41.6% of patients abandoned care (n=77). Factors significantly correlated with abandonment included travel distance greater than 60 km to the treatment center ($X^2=4.2$; $p=0.04$), and age < 5 years ($X^2=5.18$; $p=0.02$). Patients receiving weekly or biweekly chemotherapy were less likely to abandon care when compared to monthly treatment ($X^2=3.82$; $p=0.05$). Patients with retinoblastoma had the highest abandonment rate (65%) and Hodgkin lymphoma the lowest (16.7%).

Conclusion: Reasons for abandonment of cancer care are multifactorial. We demonstrate that prolonged distance to treatment center, frequency of therapy, and younger patient age correlate with increased treatment abandonment. Future interventions to reduce treatment abandonment will target methods to reduce the travel burden of our patients and their families.

P-0252 | Choc Remembrance Services – A Platform to Reconnect

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Background/Objectives: A significant support system to help families cope with the trauma of the diagnosis and treatment of cancer or a life threatening blood disorder in their child is the bond they form with the multi-disciplinary treatment team (medical-, nursing-, psychosocial staff and volunteers). Families whose children have died, shared with the author, a palliative care and bereavement support volunteer at the then Johannesburg Hospital, how much they missed this support after the death of their child.

Design/Methods: Twenty two years ago, after discussions with bereaved families and the treatment team the author identified the need for a platform where bereaved families and members of the treatment team could once again interact. The author together with two bereaved parents formed a committee and the first Remembrance Service was held during November 1993. The service took the form of a short interdenominational message of support and the opportunity to light a candle and release a balloon with a special message in memory of the children.

Results: Bereaved families were grateful for the opportunity to celebrate the lives of their children with members of the treatment team and together shared both happy and sad memories. The service grew and bereaved families now look forward to November of each year. In 2010 CHOC Childhood Cancer Foundation adopted the Remembrance Service as a support programme to be held during the last weekend of November each year.

Conclusion: To lose a child is one of the most difficult times in the lives of a family. In most cases a family never gets over the death, however, learns to adjust and find new meaning in life. The CHOC Remembrance Service is there as a support for families as they journey on this "Road Less Travelled".

P-0253 | The Absence of Vincristine Neuropathy in Kenyan Children with Cancer: the Good, the Bad, and the (Possibly) Ugly

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Background/Objectives: Vincristine is utilized as part of therapy in over half of all paediatric malignancies and is associated highly variable dose-dependent peripheral neuropathy (VIPN). Despite its broad use, little is known regarding vincristine disposition and optimal dosing in relation to genetic factors including ethnicity. Thus, current dosing strategies for vincristine are largely empiric.

Design/Methods: This prospective cohort study was conducted in Kenyan children with cancer (n=78) who received vincristine as part of their anticancer treatment. Saliva Oragene kits for DNA extraction and genotyping for variants in the vinca alkaloid pharmacologic pathway was carried out. Vincristine exposure was determined by collecting whole blood via finger stick on dried blood spot cards for analysis of vincristine area under the concentration-time curve (AUC) via HPLC-MS/MS. VIPN was assessed prospectively using five different neuropathy assessment tools.

Results: Seventy-one of the 78 subjects (91%) were CYP3A5 high-expressor genotype. CYP3A5 low-expressor genotype subjects had a significantly higher vincristine AUC than CYP3A5 high-expressor genotype subjects (0.51 ± 0.84 hr/L vs. 0.21 ± 0.12 hr/L, $p=0.006$). All subjects experienced minimal detectable VIPN regardless of which neuropathy assessment tool was utilized. Disease-free survival (DFS) at 1 year was higher in CYP3A5-high-expressor genotype group compared to the low-expressor group (42% vs. 14%, $p=0.001$). There was no statistically significant difference in DFS beyond 1 year.

Conclusion: Kenyan children are more likely to be CYP3A5 high-expressors and as such may metabolize vincristine more efficiently. The significantly lower vincristine AUC of Kenyan children who are CYP3A5 high-expressor genotype as well as the relative absence of neuropathy indicates that Kenyan children are likely being significantly under dosed with vincristine.

Kenyan children could both tolerate and potentially benefit from vincristine dose escalation to achieve more optimal vincristine exposure.

EPIDEMIOLOGY

P-0254 | Socio-Demographics, Culture and Family History of Patients with Retinoblastoma in Ghana

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Background/Objectives: Despite the increasing burden of paediatric cancer in developing countries, there is little understanding of the problem, trend and characteristics of affected populations; due to limited information. Analysis of Paediatric Oncology Networked Database (POND) data from January 2010 to December 2015; revealed leukaemia (14.80%) is the most important childhood cancer in Ghana, followed by retinoblastoma (14.20%) and Burkitts Lymphoma (14.20%). This study examines the effects of socio-demographics, culture and family history on health seeking behaviour of families caring for children with retinoblastoma.

Design/Methods: Trend analysis was conducted using data in POND at Korle Bu Teaching Hospital, Accra. Multi-stage sampling method was adopted. First, all database entries (708) were organized according to cancer types. Further, retinoblastoma cases (118) were grouped according to management outcomes. Seventy five (75) parents/caretakers who had their wards alive were shortlisted for interview between January and March 2016. STATA (version 12) was used for the analysis; and descriptive statistics employed to present the results.

Results: Response rate for the study was 69%; involving mothers (58%), fathers (27%) and others (15%). Data was collected on 52 children (46% males, 54% females). Local remedies were commonly used; and 27% of respondents had used "breastmilk drops" on the eyes before. For 73% of the children, symptoms were noticed before age two. Majority (65%) presented at two or three hospitals before referral; but among 43% waiting-time ranged from 1 month to 1 year, before seeking specialist care. Some families (25%) sought help at prayer camps; while 18% tried herbs. Other family members, including siblings (19%), parents (34%) and grandparents (23%), had reported eye problems before.

Conclusion: Culture and religion influenced health seeking behaviour of respondents. Though 73% of the respondents identified symptoms of retinoblastoma before age two; trust in local remedies and spiritual help contributed to delays in seeking specialist care, even after referral.

P-0255 | The Role of Public Education in Contributing to Childhood Cancer Case Presentations in Ghana

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Background/Objectives: More than 85% of paediatric cancers occur in developing countries where treatment outcomes are poor due to limited government funding and low public awareness. In Ghana, 1,000 children are estimated to develop cancer annually; but 25% presented at the two major treatment centres between 2010 to 2014. Up to 40% of families abandoned treatment due to cost. This paper examines strategies adopted by an International Twinning Programme facilitated by World Child Cancer to promote public and professional awareness about childhood cancers in Ghana; and its contributory effects on number of cases presented for specialist care in 2015.

Design/Methods: With funding from the UK Government, the project invests in training health staff through workshops, online training, internships and treatment support. Public engagement activities include sustainability planning with stakeholders, awareness campaigns and support groups mobilisation and training. Activities implemented in 2015 include seminars at schools, volunteers training, public education at churches and mosques; health reporters training; and collaboration with local Civil Society Organisations (CSO), musicians and film actors. Materials used for public education include stickers, roll up banners, calendars, posters, handbills and multimedia canals.

Results: The type of activities and participation in public engagement activities intensified in 2015 compared to previous years. The health reporters training laid strong foundation for media campaigns involving radio, print newspapers, television networks, online news channels and social media. Involving personalities from the entertainment industry and government functionaries contributed to sustaining the campaigns. The number of children presenting with cancer for specialist care increased to 31% by December 2015; with treatment abandonment reduced from 40% to 11.30%.

Conclusion: Expanding the stakeholder base and training health reporters contributed greatly to improving professional and public awareness about childhood cancers in Ghana. CSO involvement in sustainability planning holds potential to protecting the gains made in improving public awareness about childhood cancer in Ghana.

P-0256 | Economic and Social Impact of Long Stay at a Hospital Based Hostel During Treatment in Accra, Ghana

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Background/Objectives: Hospital based treatment is very important for every patient, particularly children with cancer. However, due to limited number of beds, patients are discharged early. In this light, a "Hostel" was established to accommodate patients who require long periods of care and emergency, hopefully to reduce treatment abandonment. Residence in the hostel is free of cost for paediatric oncology patients and their families. The objective of this study is to examine the economic and social impact of long stay in the hostel.

Design/Methods: The study was undertaken from January to March 2016 at Korle Bu Teaching Hospital in Ghana. The data were obtained from relatives of patients who patronized the hostel with the aid of questionnaire. Out of the twenty (20) respondents, 75% were females and 25% males. Descriptive statistics made up of frequency tables and pie charts were employed to show the result. Statistical Package for Social Sciences was used to analyze the data.

Results: Eighty percent (16 out of 20) of the study participants who stayed in the hostel for seven months or more were persons caring for children with cancer. Majority of the mothers (50%) complained that nobody took care of their business, with 35% saying their businesses were mismanaged but only 15% said their absence had no effect on their jobs. The study also revealed most patrons (90%) depended on themselves, families and National Health Insurance Scheme as their sources of support for cost of feeding and medication.

Conclusion: Despite the high cost of transportation, most participants think that they should bear their own transport cost with the help of their families, whilst a few respondents think NGOs should support. Eighty five percent of the respondents recommended that Non Governmental Organizations (NGOs) and the hospital should continue to support their feeding and medication.

P-0257 | Need of Capacity Building in Paediatric Haematology/Oncology in Low Income Countries: Challenges Faced by the Children's Hospital Lahore Pakistan

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Background/Objectives: The Children's Hospital Lahore is the Principal Treatment Center in public sector in Punjab Pakistan with total 3300 admissions (1000+2300) in the Haematology/Oncology Department in 2015 with 750 new childhood cancer and 300 blood disorders patients. The aim of this study was to analyze mortality cases to outline challenges faced due to this overload with limited intensive care facilities.

Design/Methods: Retrospective review of 200 patients expired in the haematology /oncology department between January 2015 – December 2015 was done. Data regarding their age, sex, initial and final diagnosis, course of therapy, duration of hospital stay and cause of death analyzed.

Results: Total 200 patients with age ranging from < 1 to 15 years (47% <5 yrs) were included. M: F Ratio was 1.6:1. 69/200 (34%) patients presented with acute Leukaemia with 36/69 (52%) mortality due to infection and rest due to progression of disease and 80/200(40%) with solid tumors with deaths due to infection 40% and remaining due to progressive disease and 51/200 (26%) had benign hematological disorders with 47% deaths due to sepsis (p-value=0.062).26/200(13%) mortalities were due to relapses put on palliative treatment and 86/200(43%) were not diagnosed on admission and 25% had even no final diagnosis and 114/200(57%) cases did not receive any definitive treatment before death (p-value=0.000) 28/200(14%) had stay <24 hours and 78% stayed less than a month.134/200 (67%) traveled >100 Kilometers from their home to hospital.

Conclusion: Mortality 94/200(46%) due to infection can be decreased by implementing effective infection prevention and control measures devised by St Judes Infection control committee and My Child Matters project and better intensive care and supportive care facilities and early diagnosis and treatment in resource limited settings can only be achieved by capacity building and establishing more centers having trained health professionals with adequate infrastructure and increased collaboration among different centers in Pakistan and abroad.

P-0258 | From Theory to Practice: Implementation of the Toronto Consensus Principles and Guidelines for the Recording of Paediatric Cancer Stage

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Background/Objectives: Access to consistent, population-wide data on cancer stage is essential for meaningful international comparisons of incidence and outcomes. The recently endorsed Toronto Consensus Principles and Guidelines for the collection of cancer stage by population registries are yet to be tested in practice. Our objective was to evaluate the feasibility of collecting data on stage at diagnosis for a wide range of childhood cancers within a population-based cancer registry (the Australian Paediatric Cancer Registry). This work was supported as part of a national initiative by Cancer Australia to improve cancer staging data for all Australian patients.

Design/Methods: Business Rules were developed for 16 diagnostic subgroups, in line with the Toronto Consensus Principles and Guidelines, for both low (Tier 1) and high (Tier 2) resource settings. A sample of 1438 cases diagnosed during the period 2006-2010 was selected at random from seven hospitals located across all six Australian states. The proportion of cases that could be staged by a clinical coder using the Business Rules and based only on information available in medical records was assessed. Information required for staging that was missing from the medical record was noted, when this occurred.

Results: Results to date indicate that stage at diagnosis can be assigned for the majority of cases using the detailed Tier 2 criteria. Of 277 cases assessed thus far, over 90% had sufficient information in the medical record to allow stage (as per the Toronto Guidelines) to be assigned by a clinical coder. Stage could be assigned for over 95% of children diagnosed with osteosarcoma, hepatoblastoma, medulloblastoma or Ewing sarcoma.

Conclusion: The Toronto Consensus Principles and Guidelines provide the first comprehensive and useable framework for population cancer registries to collect uniform information on stage at diagnosis for most childhood cancers.

P-0259 | Promoting Consistency, Fairness, and Transparency: Development and Implementation of Partnership Eligibility Criteria and Selection Process Guidelines for the Global Health Initiative

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Background/Objectives: The Global Health Initiative (GHI) at Dana-Farber / Boston Children's Cancer and Blood Disorders Center establishes partnerships with institutions in low- and middle-income countries (LMIC) to improve the lives of children with cancer and blood disorders. In an effort to promote consistency, fairness, and transparency in its selection of partner institutions, the GHI seeks to standardize this process through the development of guidelines and a tool that rely on clearly defined criteria.

Design/Methods: The decision-making methodology was based on three main sources. First, qualitative interviews were conducted with GHI members to explore case-by-case scenarios and current practices. Second, GHI site visit reports and agreements were examined to understand policies and criteria used in the past. Finally, a literature review was conducted to assess decision-making theories as well as standards employed by comparable organizations and to justify reliance on identified criteria. Eligibility and disqualifying factors were, then, summarized and agreed upon during GHI working meetings.

Results: The GHI partnership eligibility analysis is bifurcated into two steps: first, a candidate institution must meet five eligibility criteria; and, second, the GHI assesses four additional considerations. The five criteria, ranked in terms of temporal and logical sequence in the analysis, include: LMIC designation according to the World Bank; political, social, and environmental context; legal status of the institution; hospital leadership and external support; and host government receptiveness to foreign collaboration. If all eligibility criteria are met, the GHI evaluates: local burden of disease; the candidate's paediatric oncology/haematology team; its physical infrastructure; and alignment with the GHI's mission, scope and priorities.

Conclusion: This project is critical to promoting the efficacy, ethicality, optimal resource allocation and future direction of GHI programs toward its mission of improving outcomes for children with cancer globally.

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P-0260 | More Boys are Diagnosed with Cancer than Girls Worldwide: Another Sign of Gender Inequality?

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Background/Objectives: Gender is not considered as a risk factor for childhood cancer. Sexual hormones which are known risk factors many cancers are absent or too low, boys and girls usually share the same environment and are exposed to same carcinogens, and genetic factors usually do not favor any gender. Thus, the incidence should be similar in boys and girls. However, according to Reports from many national registries more boys are diagnosed with cancer than girls.

Design/Methods: We analyzed worldwide incidence of the childhood cancers to evaluate national and regional differences in gender distribution. Globocan 2012 data was used in this study. Estimates of incidence and mortality for the age population 0-14 were extracted for each country and region. The data collected was used to analyze the gender imbalance for various demographic and economic indicators.

Results: In 2012 a total of 163,284 new childhood cancers were estimated worldwide (94,518 males and 68,766 females). M/F is 1.37 globally. The incidence rate per 100,000 is 9.8 for males and 7.6 for females (M/F is 1.29). Estimated mortality is 46.031 for males and 33.925 for females (M/F is 1.36). The difference between geographical regions and income groups is evident. M/F for total number of incidence is 1.09 in Northern America but 1.66 in South-Central Asia; 1.20 in More Developed Regions and 1.42 in Less Developed Regions. M/F figures for incidence rates and mortality follow a similar trend.

Conclusion: More boys are diagnosed with cancer than girls globally and the ratio changes in regard to geographical regions and economic income groupings, the difference is associated with the human development. At the moment we can only speculate that the results of this study present a gender inequality in childhood cancers where girls are under diagnosed, which is a typical health issue in many parts of the world.

P-0261 | A Profile of Paediatric Solid Tumours: A Single Institution Experience in Kashmir

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Background/Objectives: The purpose of this retro-prospective study was to study the epidemiological characteristics and outcomes of children with solid tumours at our institution.

Design/Methods: Three hundred and three paediatrics patients registered at regional cancer centre (RCC), Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Srinagar, Kashmir between January 2008 and June 2014, were analysed with regard to demographic status,

presenting complaints, investigations, treatment, morbidity and outcomes. Standard statistical methods were used for analysis.

Results: Among 19,880 patients registered at RCC, SKIMS from January 2008 till June 2014, 986 (4.9%) were of paediatric age group. Of these, 303 (30.7%) patients had paediatric solid tumours. Male to female ratio was 1.04, there were no infants (up to 27 days), 6% were infants and toddlers (28 days-23 months), 39% were children (2-11 years), 55% were adolescents (12-19 years). There were 86% rural patients and 14% urban patients. Most common were CNS tumours (25.74%) followed by germ cell tumours (14.52%), PNET/Ewing sarcoma (13.86%), Wilms tumour (8.9%), osteosarcoma (6.6%), rhabdomyosarcoma (5.6%), colorectal cancer (5.28%), neuroblastoma (4.9%), retinoblastoma (2.6%). Outcomes: 33.9% patients went into remission, 35.64% were defaulters, 2.97% had stable disease, 2.31% had partial response, 20.79% expired and 3.96% were still on treatment. Of all these patients, 5.28% had a relapse.

Conclusion: There were some differences in the spectrum of diseases in Kashmir as compared with the rest of India and western series. Across the series, an advanced stage of presentation, a high incidence of default and poor follow-up was seen. Multiple inter-related factors are responsible for the poorer outlook of childhood cancer in Kashmir.

P-0262 | Children and Adolescent Cancer Incidence and Survival in Spain: The Comunitat Valenciana Childhood Cancer Registry

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Background/Objectives: Information on cancer epidemiology and survival in adolescence in Spain is scarce. The Comunitat Valenciana (CV) has one of the few Spanish population-based registries. We analyzed incidence, site of care and survival of adolescents (15-19 years) with cancer, and compared them to children (0-14 years).

Design/Methods: All incident 0-19 year-old cancer cases registered in the Comunitat Valenciana Childhood Cancer Registry (RTICV) from 2007 to 2011 were included. Diagnoses were recorded according to the International Classification of Childhood Cancer Third Edition (ICCC-3). Population at risk was 4,975,884 person-years. Site of care was aggregated into: Pediatric Oncology Centers (POCs) and Medical Oncology Centers (MOCs). Overall survival was calculated by the Kaplan-Meier method and compared by the log-rank test. Overall survival probabilities were adjusted by survival probabilities from matched population data according to the method of Pohar-Perme. All analyses were performed in R statistical software version 3.2.3.

Results: From 2007 to 2011, 877 patients 0-19 years-old resident in the CV were diagnosed with a new cancer (0-14 years: 642; 15-19 years: 235). Overall age-adjusted incidence (AsrW) was 178.7 cases per million (95% CI: 166.9-190.6). Observed survival was 89.9, 81.3 and 78.7% at 1, 3 and 5 years, respectively. Overall survival did not depend on sex, age group nor region of residence. We only found differences among age groups in survival of leukaemia ($p=0.001$). All patients ≤ 14 years were treated in one of the 3 POCs in the CV. Patients > 14 years were mainly treated in MOCs (97%), 113 of them (49.7%) in 3 MOCs with a POC in the same institution and 114 patients (50.3%) in 22 MOCs without a POC.

Conclusion: Centralization of care and a strong collaboration between paediatric and medical oncologists is warranted to provide the best quality of care in adolescents with cancer.

P-0263 | Global Trends in Survival from Acute Myeloid Leukaemia in Children: Is Survival Approaching the Levels for Acute Lymphoblastic Leukaemia? (CONCORD-2 STUDY)

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Background/Objectives: Despite substantial improvement in diagnostic techniques and treatment of childhood leukaemia over several decades, survival for children with acute myeloid leukaemia (AML) is still lower than for children with acute lymphoblastic leukaemia (ALL).

Worldwide, health inequalities remain, and children with leukaemia do not all have access to the best available care. In low- and middle-income countries, treatment will often be discontinued for financial or practical reasons.

Whereas survival estimates from clinical trials are essential in improving care, population-based cancer survival estimates are key for surveillance and informing policy-makers, patients' families and clinicians.

Design/Methods: Data on children (0-14 years) diagnosed with leukaemia during 1995-2009 and followed up to 31 December 2009 were provided by 198 population-based cancer registries in 53 countries.

Following standardised quality-control procedures, we will analyse data for children with AML and ALL, by country and calendar period of diagnosis (1995-1999, 2000-2004, 2005-2009). We will estimate age-standardised net survival up to 5 years after diagnosis, to control for competing risks of death and to allow for international comparison of the survival trends.

Results: Data for more than 14,500 children diagnosed with AML from 49 countries are available for analysis.

We will present survival trends for AML over 15 years for each participating country. We will compare these survival trends with those for ALL.

Conclusion: These analyses will quantify world-wide patterns of improvement in survival for children up to 5 years after a diagnosis of AML. We will assess the extent to which survival from AML has been approaching the level of survival reached for ALL in each country.

In order to understand worldwide inequalities in care of childhood leukaemia, it is essential to quantify the global differences in survival. This information will guide policy-makers on the effectiveness of health systems and on the policies required to reduce inequalities in survival.

P-0264 | Delays to Diagnosis of Childhood Cancer: A Qualitative Study of Specialist Health Care Professionals' Views

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Background/Objectives: Despite various initiatives, childhood cancer survival rates have plateaued, and the UK continues to fall behind countries with similar healthcare systems. Furthermore, when children survive cancer, they are frequently left with treatment related disability and reduced quality of life. Facilitating early cancer diagnosis is a UK priority. However, for children's cancer, the determinants and consequences of a delayed diagnosis remain unclear. Specialist health care professionals (SHCPs) working in National Health Service (NHS) Paediatric Oncology departments can provide invaluable insights into care pathways and the consequences of diagnostic delay, yet no studies have explored SHCPs' perspectives of diagnostic delay in childhood malignancy.

This pilot study will explore the opinions of SHCPs towards delays in diagnosis of childhood malignancy. This qualitative approach aims to add to the evidence body and will address a gap in the current literature.

Design/Methods: Purposive sampling will be used to obtain two sample groups: a local sample comprising SHCPs working for the Great North Children's Hospital's Department of Paediatric and Adolescent Haematology and Oncology and a national sample of SHCPs attending the Children's Cancer and Leukaemia Group's (CCLG) 2016 Summer Meeting. Each SHCP will take part in an individual face-to-face semi-structured interview. The interview will be audio recorded and transcribed verbatim. Data will be analysed using thematic analysis.

Results: Preliminary results will be presented. Final results will provide insight into current practice, including the use of referral guidance and pathways to specialist care, and identify potential barriers and facilitators in the diagnostic pathway for children and adolescents with cancer.

Conclusion: By improving our understanding, current diagnostic pathways could potentially be streamlined. In addition, a better understanding of the consequences of diagnostic delay could encourage further research and strategies to reduce time to diagnosis of childhood malignancy.

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P-0265 | Childhood Cancer Incidence and Time Trends in the National Hospital of Paediatrics, Vietnam from 2008 to 2014

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Background/Objectives: Childhood cancer is relatively rare. This report aims to determine the incidence of childhood cancer and time trends in NHP Vietnam for the last 7 years.

Design/Methods: All patients who had been suspected of or diagnosed with cancer (except CNS tumors) admitted NHP from January 2008 to December 2014. Information was obtained from registration forms. Patients were followed up periodically. Data was analysed using SPSS.

Results: This study involved 2,485 patients. The most common cancer was acute leukaemia (1,190, 47.9%), followed by neuroblastoma (354, 14.2%), germ cell tumour (GCT) (255, 10.3%), lymphoma (178, 7.2%), kidney tumour (166, 6.7%), soft tissue sarcomas (131, 5.3%), liver tumour (114, 4.6%), bone tumour (21, 0.8%), retinoblastoma (16, 0.6%), other tumours (60, 2.4%). Average male:female ratio was 1.45:1, in acute leukaemia 1.6:1, in lymphoma 2.5:1, and in renal tumours 1.4:1. Acute lymphoblastic leukaemia (ALL) was the most common (67.7%), followed by acute myeloid leukaemia (AML) (21.4%). The most common of lymphoma was Non-Hodgkin lymphoma (NHL) (66.3%), followed by Hodgkin disease (HD) (17.4%). Wilms tumour (WT) accounted for 71.7% of kidney tumours. GCT included teratoma (57.6%) and yolk sac tumour (32.5%). 85.1% were hepatoblastoma and 12.3% were hepatocellular carcinoma (HCC). Half of soft tissue sarcomas were rhabdomyosarcoma (RMS) (51.1%). Leukaemia, neuroblastoma, retinoblastoma, WT, hepatoblastoma, RMS and GCT commonly occurred in children under 5 y/o while HD, osteosarcoma commonly occurred in children over 5 y/o. Childhood cancer incidence per year was quite stable (approximately 350 pts/year) whereas abandonment had been decreasing (54.6% in 2008 to 23.4% in 2014).

Conclusion: Three most common childhood cancers in NHP Vietnam were acute leukaemia, neuroblastoma, and GCT. There were more males than females. ALL, NHL, WT, teratoma and hepatoblastoma accounted for the highest percentage in each organ-specific disease. Childhood cancer incidence per year was stable but abandonment had been decreasing.

P-0266 | The Best Chance from the Start: Improving Support to Identify Cancer in Children and Young People

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Background/Objectives: The research explores the experiences of young cancer patients and parents of diagnosis. It also provides an insight into some of the barriers GPs face in identifying suspected cancer in children and young people.

Design/Methods: A literature review was undertaken, informing the design of two online surveys: one with young people aged 16-24 and one with parents of children who have/had cancer. A total of 147 young people and 186 parents responded. Interviews were conducted with four CLIC Sargent nurses, seven social workers and two parents, along with three focus groups of 13 young people. CLIC Sargent also commissioned a representative online poll of 1,002 GPs.

Results: Half of young people (52%) and parents (49%) surveyed visited their GP at least three times before diagnosis and a third of parents (34%) and over half of young people (53%) felt their diagnosis was delayed. Nearly half of the young people surveyed (44%) said they felt their GP did not take their concerns seriously and a third (34%) felt their GP did not have time to

listen to them talk about their symptoms. Nearly half of GPs polled ranked lack of training as a top barrier to identifying cancer.

Conclusion: While a substantial proportion of young people and parents have positive experiences prior to diagnosis, a significant number do not. Many visit their GP multiple times before a diagnosis is made and many experience a delay in obtaining a diagnosis. Parents and young people often felt their GP did not have enough time to listen to them talk about symptoms and did not always take their concerns seriously. Many GPs feel they do not have enough opportunities to be trained in how to identify cancer in this age group and don't always have access to the expert support they need.

P-0267 | Cancer in Patients with Primary Immune Deficiency

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Background/Objectives: Patients with immune deficiency, comprise a high risk group in term of cancer development. In this study, cancers in immune deficiency patients have been evaluated.

Design/Methods: There were 1480 children with cancer treated between the years 1998-2015. Demographic features, primary immune deficiency and cancer diagnosis, mean following period, administered treatment, remission status and cause of death are evaluated.

Results: Eight patients (0.54%) who are followed up for primary immune deficiency had got malignancy. Male/ female ratio was 6/2. Immune deficiency diagnosis age was median 6 years (1.25-10 years), malignancy diagnosis age was median 9 years (3-18 years). Period between immune deficiency diagnosis and development of malignancy were median 3 years (0-11 years). There were two patients diagnosed with primary immune deficiency concurrent with malignancy. Types of primer immune deficiency diagnosis were like that; five patients were ataxia telangiectasia, two patients were common variable immune deficiency (CVID), one patient was Wiskott-Aldrich syndrome. Six of those patients have developed Non-Hodgkin Lymphoma (NHL), one of patients developed Hodgkin Lymphoma and one of patients developed hemangiopericytoma. Complaint period before diagnosis of malignancy were median 22 days (1-90 days). One of patients was administered surgery and this patient were applied only radiotherapy due to relaps. Six patients were received only chemotherapy, one patient got both chemotherapy and radiotherapy. Dose of chemotherapy was reduced. In four patients, post-treatment remission observed, four patients died during treatment. Three of patients died without remission during treatment, one of patients died during remission due to sepsis. Three patients are still in remission and followed up.

Conclusion: Cancer which developed in patients were followed up with primary immune deficiency was usually lymphoma. Shortness of complaint period was associated with that majority of patient group were ongoing follow-up. All mortalities associated with cancer had been observed during treatment.

P-0268 | Access to Principal Treatment Centres for Children and Young People in Yorkshire and the Effect on Survival

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Background/Objectives: Principal Treatment Centres (PTC) aim to provide age appropriate care and clinical expertise for children and young people with cancer. We aimed to describe patterns of care at PTCs in children and young people in Yorkshire, UK between 1998 and 2009 and assess the association with survival trends.

Design/Methods: Patients diagnosed from 1998-2009 aged 0-29 years were extracted from the Yorkshire Specialist Register of Cancer in Children and Young People, including information on all treating hospitals, followed-up until 31st December 2015. The six commonest cancer types were included: leukaemia (n=751), lymphoma (n=793), CNS tumours (n=685), bone tumours (n=184), soft tissue sarcomas (n=240) and germ cell tumours (n=691). Treatment was categorised into three groups: 'all', 'some' or 'no' treatment received at a PTC. Treatment at PTC was examined by diagnostic group and patient characteristics. Overall survival was modelled using Cox regression adjusting for case-mix including stage and treatment.

Results: 64% of individuals aged 0-29 years received all their treatment at PTC while 15% received no treatment at PTC. This differed by diagnostic group and age at diagnosis. In unadjusted analysis patients with leukaemia who received 'some' or 'none' of their treatment at PTC had an increased risk of death but this was not significant in the adjusted model (HR=1.35 (95%CI 0.75-2.42) for 'some' and HR=1.61 (95%CI 0.85-3.06) for 'none'). Soft tissue sarcoma patients who received 'some' of their treatment at PTC had a significantly reduced risk of death compared to those who received 'all' their treatment at PTC, an effect which remained after adjustment for case-mix: adjusted HR=0.50 (95%CI 0.28-0.87). There were no significant differences in outcomes for other diagnostic groups.

Conclusion: Access to PCT varied by diagnostic group and age, however there was little evidence of differences in outcome after considering patient case-mix, except for soft tissue sarcomas.

P-0269 | Measuring the Efficacy of a Project Dedicated to Adolescents and Young Adults with Cancer: A Study from the Milan Youth Project

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Background/Objectives: Various projects dedicated to adolescents and young adults (AYA) with cancer have been developed in the last years. A key point of a dedicated AYA program should concern the capability to demonstrate its value, and therefore how to define and measure the desired outcome.

Design/Methods: This study aimed to identify a list of metrics to be considered to demonstrate the advantages of an AYA program. These parameters are related to the number of patients and the proportion of them involved in clinical facilities and support projects, the patient satisfaction, and the scientific and community recognition. The parameters were used to evaluate the activity of the Youth Project of the Pediatric Oncology Unit of the Istituto Nazionale Tumori (INT) in Milan.

Results: During 2015, 205 new patients with solid tumors were treated at the Pediatric Oncology Unit and 81 were AYA, i.e. ≥ 15 years (39%). The number of AYA patients admitted each year increased after the start of the Project, i.e. 65 cases/year in the 2006-2010 period; 81.2 in the 2011-2015.

All AYA patients with malignant tumors seen in 2015 were included in a national or international cooperative clinical trial (82.7%) or registered in a prospective observational study (17.3%).

Fertility preservation measures were done in 59% of AYA patients considered at risk, while specific psychological support was provided in 71%. Support projects (e.g. creative laboratories) were attended by 77% of AYA patients. In 2015, 7 research peer-reviewed papers have been published, as well 51 articles on mass-media.

Conclusion: This study proposed a list of metrics for support the sustainability of an established program dedicated to AYA. Second, it demonstrated the efficacy of the INT Youth Project as a referral center for patients in this age group.

P-0270 | Actions to Improve Early Diagnosis of Childhood Cancer in Developing Countries

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Background/Objectives: Introduction: In developed countries the cure rate of cancer children exceeds 75%, this reality is far from being achieved in Brazil and the main reason is the difficulty that health professionals have to diagnose the disease early. The Cancer Hospital of Cascavel - UOPECCAN in partnership with the Ronald McDonald Institute through the early diagnosis of cancer children and adolescents program, train professionals of health and paediatrics of the municipalities of Parana-Brasil.

Objective: Train professionals of health and paediatricians to contribute to the early identification of cancer in children and adolescents, reducing the time between the onset of signs and symptoms and diagnosis in a specialized center providing an increase of the probability of cure.

Design/Methods: Health professionals from several cities of parana, were trained from April /2008 to march /2016, received basic information about children cancer and adolescents (Epidemiology; signs and symptoms of suspicion; care needed for the attention to children and adolescents with cancer). The groups were formed with 40 professionals, 20 hours /course.

Results: 1809 professionals, 112 doctors, 196 nurses, 282 technicians / nursing assistants, 894 community health agents, 162 upper level and 163 medium-level professionals or auxiliary were trained.

Conclusion: Among the diagnosed cases of cancer in children in Brasil, many are referred to treatment centers with the disease at an advanced stage. One goal of the campaign is to encourage educational and preventive actions, becoming known to more people about symptoms and signs of disease. Shortening the time between the suspicion of cancer and early diagnosis and treatment, will certainly contribute to the increasing expectations of cure in developing countries.

P-0271 | Disease Profile and Outcome of Paediatric Cancer in Three Consecutive Periods in Tygerberg Hospital, Cape Town, South Africa

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Background/Objectives: Aim: This study compares disease profile and outcome of all children younger than 15 years, diagnosed with cancer at Tygerberg Hospital, South Africa during three consecutive time periods.

Design/Methods: All children were treated with appropriate standard treatment protocols. Data entered into the South African Children Cancer Study Group (SACCSG) Tumour Registry, were analysed anonymously. The three time periods were 1983 to 1993 (1st period; previously published), 1994 to 2003 (2nd period) and 2004 to 2013 (3rd period). Study exit was 60 months (3rd period analysed till 24 months for survival).

Results: The three time periods had consecutively 492, 404 and 437 patients per period. Ethnicity was similar in all three periods with more cancers diagnosed in children of mixed race (so called "coloured"), respectively 48.3%, 67.6% and 61.6%, reflecting population demography of the region. The most common cancers in the 3 time periods were leukaemia (respectively 22.8%, 30.9% and 25.5%), brain tumours (respectively 20.5%, 21% and 14.9%), lymphomas (respectively 15.2%, 11.9% and 14.9%), nephroblastomas (respectively 10%, 7.4% and 9.4%), neuroblastomas (respectively 8.5%, 3.7% and 6.4%) and retinoblastomas (respectively 5.7%, 2.2% and 6.4%). Improved overall survival was demonstrated for most of these common cancers: ALL improved from 63% (whites only) to 75% in the following 2 time periods, Hodgkin lymphoma from 70% to 80% and 85%, and 65% for nephroblastoma (stages 1 and 2 only) during the first period to 90% in the two consecutive time periods. Neuroblastoma is still diagnosed late and overall survival was only 40% during the last 2 time periods. Other less common cancers' outcome will be demonstrated.

Conclusion: The number of newly diagnosed cancers was decreased in the 2 consecutive time periods. Survival improved for most of the common cancers, especially for ALL to 75% and nephroblastoma to 90%.

P-0272 | Paediatric Tumour Boards in Europe: Current Situation and Results of An International Survey in EXPO-r-NeT

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Background/Objectives: Multidisciplinary care is the hallmark of high quality cancer management. Individual opinions have been displaced by collective decisions in the approach of paediatric cancer. Under the EXPO-r-NeT project (European Expert Paediatric Oncology Reference Network for Diagnostics and Treatment), the actual picture of multidisciplinary paediatric tumour boards in Europe has been studied in depth.

Design/Methods: A 20 question survey regarding several features of tumour board practice was designed. Data collected included infrastructure, organization and clinical decision-making information from the centres. The survey was distributed to the National Paediatric Haematology and Oncology Societies (NaPHOS), that forwarded the survey to the sites. For comparative analysis, respondents were grouped into four geographical regions: Northern, Central, Southern and Eastern Europe. Statistical significance among regions was assessed by multinomial logistic regression and $p < 0.05$ was considered as statistically significant.

Results: The questionnaire was distributed amongst 30 countries. Response was obtained from 23 NaPHOS (77%) that altogether have 212 paediatric oncology treating centres. A total of 121 institutions answered (57%). Ninety-one percent of the centres hold multidisciplinary boards, however international second consultations are performed in 36% and only 15% participate on virtual tumour boards. Videoconferencing facilities and standard operational procedures (SOPs) are available in 49% and 43% of the centres respectively. There were statistically significant differences between European regions concerning meeting infrastructure and organization/logistics: specific room, projecting equipment, access to medical records and PACS (Picture Archiving and Communication System) videoconferencing facilities and existence of SOPs.

Conclusion: Pediatric tumour boards are a common feature in Europe. In order to reduce inequalities and have equal access to healthcare a virtual network is needed. Important differences on the functioning and the access to IT technology between regions in Europe have been observed and need to be addressed.

P-0273 | Burkitt Lymphoma (BL): HIV/AIDS Prevalence and Outcome of Treatment in Cameroon

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Background/Objectives: Cameroon has approximately 20 million inhabitants, of whom 40.5% are age 0 to 15 years, and of whom 1% were HIV positive in 2013. Pregnant women in the Northwest (NW) and Southwest regions (SW) have a HIV prevalence of 4.6% to 6.8% and the mother to child transmission rate in 18 month old breastfed children in 2013 was 25%. Patient with BL are treated with standardized chemotherapy at Banso, Mbingo and Mutengene Baptist hospitals in the NW and SW.

Our objective was to record the prevalence of HIV, and response to treatment in these patients.

Design/Methods: Our database is a POND registry for the period 2003 to 2013. We analyzed the number of HIV positive patients, the St Jude stage, whether antiretroviral (ARV) treatment was given, and the long term outcome.

Results: Of 979 patients treated, 717 (73%) were tested for HIV, and 11 (1.5%) were positive. The age ranged from two to 13 years (mean 7 years). One patient had stage IV, 8 patients stage III and 2 patients stage II disease. Eight patients received ARV, three of whom with stage III disease, are alive at 56, 72 and 76 months follow-up respectively. The CD4 count in 4 patients ranged from 30 to 559 cells/ul.

Conclusion: The prevalence of HIV (1.5%) was comparable to that of the general population (1%). HIV positive BL patients have a good chance of cure with chemotherapy and long term ARV treatment.

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P-0274 | Testicular Tumors: Experience of 16 Years in the Rebagliati Hospital

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Background/Objectives: Testicular tumors (TT) in children are rare and distinct from adult TT. This study was to focus on children to evaluate clinical features among various testicular tumors with follow-up.

Design/Methods: A total of 45 children who were treated for TT at Rebagliati's Hospital from 2000 to 2016 were retrospectively reviewed. Histopathological findings, age, clinical stage, and outcomes were analyzed. We separated two groups: Group 1 were boys less than 12 years old. Group 2 were 12 to 17 years old.

Results: The median age at operation was 23 months in group 1 and 187 months (15.8 years old) in group 2. Germ-cell tumors (GCT) were the most common in both groups (81% and 75%). They had characteristics: Premature (2), Cryptorchidism (2), low birth weight (1) and retractile testicle (2). In prepubertal group, mainly with yolk sac tumour, YST (75%). In pubertal boys, mixed malign GCT was more prevalence (66.6%), none was YST. Children with immature teratomas were neonates. Of the total patients 28.8% (46.15% were mixed malign GCT) had metastasis. Management after surgery included combination with chemotherapy in 70%, 15% need second line of chemotherapy and 7.4% need radiotherapy. Outcomes at the last followup (average 80 months) were 91% of patients alive.

Conclusion: Demographic data on paediatric testicular tumors in Peru will lead to a better understanding of the biological behavior and optimal management of these tumors in these children. The most common TT in this study was Germ Cell Tumour No seminoma. The incidence of yolk sac tumour was markedly higher in the present study in both groups.

P-0275 | Assessing the Role of Apoptosis Genotypes on Biomarkers of Symptom Severity in Children Undergoing Acute Lymphoblastic Leukemia Treatment

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Background/Objectives: Patients being treated for childhood acute lymphoblastic leukaemia (ALL) experience adverse physical and psychological symptoms, which may compromise treatment efficacy and long-term quality of life. There is growing evidence that cerebral spinal fluid (CSF) biomarkers of apoptosis, including caspase 3/7, are associated with the severity of symptoms experienced by children during ALL therapy. Because genetic variation likely contributes to the symptom experience, we assessed the role of apoptosis genotypes on biomarkers of treatment-related symptoms in children during the most intensive phase of ALL therapy.

Design/Methods: Our study population included 81 children newly diagnosed with ALL at two paediatric cancer centers in the Southwestern United States. We measured CSF caspase 3/7 concentrations collected before the beginning of consolidation. Common functional variants in *CASP3* (rs4647603, G>A) and *CASP7* (rs 12415607, C>A) were genotyped using TaqMan assays. Based on minor allele frequencies, genotypes were coded using a dominant model of inheritance. Beta coefficients and P values were calculated using linear regression to evaluate the role of *CASP3* and *CASP7* genotypes on caspase 3/7 concentrations.

Results: The majority of patients with ALL were female (55%), and the mean age at diagnosis was 6.8 years. We did not detect significant associations with *CASP3* rs 4647603 and CSF caspase 3/7 concentrations. Notably, the mean concentration of caspase 3/7 among those without a risk allele of *CASP7* rs 12415607 was 34.4 units/L (n=49) compared to 49.4 units/L among those with at least one risk allele (n=32). *CASP7* rs 12415607 was significantly associated with log-transformed CSF caspase 3/7 in linear regression models (beta=0.33, P=0.04).

Conclusion: Our results suggest *CASP7* rs4647603 is associated with a biomarker of adverse symptoms during a critical period of ALL therapy. Physiologic biomarkers and relevant genotypes may improve our limited understanding of treatment-related symptoms and inform risk prediction models, which may ultimately be used to limit the adverse consequences of therapy.

P-0276 | Biobank Participation Beliefs and Attitudes: Analysis of Factors Influencing Participation in a Paediatric Cancer Research Biorepository - Egypt

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Background/Objectives: Biobanks have become a powerful tool that can foster many types of research. The success of biobanks depends upon people's perception and willingness to donate their samples for future research. This is the first paediatric biorepository in the middle-east, hence, little is known about the beliefs and attitudes of parents towards their children participation in a research biorepository.

Aim: To investigate the level of willingness to donate samples for research in an Egyptian Children's cancer hospital and understand factors influencing enrollment.

Design/Methods: A Standardized questionnaire was designed covering multiple items expected to affect the enrollment. This was conducted in-person and data collected included, demographics data, socioeconomic level, educational and religious constraints. Additionally, in the case of refusal, participants were asked about reasons for nonparticipation.

Results: We succeeded to enroll 7,000 paediatric participants from November 2012 till March 2016. Yet, approximately 3.1% of patients have refused to participate and 0.3% have withdrawn. Three demographic factors were found having disparate trends in the parents decision making process to participate or not: father's education (p-value = 0.0001), mother's education (p-value = 0.0001) and father's age (p-value = 0.034).

Conclusion: More intense awareness programs need to be designed specifically for parents with a higher level of education and who are of older age, as they tend to be more unwilling to participate in a research biorepository.

P-0277 | The Adolescent and Young Adults Program in Lyon, France (DAJAC): Report on the 3,5 Year Experience

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Background/Objectives: In 2012, the INCA (Institut national du cancer) launched 8 programs to improve the management of French AYAs(15-25y) with cancer. The Centre Léon Bérard (cancer institute) and the IHOP (paediatric university hospital) implemented the DAJAC in

June 2012. This program is based on a multidisciplinary team: 1 "adult" oncologist, 1 paediatrician, a nurse, a psychologist and a social worker. It allows patients to decide where they want to be treated (adult or paediatric ward) and to be managed by a specialist team. We report on the first 3.5 years of this program.

Design/Methods: A database was created in 2012 (CNIL:1552730). An analysis was performed in 2016 to describe the characteristics of the population and to evaluate the benefit of the program.

Results: Between June 2012 and December 2015, 436 AYAs (176♀/260♂) were referred to our institutions (mean 125/year) and managed within the DAJAC. Median age at diagnosis was 19.7y. 217 decided to be treated in an adult ward (median age=22.2y) and 219 in a paediatric ward (median age=17.4y). There were 142 sarcomas, 100 lymphomas, 56 germ cells tumours, 52 leukaemia, 32 brain tumours, 28 carcinomas, 13 other malignancies and 12 benign tumours. At initial diagnosis, 100% patient's case was discussed at a mixt (paediatric/adult) multidisciplinary tumour board meeting (versus 20% before 2012). 95% patients had systematic psychological assessment and follow-up (vs 20%). 129 patients (30%) were enrolled in one or more (230 inclusions) clinical trial (vs 6%). During this period, 174/260 males benefited from a freezing of sperm and since 2014 100% of girls have a clinic appointment with a fertility specialist at diagnosis.

Conclusion: The implementation of a specific program to manage AYAs with cancer allowed the improvement in their medical and psychosocial care. Extending this sort of approach nationwide could lead to improving further the quality of care for this population.

P-0278 | Diagnostic and Treatment Intervals for Patients Presenting with Solid Tumours to Secondary/Tertiary Care: A UK-Based Retrospective Observational Study

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Background/Objectives: Timely diagnosis of cancer is dependent on the patient, doctors and the health care system to which they present. The secondary/tertiary care component of the diagnostic pathway is rarely interrogated. This study evaluated diagnostic and treatment intervals for patients with solid tumours with the aim to identify opportunities to improve timely diagnosis within secondary/tertiary care.

Design/Methods: This 1 year retrospective observational study evaluated newly diagnosed patients with solid tumours. Data were collected from 1 tertiary oncology centre and 7 paediatric oncology shared care units in secondary care.

The diagnostic and treatment intervals were as defined by the Aarhus statement. Primary outcome was the treatment interval, time to start treatment from date of diagnosis. Secondary outcomes were the diagnostic intervals, time to diagnosis from referral to secondary care and from first specialist visit.

Results: The diagnostic pathway of 49 patients was evaluated, mean age 8 years (range 1 month-17 years). The median time to treatment from date of diagnosis was 10 days (range 2-23) for all patients. Patients with bone tumours (n=5) were analysed separately as they require referral to a supra-regional quaternary service for surgical management. Treatment interval for bone tumours was 15 days (range 10-18). The diagnostic interval from referral to secondary care to diagnosis was 10 days (range 0-76) for all patients and 38 days for patients with bone tumours (range 36-81). From first specialist visit to diagnosis was 3 days (range 1-11) for all patients and 10 days for patients with bone tumours.

Conclusion: These findings are important for setting standards, evaluating the performance of the diagnostic multi-disciplinary team and managing patient's/families expectations. The data suggests that patients with bone tumours have longer diagnostic and treatment intervals than other solid tumour patients. Critical review of this data has identified factors influencing the diagnostic pathway.

P-0279 | A Project Initiative Approach: Shaping the Future of Teenage and Young Adult Cancer Services in Northern Ireland

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Background/Objectives: To scope the current service provision for teenage and young adults (TYAs) with cancer in Northern Ireland (NI), measuring against national and international guidance. To make recommendations as to how all aspects of care should be coordinated to ensure there is a balance of service provision and allocation of resources.

Design/Methods: The Northern Ireland Cancer Network TYA Project Steering Group was established in 2014 to manage the project. A scoping exercise was conducted with all five health and social care trusts and the voluntary sector in NI in 2014. A review of TYAs with cancer literature including patient experience surveys; semi structured interviews with key stakeholders, reviews of cancer incidence datasets and supplemented by best practice visits to mainland United Kingdom TYA principle cancer treatment centres and a comparative analysis of service level baseline assessments from 2010 and 2014.

Results: Gaps in the workforce profile were identified with a subsequent options appraisal produced outlining additional nursing, social work and psychosocial staff. Incidence data indicates a geographical spread of place of treatment for TYA patients with cancer across NI, highlighting the need for a regional approach to service delivery. 41.8% of TYAs may not have had access to an age appropriate cancer service in NI. Implementation of a regional service with additional workforce has been agreed.

Conclusion: Overall, the project identified a responsibility to offer an equitable service to all TYA patients with cancer in NI. The reconfigured TYA cancer service ensures TYAs with cancer attain the best possible outcomes and have access to appropriate specialist service, as locally as possible, that are both safe and sustainable, supported by consistent pathways of care, regardless of where they live in NI.

P-0280 | Long-Term Experience in the Management of Adolescents and Young Adults with Cancer Referred to A Regional Tertiary Centre for Multidisciplinary Care

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Background/Objectives: Adolescents and Young Adults (AYA) with cancer constitute a heterogeneous group in which improvements in survival rates (OS) have not kept pace with those achieved in younger patients.

Design/Methods: Retrospective review of AYA (15-29 years) patients with cancer, except leukaemias, referred for multidisciplinary treatment (1992-2014). Baseline characteristics, pathological type and stage, 1st -line treatments and OS were reviewed. Differences between three age groups (15-19, 20-24, 25-29 years) assessed with Chi-square and log-rank tests. A p-value < 0.05 was considered significant.

Results: 286 patients. Median age 23 years (15-29); 33.1% (15-19 years), 23.6% (20-24 years) and 43.3% (25-29 years).

Tumour types (% in age-groups): Paediatric-bone tumours 15.7% (28.7-13.4-7.3), germ-cell tumours (both sexes) 15.5% (11.7-17.9-17.1), adult-type epithelial tumours 14.1% (6.4-10.4-22.0), Hodgkin lymphoma 12% (11.7-11.9-12.2), non-rhabdomyosarcoma soft-tissue tumours 9.5% (4.3-10.4-13.0), glial-derived brain tumours 7.7% (9.6-7.5-6.5), paediatric-type brain tumours 7.7% (8.5-9.0-6.5), non-Hodgkin lymphoma 4.9% (5.3-6.4-1%), endocrine tumours 2.8% (3.2-1.5-3.3), paediatric-type solid tumours 2.1% (4.3-3.0-0.0), other bone tumours 2.1% (0-4.5-0-2.4), melanoma 2.1% (1.1-1.5-3.3), liver tumours 1.8% (1.1-1.5-2.4) and rhabdomyosarcoma 1.8% (4.3-1.5-0.0).

Locally advanced or metastases: 43.7% (45.8-37.3-45.6). 1st-line treatment: 62.5% surgery, 73.7% chemotherapy and 32.5% radiotherapy; 2.1% included in clinical trials.

Median follow-up: 110 months (6-314 months). 5 and 10-year OS: 64 and 57%. No differences between age-groups in treatment patterns and pathology, except in incidence of paediatric bone tumours and adult-type epithelial tumours. There was a trend for worse OS in the 25-29 age group; 5 and 10-year OS were 68 and 64%, 66 and 53% and 56 and 36%, respectively (p 0.06).

Conclusion: Patients in the 25-29 years-group fared worse than younger patients. More biologically aggressive presentations and a higher rate of adult-type epithelial neoplasms could justify these findings. Inclusion in clinical trials remains disappointingly low. Closer collaboration with Paediatric Oncology Departments and better knowledge of the biology of these rare tumour presentations are needed.

P-0281 | Childhood Cancer: Incidence Trends in Argentina. Report from the National Paediatric Cancer Registry, ROHA Net. 2000-2013

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Background/Objectives: The aim of this study was to present information regarding childhood cancer incidence trends in Argentina. Data obtained from the ROHA, hospital-based registry with national coverage belongs to the National Cancer Institute, showed that 18,069 newly diagnosed paediatric cancer cases were registered between 2000 and 2013. Estimated coverage is 93% of the country's cases. Incidence trends of common primary cancers diagnosed in children under age 15 years between 2000 and 2013 were assessed.

Design/Methods: Overall and age-adjusted incidence rates trends were calculated using joint regression to analyze annual percent change (APC) in rates (with 95% confidence intervals [95% CI]).

Results: Between 2000 and 2013, a modest or no change in the average annual incidence rate (APC: -0.4%; 95% CI, -1.0%; 0.3%.p:0.2) was observed for all common paediatric cancer diagnoses combined, including leukaemia (APC:0.1%; 95% CI, -0.6%; -0.8%.p:0.7), brain tumors (APC: 0.4%; 95% CI, -0.5%; 1.3%.p:0.3), and lymphomas (APC: -2.6%; 95% CI, -3.8%; -1.4%.p:0.0).

Conclusion: There was no substantial change in incidence for the major paediatric cancers and rates have remained relatively stable, although incidence of lymphomas decreased modestly but statistically significantly.

P-0282 | Characteristics of Intermediate Care Transfers in a Resource-Limited Paediatric Oncology Hospital in Guatemala

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Background/Objectives: The intermediate care unit (IMCU) provides a cost-effective alternative for patients requiring frequent monitoring or increased nursing care, but not intensive interventions. Little data exists on patients best suited for IMCU transfer, especially in resource-limited hospitals or among oncology patients at high risk for deterioration. Patients improperly triaged to IMCU may require early transfer to ICU, resulting in treatment delays and poor resource utilization.

Objective: Describe patients requiring transfer to IMCU at Unidad Nacional de Oncología Pediátrica (UNOP), a resource-limited paediatric oncology hospital in Guatemala, and identify patients at risk for early ICU admission.

Design/Methods: Data on patients at UNOP requiring IMCU transfer from January to June 2015 were collected. Demographics and transfer characteristics were collected via retrospective chart review. Patients requiring transfer to ICU within 24 hours of IMCU admission were compared with those remaining in IMCU.

Results: Thirty-nine patients required IMCU transfer during the study period. Of these, 77% had Acute Lymphocytic Leukaemia. Most common transfer diagnoses included fever and neutropenia, pneumonia, respiratory distress, mucositis, and fever without neutropenia. The majority (51.35%) were neutropenic at time of transfer. Six patients (15.38%) required transfer to ICU, 5 within 24 hours of IMCU admission. Of these, 2 died (30%). Compared with patients remaining in IMCU, those requiring early ICU transfers had higher Pediatric Early Warning Scores (PEWS) prior to IMCU admission (3.1 vs 5.6, $p=0.03$), respiratory distress as a reason for transfer (2.9% vs 40%, $p=0.04$), and a trend to more neutropenia (45.2% vs 80%, $p=0.17$).

Conclusion: We describe characteristics of patients requiring transfer to IMCU at UNOP. They are generally neutropenic with infectious diagnoses. Early transfer to ICU among these patients are common and result in poor outcomes. In this setting, the PEWS tool is effective in identifying patients requiring ICU vs IMCU level care, and may lead to better resource utilization.

P-0283 | Epidemiology of Head and Neck Paediatric Tumors. 30 years' Experience

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Background/Objectives: Primary paediatric head and neck tumors (TPCC) are a rare and heterogeneous group. There are few epidemiological reports of TPCC. The objectives of this study are to describe epidemiological characteristics of patients (p) with TPCC and to correlate age, location and histology.

Design/Methods: We reviewed records of p with TPCC admitted to Oncology Unit Hospital de Niños Ricardo Gutierrez between January 1986 and March 2016. Infectious disease, thyroid tumors and hematological malignancies were not included.

Results: 3300p with solid tumors were admitted and 303p with TPCC with inclusion criteria (9%). Male/female ratio: 1. Malignant 94% and benign 6%. Histological types: retinoblastoma 157p (52%), rhabdomyosarcoma 39p (13%), sarcomas not rhabdomyosarcoma 31p (10%), histiocytosis 27p (9%), carcinomas 16p (5%), plexiform neurofibromas 7p (2.3%), bone tumors 5p (1.6%), neuroblastomas 5p (1.6%), fibrohistiocytomas 3p (1%), pleomorphic adenomas 3p (1%), melanomas 2p (0.6%), Rosay Dorfman disease 2p (0.6%), spindle epithelial tumour with thymus like differentiation 1p (0.4%), rhabdoid tumour 1p (0.4%) and others 4p (1.5%). Localizations: eye 158p (52%), calota 32p (10%), base skull 27p (9%) cavum 19p/ptergomaxilar fosa 4p/sphenoid 4p, neck soft tissue 24p (8%), orbit 18p (6%), cheek 11p (3.5%), salivary glands 9p (3%) and tongue 7p (2%), scalp 5p (1.2%), lower jaw 4p (1.3%), maxillar sinus 3p (1%), nose 3p (1%), medium hear 1p (1%) and palate 1p (1%). Forty seven percent were between 1 and 4 years old. Age groups and localization were also correlated with histology.

Conclusion: TPCC represent a small proportion of patients admitted to our Unit. Near half of the evaluated p are between 1 and 4 years. Retinoblastoma, sarcomas and histiocytosis were the most frequent TPCC. Eye, calota and base skull were the most frequent localizations. This study reports a low number of benign tumors probably because they require only surgery and aren't referred to our Unit.

P-0284 | Prospective, Observational Nationwide Study on Pharmacogenomics/Genetics of Childhood Cancers in a Cohort of Turkish Paediatric Oncology Group (TURKPEDPGX)

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Background/Objectives: Standard chemotherapeutic regimes are applied in the management process of childhood cancers and observed consequences can be various, in terms of treatment responses and toxicities. Personal variations in genetic structure have role on the functions of drug-metabolizing enzymes, as well as effectiveness of therapy and toxicity. The aim of this study, determination of the polymorphisms on drug-metabolizing enzymes and identify paediatric cancer patients at risk of therapy-related complications according to personal polymorphism profile in a nationwide cohort study.

Design/Methods: In this context, Turkey Childhood Pharmacogenomics/Genetic Cohort Study (TURKPEDPGX) has been initiated as a nationwide, prospective and observational cohort study between 2015 and 2020. The main outcome measure will be toxicity and therapeutic response throughout five year follow-up. Polymorphism analysis was performed with pyrosequencing by using genomic DNA extracted from blood.

Results: From March, 2015 to March, 2016; 67 patients have included to study. Lymphomas/reticuloendothelial neoplasms (n=21); CNS/miscellaneous intracranial and intraspinal neoplasms (n=9), soft tissue-other extraosseous sarcomas (n=9), neuroblastoma and other peripheral nervous cell tumors (n=8), Malignant bone tumors (n=6), renal tumors (n=5), retinoblastoma (n=1), hepatic tumors (n=1), germ cell tumors (n=1), other malignant epithelial neoplasms (n=3) and unspecified malignant neoplasms (n=3) were observed. ERCC1 C8092A (35%), ERCC1 T19007C (70%), XRCC1 G28152A (65%) and GSTP1 A313G (65%) variants were detected.

Conclusion: The observation of toxicity on the paediatric cancer patients, who were applied chemotherapeutic regimes, may be responsible on the variations of drug metabolizing enzyme polymorphisms and metabolism of drug. Usage of same chemotherapeutic agents even with same dosing schedule, can present different responses between individuals. Pharmacogenomics will allow us to identify paediatric cancer patients at risk of therapy-related toxicity and predict therapeutic responses according to personal polymorphism profile.

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P-0285 | Health Seeking Attitudes of Caregivers at the Paediatric Cancer Clinic of a Teaching Hospital in Ghana

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Background/Objectives: The Paediatric Cancer Unit (PCU) of the Komfo Anokye Teaching Hospital (KATH) in Kumasi, Ghana was established in 1998 as part of a larger Unit including Paediatric Neurology and Haematology Units. 129 new cases of cancer were registered in 2015 with average weekly clinic attendance of 20. 34% of patients default treatment and 31% die. Our goal was to determine the health seeking attitudes of caregivers attending the PCU compared with the Paediatric Neurology and Sickle Cell Disease (SCD) Clinics of KATH.

Design/Methods: This was a prospective, cross-sectional survey from November, 2015 to February, 2016 using a pretested e-questionnaire at the various Outpatients Clinics and data analyzed with STATA IC 12.0[®] statistical software.

Results: 133 participants were interviewed: Cancer, 46(35%); Neurology, 34(25%) and SCD, 53(40.0%). Average age of caregivers was 36 years with biological mothers constituting 74%. A larger proportion of cancer participants (15%) had no formal education compared with Neurology (6%) and SCD (7%). Participants were mostly petty traders (47%), artisans (20%) and peasant farmers (15%) with approximate average earning of 6.0USD daily. 50% of SCD participants rented houses compared to 29% Neurology and 39% Cancer participants. 33(72%) of Cancer participants reported initially to a health facility compared with 88% Neurology and 100% SCD. The mean onset time to reporting was 68days (Cancer), 11days (Neurology) and 6 days (SCD). Awareness of disease was 9% (Cancer), 30% (Neurology) and 28% (SCD). Most participants - Cancer, 93%; Neurology, 70%; SCD, 60% - were referred from primary/secondary health facilities. At presentation, 65% of the cancers were advanced.

Conclusion: Caregivers at PCU, KATH were women of low socioeconomic status who reported to primary healthcare facilities from where they were referred. They presented with advanced disease. We suggest more strategies for caregiver and primary healthcare provider education on early signs of childhood cancers to improve early diagnosis.

P-0286 | Caregivers' Perception of Treatment Outcome and Challenges at the Paediatric Cancer Unit of a Tertiary Center in Ghana

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Background/Objectives: The Paediatric Cancer Unit (PCU) of the Komfo Anokye Teaching Hospital (KATH) in Kumasi, Ghana is one of two main treatment centres. Since 1998 about 2,500 children have accessed services at the centre which has one Paediatric Oncologist. 129 new cases of cancer were registered in 2015 with average weekly clinic attendance of 20. 34% of patients die as same abandon treatment. Our aim was to determine the caregiver perceptions of overall treatment outcome and their challenges compared with the Paediatric Neurology and Sickle Cell Disease (SCD) Clinics of KATH.

Design/Methods: This was a prospective, cross-sectional survey from November, 2015 to February, 2016 using a pretested e-questionnaire at the various Outpatients Clinics. Data was analysed with STATA IC 12.0[®] software.

Results: Overall 133 caregivers participated: Cancer, 46(35%); Neurology, 34(25%) and SCD, 53(40.0%). Mean daily wage was \$6.00 and most caregivers were self-employed (72%) and Petty traders (47%). More Cancer participants (15%) relative to Neurology (6%) and SCD (7%), had no formal education. 89% Cancer, 96% SCD and 87% Neurology participants reported their children were improving on current clinical managements. More Cancer caregivers (62%) were willing to disclose their wards' diagnoses to others compared with Neurology (39%) and SCD (29%). All Cancer participants admitted to financial constraints for treatment for their wards (75% SCD and 85% Neurology). 12% of Cancer participants spent twice as long (2.5hours) as 15% each of SCD and Neurology participants (1hour) traveling to access care on average.

Conclusion: Caregivers in PCU compare favourably with counterparts in Neurology and SCD clinics on their perception of treatment outcomes for their wards. They were however, more likely to face financial constraints but more willing to disclose their wards' diagnoses to other parties. Can this fact guide experts in exploring advocacy strategies for caregivers seeking care for their wards with suspected cancer?

P-0287 | A 5 Year Review of Mortality Trends at a Paediatric Oncology Unit of a Tertiary Center in Ghana

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Background/Objectives: From 1998 to 2015 about 1550 new cases were registered at the Paediatric Oncology Unit (POU) of the Komfo Anokye Teaching Hospital (KATH) in Ghana

with 614 registered from 2010 to 2015. Our goal was to review the clinical case notes marked as "death" stored at the POU, KATH from January, 2010 to December, 2015.

Design/Methods: Data was retrospectively extracted from archived clinical case notes and stored electronically from January, 2010 to December, 2015. Data was analysed with STATA IC 12.0[®] software.

Results: Overall, 155 clinical case notes were found and archived as "died" from which data was extracted. The overall top 5 oncological diagnoses included Burkitt Lymphoma, 38%; Acute Leukaemias, 21% (Acute Lymphoblastic Leukaemia, 14% and Acute Myeloid Leukaemia, 7%); Retinoblastoma, 7%; Neuroblastoma, 6%; and Wilms Tumour, 5%. The others were Non-Hodgkin Lymphoma, 4.5%; Rhabdomyosarcoma and Nasopharyngeal Carcinoma, 3% each. 6.5% of cases lacked any oncological diagnoses. The clinical causes of death were not indicated for almost all the cases reviewed. Mortality per total cases was 10% with highest in 2014 (4%) and lowest in 2010 (1%) with 3% in 2011 and 2% in 2012, 2013 & 2015. Mean age was smallest (67months) in 2010 and highest (90 months) in 2015. The average duration of clinic contact from first and last visits to documented time of death were as follows:

Year Under Review	Duration of Clinic Contact/Days	Duration Between Last Visit and Death/Days
2010	49	15
2011	75	8
2012	71	16
2013	128	78
2014	164	42
2015	194	148

Conclusion: Burkitt lymphoma, Acute Leukaemias and Retinoblastoma underlie most deaths in POU, KATH. The mortality rates were well below figures available in literature. We suggest effective documentation of clinical causes of death and improved storage of data electronically, for the development of interventions to reduce childhood cancer mortality.

P-0288 | Disparity in Outcomes for Adolescent and Young Adult Patients Diagnosed with Paediatric Solid Tumors Across Four Decades

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Background/Objectives: Cancer mortality is a leading cause of disease-related death in the adolescent and young adult (AYA) population. Compared to older and younger patients, AYA patients often experience worse cancer specific outcome. Here, we compare AYA and paediatric overall survival (OS) in the most common paediatric extra-cranial solid tumors.

Design/Methods: Using the U.S. Surveillance, Epidemiology, and End Results (SEER) database, we studied patients age 0-39 years diagnosed with Ewing sarcoma, neuroblastoma, osteosarcoma, rhabdomyosarcoma, and Wilms tumour.

Results: There were 12,375 patients age 0-39 years diagnosed between 1973-2010 (8,247 paediatric and 4,128 AYA patients). AYA patients with rhabdomyosarcoma and Ewing sarcoma were more likely to present with metastatic disease. OS was significantly worse in the AYA cohort for all tumour types ($p < 0.001$) with the exception of osteosarcoma ($p = 0.29$). Across two treatment time periods (1973-1989 & 1990-2010), there was a significant improvement in 5-year OS in all tumour types with the exception of rhabdomyosarcoma, however AYA patients continued to experience worse OS in the modern treatment cohort with the exception of osteosarcoma patients. Multivariate analysis using Cox proportional hazards model showed AYA age group to be associated with worse OS in Ewing tumour, neuroblastoma, rhabdomyosarcoma and Wilms tumour independent of the presence of distant disease and advances in treatment over time.

Conclusion: For the most common paediatric extra-cranial solid tumors, AYA patients experience significantly worse OS than paediatric patients. While improvements in therapy have led to gain in survival for paediatric patients, with the exception of osteosarcoma, AYA experienced no increase in survival over the study period. Our findings are unique in comparing outcomes of five common paediatric solid tumors in the AYA and paediatric cohorts in large number of patients over four decades. This investigation demonstrates the importance for further research in the AYA population.

P-0289 | Trends in Cancer Incidence among Adolescents and Young Adults (AYA) in Sao Paulo, Brazil, 1997-2010

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Background/Objectives: This study aimed to analyze trends in cancer incidence among adolescents and young adults (AYA) (15-29 years) in São Paulo, Brazil, in the period from 1997 to 2010.

Design/Methods: This is an ecological time-series study, which used cases reported to the population-based Cancer Registry of São Paulo, Brazil, classified according to Birch & Alston classification. Age-standardized (world population) were reported for every 100,000 inhabitants, according to group and gender. Annual percentage changes (APC) were calculated using

the Joinpoint method, with the calendar year as regressor variable. The null hypothesis that $APC = 0$ was rejected when $p < 0.05$.

Results: During the study period, 14,011 cases of cancer among AYA were registered in São Paulo. There was a non-significant decline in the incidence of all malignancies in men ($APC = -1.04\%$, 95% CI $-2.76; 0.71\%$) and a significant increase in women ($APC = 2.55\%$, 95% CI $0.71; 4.42\%$). Among males, there was a significant increase in the incidence of carcinomas (except skin) ($APC = 4.60\%$, 95% CI $1.95; 7.33\%$) and a significant decline for leukaemias ($APC = -8.46\%$, 95% CI $-11.36; -5.46\%$), CNS tumors ($APC = -6.77\%$, 95% CI $-10.05; -3.36\%$), and bone tumors ($APC = -6.42\%$, 95% CI $-10.16; -2.53\%$). Among females, there was a significant increase in the incidence of carcinomas (except skin) ($APC = 4.95\%$, 95% CI $2.27; 7.70\%$) and unspecified malignant neoplasms ($APC = 8.32\%$, 95% CI $4.04; 12.76\%$), and a significant decline in the incidence of CNS tumors ($APC = -6.87\%$, 95% CI $-10.76; -2.81\%$), bone tumors ($APC = -7.30\%$, 95% CI $-10.99; -3.45\%$) and soft tissue sarcomas ($APC = -4.74\%$, 95% CI $-8.00; -1.37\%$). No significant trends in incidence were observed for lymphomas and skin cancers.

Conclusion: Distinct trends in cancer incidence among AYA were observed in São Paulo, Brazil, including increasing rates of carcinomas among women. These patterns and trends must be analyzed in order to tailor better strategies for cancer prevention and control in adolescents and young adults, more adequate their specific needs.

P-0290 | Advancing Parental Age and Risk of Solid Tumors in Childhood: Evidence from a Case-Control Study and A Meta-Analysis of Epidemiological Studies

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Background/Objectives: Advanced parental age has been suggested as a risk factor for childhood cancer in several observational studies; however, the existing results are inconsistent. We conducted a case-control study and a subsequent meta-analysis to examine an association between parental age and childhood solid tumors.

Design/Methods: We conducted a hospital-based case-control study (310 cases/620 controls, matched by age and gender). Risk estimates comparing categories of advancing parental age with and without adjusting for possible confounding factors were calculated. We performed a comprehensive meta-analysis researching the association between parental age and childhood solid tumors (retinoblastoma, non-Hodgkin lymphoma, hepatoblastoma, Wilms tumour and brain tumors) in PubMed, LILACS, SciELO, Scopus and the Cochrane Library. The initial electronic database search identified 516 citations and according to eligibility criteria 15 articles were included in the meta-analysis (21,524 cases). Reference lists were thereafter hand-searched for additional articles. The result was assessed based on pooled odds ratios (ORs) with 95% confidence intervals (CIs). The quality of each study was assessed using the Newcastle-Ottawa Scale. This study was conducted in accordance with international guidelines for meta-analysis of observational studies (PRISMA).

Results: In our case-control study, the risk of childhood retinoblastoma was significantly higher among children of mothers aged >35 years (adjusted OR 1.21; 95% CI, 1.09-6.08) and significant trend with increasing mother's age was found ($p = 0.037$); whereas no association was found with other cancer types. There was a strong protective effect of increasing parity on risk of childhood solid tumors ($p = 0.0015$). Further meta-analysis did not show an association between mothers or fathers aged 35 years or over and risk of retinoblastoma, non-Hodgkin lymphoma, hepatoblastoma, Wilms tumour and brain tumors. No publication bias or heterogeneity among these studies were detected.

Conclusion: These findings provide strong evidence to date that advancing parental age is a not associated with an increased risk for childhood cancer in the offspring.

P-0291 | A Framework for the Development of System Performance Indicators for Adolescent and Young Adult (AYA) Cancer Care in Canada

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Background/Objectives: To develop a framework for identifying consensus-based indicators to monitor and evaluate the performance of cancer control systems pertaining to adolescents and young adults (AYA, ages 15-39 years) in Canada.

Design/Methods: AYA with cancer are a distinct patient population within oncology. Their unique biology and extraordinary psychosocial challenges, intrinsic to this juncture in life, renders their management complex. Metrics are important to address issues unique to this cohort and evaluate interventions in order to improve outcomes. A stakeholder working group has been assembled by the Canadian Task Force on AYA with Cancer to develop and report on indicators for cancer care in this age group. An environmental scan of the literature was undertaken, modifying the search strategy utilized by the Pediatric Oncology Group of Ontario (POGO) to develop childhood cancer indicators. The literature guided both the development of the framework and method for identifying indicators. The group brainstormed indicators based upon the AYA cancer care framework.

Results: The framework for indicator development was based on two multi-stakeholder workshops that developed principles and recommendations for AYA cancer care in Canada. The domains include: active care, survivorship, palliation, psychosocial, research, awareness, prevention and education. A total of 114 unique indicators were identified in the brainstorming exercise (e.g. proportion of AYA accrued to clinical trials; proportion of AYA referred to fertility specialist). A survey of group members will assess proposed indicators using three criteria: importance, relevance, and usability. A consensus meeting will be held to review results and produce a ranked list of indicators.

Conclusion: Involvement of multiple stakeholder groups in this process will ensure a comprehensive set of indicators, and enhance uptake of the indicators. The metrics developed will identify opportunities to improve quality of care and benchmarks to achieve improvement goals in AYA cancer control in Canada.

P-0292 | Medical Care for Children with Cancer in the Russian Federation

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Background/Objectives: The large size of the Russian Federation, different density of the child population in the regions require careful planning organization of cancer care for children and the rational use of available resources.

Design/Methods: Our study included reports of regional departments of health of 83 subjects of the Russian Federation for 2014.

Results: The highest incidence of malignant tumors (per 100 thousands aged 0 - 17 years) registered in the Lipetsk region - 21.7, the lowest - in the Republic of Tyva - 5.5. The number of patients with newly diagnosed in 2014 was the highest in the Central and Volga federal districts - 775 and 653. The smallest - in the Far Eastern Federal District - 138. The number of primary patients referred to the federal clinic, was the largest in the North Caucasus Federal District (NCFD) - 80%, the lowest - in the South - 32.5%, the largest number of doctors who do not have primary specialization in "Paediatric oncology", registered in the NCFD - 50%, the lowest - Urals - 14.2%. Total in Russia operates 51 children's oncology departments, while the number of beds is 2021. The number of doctors who treat children with cancer, is 390, of which 252 (64.6%) did not have a certificate. In 2014, 3378 children with cancer were registered, of which 1705 (50.5%) were directed for treatment in Moscow clinics. Features of high-dose chemotherapy, there are 36 (42%) of the 85 regions, radiation therapy - in 62 (73%) with the restriction of the lower limit of age (6 - 15 years), high-tech operations - only in the several clinics.

Conclusion: Requires further improving of high-tech medical care for children with cancer, the creation of regional cancer registers, certification of specialists and improving the quality control of medical care through the implementation of internal and external audit.

P-0293 | Epidemiology of Malignant Tumors in Children in Russia and its Provision of Medical Care (Doctors, Bedspace, Technologies): Analysis of Statistical Data for 2011 - 2015

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Background/Objectives: Cancer is the second most common cause of death in children. The organization of cancer care for children requires further reforming and rational use of available resources.

Design/Methods: The study investigated reports of regional ministries and departments of health of 85 subjects of the Russian Federation (RF) for 2011 - 2015. It was analyzed the morbid (newly diagnosed cases of cancer) of children aged 0-17 years, the provision of bedspace, doctors, diagnostic and therapeutic technologies.

Results: In 2011 - 2015 it was registered 3378 children with cancer. The average incidence rate in Russia amounted to 12.4 per 100 thousand of the child population, in the RF subjects index values ranged from 5.5 to 21.8. 1705 (50.5%) patients were sent to federal clinics. In total, in 2013 in Russia there were 51 children's oncology departments with 2021 beds (including beds in non-core departments), therewith, the provision of bedspace varied by FD from 0.40 to 1.13 per 10 thousand of the child population. Treatment of children with cancer was carried out by 390 doctors, 138 (35.4%) among them did not have a certificate of Paediatric Oncology. The provision of doctors varied by FD from 0.06 to 0.20 per 10 thousand of the child population. The availability of modern diagnostic tools in the RF remains at a relatively low level. As a result, 76.6% of all newly diagnosed cancers were stage III-IV.

Conclusion: It requires improving the organization of medical care for children with cancer and optimization of available resources depending on the density and size of the child population in different federal districts.

P-0294 | Small Steps Towards Bigger Goals: A Study of Demography and Outcome of Paediatric Cancer in a Peripheral Newly Established Resource Limited Paediatric Oncology Centre

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Background/Objectives: Pediatric cancer requires prolonged treatment and follow up which makes compliance an important factor for good outcome. Patients from peripheries in developing countries find it difficult to relocate to major cities, leading to high rate of abandonment of treatment. Here we have retrospectively analysed demography and outcome of paediatric cancer cases admitted in newly established peripheral paediatric oncology unit in a low income setting. We also analysed the Quality Of Life(QOL), psychological status and socioeconomic status of parents of 60 children diagnosed with cancer.

Design/Methods: Data of paediatric cancer cases admitted from 2011 to 2015 was analysed. In 60 parents of patients, socioeconomic status was assessed by Kuppuswamy scale, QOL by WHOQOL-Bref scale and psychological status by DASS scale. QOL and psychological status was compared with well matched controls constituted by parents of normal children.

Results: Ninetyone patients were admitted over period of four years. Median age was 5.7 years. Male to female ratio was 1.6. Leukaemias constituted commonest malignancy (58.2%), followed by brain tumours(6.5%), neuroblastoma(5.5%), Wilms tumour(5.5%), lymphomas(5.5%), germ cell tumours(5.5%), histiocytosis (4.4%) and the rest 8.8% were constituted by clear cell sarcoma, rhabdomyosarcoma, retinoblastoma, Ewing sarcoma and nasopharyngeal carcinoma. Event free survival was 75.8%. Eleven percent were defaulters, 6.6% expired and 5.5% relapsed. Out of the 60 patients, 76.6% belonged to lower socioeconomic status. Parents of these 60 cases had decreased scores in all domains of QOL and were significantly depressed, anxious and stressed as compared to controls.

Conclusion: Good outcome of paediatric cancer even in resource limited setting is achievable. Treatment abandonment rate was relatively lower probably due to involvement of proactive parallel social service personnel right from the time of diagnosis. This study highlights that decentralised cancer care centres can effectively pave the way in reducing paediatric cancer mortality in large diverse country like India.

P-0295 | Malignant Solid Tumors in >8,000 Mexican Children and Adolescents. What have We Learned?

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Background/Objectives: Cancer in Mexico is the second leading cause of death in children 5 to 14 years. About 6,000 children are diagnosed every year, with >2,300 annual deaths.

We aim to describe the epidemiology of solid tumors in Mexican children over an 8-year time frame.

Design/Methods: Newly diagnosed malignant solid tumors registered at the National Childhood Cancer Registry and/or Popular Insurance database between 2008 and 2015 were selected. For incidence calculation, population below age 18 was obtained from official records at the Health Informatics Office. Tumors were classified according to ICC-3. Overall survival and abandonment were calculated through Kaplan-Meier.

Results: We enrolled 8,197 cases (53.5% males).

Incidence increased from 3.36 in 2008 to 4.60 in 2015 (0.166/year, p<0.001).

Age: younger than one year 10.4%, 1 to 4 - 32.1%, 5 to 9 - 20.2%, 10 to 14 - 23.0%, and 15 to 17 years 14.4%.

Tumour type: Brain and other central nervous system 24.7%, germ-cell 17.7%, bone 12.2%, soft tissue sarcoma 11.4%, retinoblastoma 10.0%, renal 8.6%, neuroblastoma 5.2%, liver 4.8%, carcinoma/melanoma 4.2%, and others non-specified 1.2%.

Only 38.6% of cases had stage of disease recorded at diagnosis. Assuming this sample is representative for the whole group: Stage I 14.4%, II 21.0%, III 36.8% y IV 27.8%.

Abandonment one year after diagnosis was 6.3% (95%CI: 6.1%-6.4%). Recurrence rate 1, 3 and 5 years after diagnosis was 2.1%, 4.6% y 4.9% respectively.

Five-year overall survival was 49.9% (95%CI: 47.2%-52.7%).

Conclusion: The registered incidence of childhood cancer in Mexico has consistently increased over the past 8 years. Distribution by age and type of tumour is comparable with other international reports.

Since 65% of cases are diagnosed in advanced stages of disease, survival remains suboptimal. Early detection and effective access to care are mandatory to improve outcomes.

Further studies of epidemiological and surgical factors affecting survival are needed.

P-0296 | Technology for Global Health: A Proposal to Reduce the Gap in Childhood Cancer

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Background/Objectives: Mexico: Cancer is the leading disease-related cause of death between 5 and 14 years, with 6,000 new cases and 2,300 annual deaths. Average time to diagnosis: 8 months. 65% of cases diagnosed in advanced stages of disease. Five-year overall survival: 49%.

Design/Methods: Areas of opportunity were defined from >18,000 cases analysed from the National Childhood Cancer Registry (2008-2015).

We propose a technology-based model for early detection, effective access, and standards of care through education and research.

Results: e-DOC is an ecosystem for early detection and effective access to childhood cancer care, based on data collection, disease prevention, optimal treatment, research, and communication.

A platform allows capture of cases into a Big-Data with demographic, epidemiological, clinical, and financial information. Performs real-time analytics via artificial intelligence (Watson Oncology - IBM™). Trends in incidence, time to diagnosis, variability, and outcome disparities represent the substance for decision-making.

A digital model provides primary prevention through education on healthy lifestyles at schools, and secondary prevention through on-line courses in early detection for healthcare personnel.

Users communicate, get support, share information, and find available resources through a specifically designed app. Caregivers get useful information to identify signs and proceedings, while primary physicians get support for diagnosis and referral.

Hospitals get financial aid, quality control, education and research through twinning programs with international allies, and support from the government and civil organisations.

Results obtained favor research in epidemiology from the Big Data, education from the schools platform and medical courses, basic, clinical, and translational research from the accredited units.

The ecosystem is monitored through indicators such as number of cases diagnosed at early stages of disease.

Conclusion: Early detection and effective access to care are essential to improve results. If the model proves useful to decrease mortality through education, early detection and optimal care, it can potentially be replicated anywhere at a very low cost.

P-0297 | Are our Referral Pathways Suitable for Children with Suspected Cancer?

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Background/Objectives: Children with suspected cancer in the UK are referred for specialist review via the "two week wait" (2WW) pathway. This has been shown to be a poor use of resources as very few children referred through this system have cancer. Concurrently, children who do have cancer can experience delays in diagnosis which can impact on their outcomes. New guidance from the National Institute of Health and Clinical Excellence (NICE) is an attempt to improve this pathway. We conducted a service evaluation to establish the patient journey before children with suspected or confirmed cancer reach oncology services.

Design/Methods: We conducted a retrospective case note review of referrals to a single centre in England in 2014. This included children aged 0 – 16 years referred via the 2WW pathway for suspected cancer. The notes of all children with a confirmed diagnosis of cancer during the same period were also reviewed. Children referred directly to other specialities with suspected cancer (e.g. surgery/maxillo-facial surgery) were excluded.

Results: Seventeen children had a confirmed diagnosis of cancer: only seven were referred from primary care (four via the 2WW pathway, and three emergency referrals). Delays occurred in presenting to health services, and the primary clinician decision to refer to oncology. The most common reason for referral via 2WW was lymphadenopathy; however, children with cancer more often presented with fever, lethargy, and general malaise. Thus a high index of suspicion was required before children were referred to specialist services.

Conclusion: The 2WW pathway does not add value to the patient journey of children with cancer, and may divert attention from other referral routes. Delays still occur in presentation to, and referrals from primary care. This may reflect the non-specific presentation of childhood cancer. An improved awareness of the features of childhood cancer amongst families and non-specialist practitioners could improve this situation.

P-0298 | Complementary and Alternative Medicine Use in the French Paediatric Oncology Population: Survey in Two Centers

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Background/Objectives: The use of Complementary and Alternative Medicine (CAM) in children with cancer is commonly used. However, studies and data on this topic are still scarce in France.

Design/Methods: Our aim was to investigate the prevalence of CAM usage in paediatric cancer patients and describe the modality of use. Our study population comprised children and young treated in two French centers (Paediatric oncology Nantes, Paris) from 2011 to 2012. An anonymous self-administered questionnaire was addressed to families and data were collected from them and from the medical record.

Results: Out of the 202 patients selected, 111 families answered (55%). Fifty-four (48.6%) of respondents used CAM for their child during the treatment period. Forty-seven (87%) patients used CAM during the initial therapy of cancer. Thirty-two (59.3%) of them had discussed their CAM usage with health professionals, whose 25 (75.8%) with their child's physician. The three most common therapies used were homeopathic medicines (75.8%), chiropractic (31.5%) and faith healing (42.6%). The main reason for the use of CAM was to control conventional treatment side effects (85.2%). Overall perceived satisfaction was rated 7.4/10. A majority of CAM users (98%) would recommend CAM use to other families. The CAM use rate was significantly and independently higher if the parents used to use CAM before cancer diagnosis (OR=5.27 [2.19-12.68], p<0.001).

Conclusion: The widespread use of complementary and alternative medicines during paediatric cancer treatment is high. Although scientific evidence is limited regarding the effects, mechanisms of action and security of CAM. Research is necessary to improve the communication and council quality to families, optimize supportives cares and reinforce the pharmacovigilance.

P-0299 | Leveraging and Adapting Domestically Used Program Planning Tools to the Development of Sustainable Global Health Plans

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Background/Objectives: Program Purpose: The foundation of any successful and sustainable project is planning. Developed countries have long used planning methods in healthcare settings. Using prevailing tools facilitates the planning processes needed in global settings; although, some modifications may be necessary for cultural, strategic, political or other reasons. This is something that domestic healthcare programs must take into account as they extend their reach into global settings. Being an academic healthcare organization with 20 years' experience in domestic planning tool development and implementation in a very successful U.S.-based paediatric haematology -oncology center, we were able to review and modify our standardly used program planning tools as we applied them in global health program planning initiatives in sub-Saharan African programs.

Design/Methods: Adjustments that were made to well-used planning tools included ways to manage planning logistics across great distances with limited communication via a variety of technological approaches, relationship building over long distances with limited face-to-face interaction, and alteration of communication approaches. Additional modifications such as data gathering databases to catalogue large amounts of information rapidly during both offsite and

onsite assessment stages were implemented as well. In order to better habituate into the setting, logistics, and culture, the orthodox processes, order and methods of the steps used for planning required more adjustability. Although the infrastructures of a strong, sustainable plan were achieved, the organization, presentation and action plan required adaptation.

Results: The tactic taken to evaluate how to leverage and adapt the standard procedure reinforced the development of a strategy with a delivery method that, while different from the one used domestically, was befitting to the unique requirements of the stakeholders in the global setting.

Conclusion: The focus will be constant use, evaluation, improvement of planning tools, and training of more globally placed staff.

P-0300 | Adapting High-Income Country Standards to PODC: The Design, Renovation, and Implementation of a State of the Art PHO Facility in a Government Hospital in Malawi

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Background/Objectives: The article Worse than AIDS published in The Economist, March 1, 2014 states: "many developing countries have no trained oncologists, let alone a treatment centre". Central Malawi is an example of this challenge with no locally trained paediatric oncologist or dedicated services. The Malawi MOH, TCH, Baylor-Malawi, and AbbVie partnered towards the goal of improving facilities at Kamuzu Central Hospital (KCH) and providing dedicated PHO space and services.

Design/Methods: Our strategy was to adapt U.S. facility planning and renovation standards to local realities while stretching resources to maximize impact. We determined essential resources needed to provide state-of-the-art services including lab, pharmacy, infusion, exam and procedure rooms. We used common U.S. standards and approaches to planning and managing facilities projects including "punch lists" and progress and financial reporting. Challenges included the distance between U.S. and Malawi which impacted the ability to closely monitor renovation progress. Other challenges included variations in renovation vocabulary, standards, timing, and skill level, and determining operational sustainability and product longevity in the local environment. Adaptations to overcome these challenges included obtaining remote updates, field-modified solutions, modified tracking tools, and use of local products. Strong partnerships with key local stakeholders such as MOH, hospital matrons, local healthcare providers, community members, funders and supporters was the foundation of our strategy.

Results: Renovations started in October 2015. The first freestanding PHO Clinic in Central Malawi opened in February and a designated inpatient PHO ward opened in March. Services added include ultrasound, PHO pharmacy, and flow cytometry. All remaining paediatric ward renovations will be completed in June.

Conclusion: This renovation greatly benefited PHO care at KCH and was leveraged to improve all paediatric facilities. Cost savings were re-purposed to allow for additional improvements to the project.

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P-0301 | Hashimoto's Thyroiditis is Associated with Papillary Thyroid Carcinoma in Children and Adolescents

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Background/Objectives: Background. This study investigated the relationship between Hashimoto's thyroiditis (HT) and papillary thyroid carcinoma (PTC) in children and adolescents.

Design/Methods: We carried out a retrospective study of thyroidectomies performed during 2004–2014 at The First People's Hospital and the Tumour Hospital of Yunnan Province. The incidence and features of PTC and benign thyroid disease (BTD) in children and adolescents (age ≤ 20 years) and PTC in young adults (20 years < age ≤ 29 years) were compared.

Results: Results. We evaluated 272 consecutive thyroidectomies. Among children and adolescents with PTC, 13 cases were histopathologically confirmed as HT. Mean tumour diameter was smaller in children and adolescents with PTC than in those with BTD. Thyroid-stimulating hormone (TSH) level was abnormally elevated in a greater proportion of children and adolescents with PTC as compared to those with BTD or youths with PTC. The proportion of thyroglobulin antibody (TGAb)- and thyroid peroxidase antibody (TpoAb)-positive children and adolescents was higher in the PTC than in the BTD group. Among children and adolescents with PTC, 13 had HT as compared to two in the BTD group and nine among young adults with PTC. The proportion of children/adolescents with abnormally elevated TSH levels was higher for the PTC combined with HT group than for the PTC without HT group. A multivariate conditional logistic regression analysis showed that elevated TG and TGAb was an independent risk factor for PTC in children and adolescents.

Conclusion: Conclusions. HT is associated with an increased incidence of PTC in children and adolescents.

GERM CELL TUMOURS

P-0302 | Comparison of Gonadal and Sacrococcygeal Germ Cell Tumors in a Developing Country: The Children's Hospital Lahore Pakistan Experience

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Background/Objectives: Extracranial GCT comprise of 10% of solid tumors each year in Paediatric Oncology department of the Children's Hospital Lahore, the only public hospital in whole Punjab province providing free cancer treatment to children.

Design/Methods: Retrospective review of 100 patients with gonadal and Sacrococcygeal Teratoma (SCCT) enrolled between January 2011 – December 2015 was done. Data regarding their age, sex, and clinical classification, course of therapy, and outcome and role of MDT in these two groups analyzed. The therapy comprised of 4-6 courses of JEB.

Results: Total 100 patients with age ranging from <1 to 15 years (66% <5 yrs) were included. 53/100 originated from gonads and 47/100 had Sacrococcygeal teratoma (SCCT). M: F Ratio was 1:1.8, with females presented with advanced stages (**p-value=0.089**) and higher risk stratification (**p-value=0.003**) consequently more eventful course. 88% of tumors had size >5 cm and 70% stratified high risk. 49% had yolk sac tumour, 8% mixed malignant GCT, 8% dysgerminoma, 12% Mature teratoma, 7% immature teratoma and 12% unspecified GCT. 39% presented at stage IV, 46% with stage III and 15% with stage II. Advanced stages at presentation resulted in more eventful course in both groups, (**p-value=0.000**). Multidisciplinary team approach (MDT) was utilized in 70% cases with lesser events (**p-value=0.008**). Total 67% have completed treatment, 3% are on treatment, and 11% left against medical advice (LAMA) and 18% expired due to advanced stage, progressive disease and sepsis (**p-value=0.032**) with SCCT group with more deaths 27% (9%) and abandonment 15% (7%). Regarding events 30% had sepsis requiring hospital admission, 13% had recurrence after surgery alone, 11% had obstructive uropathy, 5% had neurogenic bladder and bowel and 4% had relapse after surgery and chemotherapy (**p-value=0.044**).

Conclusion: Decreased survival 58% (76%), increased abandonment and expiries in SCCT group as compared to Gonadal group can be improved by structured MDT and close follow up specially in female patients.

P-0303 | Clinical-Pathological Characteristics of Germinal Cell Tumour in An Ecuadorian Hospital

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Background/Objectives: Germ cell tumours are a heterogeneous group of benign and malignant neoplasms commonly associated with abdominal pain and testicular mass. These tumours occur in all age groups from fetal period to adulthood, Corresponding only to 1-3% of paediatric cancer.

Design/Methods: Evaluate the distribution of germ cell tumour in childhood using clinical-pathological characteristics in a retrospective study from 2009-2013 in a paediatrics hospital in Quito, Ecuador.

Results: From a sample of 660 patients, fourty were diagnosed with a germinal cell neoplasm. 60% were males between 7 days and 13 years old. Mean age at diagnosis was 4 years old. According to histological classification, 57.5% of the tumours were benign, such as Mature Teratoma and 42.5% malignant.

Clinical characteristics of Mature teratoma were identified as 12 cases of extragonadal localization (52.17%), 83% were males. Eleven cases (47.8%) were found in testis (72.7%) and ovarium (27.3%). Younger patient in this group was a 7 months old boy and the oldest was a 13 years old boy. Most frequent extragonadal site was retroperitonium, followed by mediastinum and CNS.

We found 17 patients diagnosed with malignant teratoma, 82.4% were male (14 cases versus 3 female). Eleven cases (64.7%) were yolk sac tumours, located in testis, the rest were Leydig and granulose cell tumours.

Conclusion: Although the incidence of germinal cell neoplasms in our study was higher than the estimated worldwide (4.1%) the distribution was the same found in literature. Most germinal cell neoplasms identified in our study corresponded to benign tumors; only 42.5% was malignant. Extraembryonic tumour, Yolk sac tumour of testis was the most common malignant pathology, males were the most affected group by cancer and female by teratoma mature.

P-0304 | Histo-Pathological Characteristics of Germinal Cell Tumour, A Descriptive Study

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Background/Objectives: Germ cell tumour are a heterogeneous group of neoplasm benign and malignant. The usually clinical presentation is testicular mass, abdominal pain. This tumours can occur in all age groups from fetal period to adulthood. Corresponded 1 to 3% of paediatric cancer.

Design/Methods: To evaluate clinico-pathological characteristics of germ cell tumour, in retrospective study from 2009 to 2013 in a paediatrics hospital in Quito, Ecuador.

Results: We found 40 patients, 24 men (60%), 16 woman (40%), between 7 days and 13 years old. Mean age at diagnosis 4 years old. According to histological classification 23 patients (57.5%) were benign as Mature Teratoma, and 42.5% malignant as Extra embryonic germ cell tumour.

Clinical characteristics of Mature teratoma showed 12 (52.17%) cases of extragonadal localization, occurring 83% in man, 16.6% in female, and 11 (47.8%) cases in testis and ovarium, 27.3% in man and female 72.7% respectively. Younger patient in this group was a boy 7 months

old, and oldest a boy 13 years old. Most frequent extragonadal site were retroperitonium, also presented in mediastinum, and brain system.

Of the 17 patients with a malignant teratoma, 14 (82.4%) cases were in male and 3 in female. In eleven cases (64.7%) a yolk sac tumour were found, Testis site principal affected. Leydig, and granulose cell tumour were the rest.

Conclusion: Most cases studied corresponded to benign tumour, only 42.5% was malignant as described. Extraembryonic tumour yolk sac tumour of testis most frequent as malignant pathology, man most affected by cancer and female by teratoma a benign tumour.

P-0305 | Clinical Characteristics and Survival in Girls with Ovarian Germ Cell Tumors (OGCT) at the Instituto Nacional De Enfermedades Neoplasicas (INEN) between 2008 and 2015

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Background/Objectives: Ovarian germ cell tumors (OGCT) represent about 4.1% of the paediatric neoplasms at the Instituto Nacional De Enfermedades Neoplasicas (INEN). The aim is our study is to determine the Disease-free survival (DFS) and overall survival (OS) in girls with OGCT at the INEN attended between January 2008 and December 2015.

Design/Methods: This is a descriptive, longitudinal and retrospective study. Thirty-three patients with OGCT under 15 years of age were seen in the study period; eight of them were excluded because inclusion criteria were not met. Patients received chemotherapy with bleomycin 15mg/m² and cisplatin 100mg/m² on day 1, and etoposide 150 mg/m² on days 1 to 3. The OS and DFS were evaluated with the Kaplan-Meier method.

Results: Between 2008 and 2015, 33 girls have been treated. Mean age was 11 years (range 5 to 14 years). The most frequent symptoms were abdominal pain and tumour in 81% and 85% of cases, respectively. The length of symptoms were between 1 and 12 months. The most common histologic types were mixed and dysgerminoma in 42% and 32% respectively. Patients presented in stage I in 12% of cases, stage II in 12%, stage III in 48% and stage IV in 28% of cases. Twelve patients had a relapse and 5 died. Five-year OS was 62%. In patients with optimal surgery, 5-year DFS was 92.9%; and those with suboptimal surgery 29.1% (p < 0.05). No significant difference was found in the DFS for histologic type, capsular involvement, vascular invasion, lymphatic involvement and stage.

Conclusion: Seventy-six percent of our patients have advanced stages at diagnosis, in our country, OGTC diagnosis carries a poor outcome due to probably advance clinical stage and suboptimal surgical approach. It is important to improve the promptness in the diagnosis and referral to the appropriate medical facility for treatment.

P-0306 | Paediatric Testicular Germ Cell Tumors (TGCT): 35 Years Experience at the Instituto Nacional De Enfermedades Neoplasicas (INEN) Peru

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Background/Objectives: Germ Cell Tumour represent 4.1% of paediatric malignancies at the INEN, of these 10% are of testicular location. The purpose of this study was to evaluate disease free survival (DFS) and overall survival (OS) for stages and lymphovascular invasion (LVI) in boys with TGCT between 1980 and 2014.

Design/Methods: Retrospective and descriptive study. Between January 1980 and December 2014, 134 boys under 15 years of age were diagnosed having TCGT; they are divided in two study groups, from 1980 to 2007 and from 2008 to 2014. Survival analysis was performed using Kaplan-Meier method.

Results: The median age was 27.2 months. Yolk sack was the most common histology (82.8%). Staging frequencies: I (56.7%), II (6%), III (15.7%), IV (21.6%). LVI was present in 19%, absent in 25% and no data in 56%. There was 24.7% abandonment in the first group, and none in the second one, 30.6% died from disease. The five year OS in group 1 was: Stage I and II 77.3% (95% CI : 66.3%-88.3%), III and IV 38.3% (95% CI : 22.2%-54.4%), and DFS for stages I and II 68.1% (95% CI : 56.1%-80.1%), III and IV 57% (95% CI: 37.6%-76.4%). The five year OS in group 2 was: Stages I, II and III (100%), IV 50% (95% CI: 19%-81%), and DFS: stages I and II 45.5% (95% CI : 19%-72%), III (100%), IV 58.3% (95% CI : 19.5%-97.1%). The five year DFS was improved when no LVI was present in both groups 73.8% (95% CI: 55.6%-92%) vs 25% (95% CI : 0%-55% p = 0.029).

Conclusion: There is marked improvement in the outcome of boys with TCGT over the study period, less abandonment and better survival. Boys with stage I and recurrence have an excellent overall survival after rescue chemotherapy. The presence of LVI is associated with a lower DFS and could be an important prognostic factor for these tumors as in the adult population.

P-0307 | Role Surgery in the Treatment of the Sacrum Area Teratoblastomas in the Children

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Background/Objectives: Assessment surgery efficiency of the combined therapy in children with diagnose of teratoblastoma in the sacrum area.

Design/Methods: There were controlled 22 patients during the 2010 to 2015, difference between female and male were 15 and 7 accordingly. Age variation was 4 month to 7 years, median age – 1 year 8 month. The primary tumour were determined after birth and verification of diagnose based on morphology and activeness of the markers (Alpha-Fetoprotein) in the blood. Volume of the tumour was from 60 to 5800 cm³, level of the AFP increased 10000 times than normal blood rate. All patients were accepted 2-4 cycle neoadjuvant chemotherapy with scheme of BEP (Bleomycin+etoposide+cisplatin) and performed radical tumour excision in the sacrum area. After surgery performed adjuvant chemotherapy till 4-6 cycle with scheme

of BEP or VEP (Vinblastine+etoposide+cisplatin) regarding to pathomorphosis of the tumour cell.

Results: After the combined therapy were revealed local recidivating of the tumour in 1 patient and long-term metastasis were 1 patient too. In 20 patients are still in the controlling and were not detected any metastasis and tumour recurrence.

Conclusion: The combined therapy with surgery in the sacrum area terblastomas is increased survival rate, keeping the non-metastasis and tumour recurrence period.

P-0308 | Primary Ovarian Tumors in Children: A Single Center Experience of 124 Patients

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Background/Objectives: Primary ovarian tumors are rare in paediatric age group and survival rates improved significantly recent years. We aimed to investigate clinical features and treatment results in children with primary ovarian tumors.

Design/Methods: Between January 1975 and October 2015, 124 girls with primary ovarian tumors were retrospectively evaluated. Clinical features and treatment results were recorded. Survival rates were estimated by using Kaplan-Meier method. The log-rank test was used to compare groups.

Results: Median age for 124 children was 11.0 year (0.73-17.63). The main complaint was abdominal pain in 85 patients (68.5%) and the most common sign was abdominal mass in 87 patients (70.1%). Ninety-three patients (75.1%) had total one-sided and five patients had bilateral salpingo-oophorectomy. The major histopathological subtypes were mature teratoma in 29 patients, dysgerminoma in 21, mixed germ cell tumors in 17, endodermal sinus tumour in 14, embryonic carcinoma in 13, and immature teratoma in 12 patients. COG stagings were stage I disease in 57.2%, stage II 10.4%, stage III 25.8%, stage IV 6.6%. Ten-year overall and event-free survival for 124 children were 82.5% and 76.3%, respectively. Age ($p < 0.017$), histopathological subgroup ($p < 0.001$), COG stage ($p < 0.003$), chemotherapy protocols ($p < 0.049$) were significant factors for survival. Patients treated with BEP protocol had better survival rates than others. Ten-year overall and event free survival rates for those treated with VAC regimen 66.7% and 50%, PVB protocol 57.1% and 42.9%, BEP protocol 82.5% and 78.5%.

Conclusion: The survival rates in children with ovarian tumors were comparable with other studies. Although patients treated with BEP protocol has better survival rates, for the patients with advanced stage, prognosis is poor. This should be a focus for further studies and improvement.

P-0309 | Super-Infection of Mature Ovarian Cystic Teratoma in a Child: An Unusual Presentation

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Background/Objectives: Mature cystic teratoma is the commonest ovarian germ cell tumour. The presentation ranges from its asymptomatic nature to various complications like torsion, rupture and malignant change. We report a case with a rare complication in the form of super-infection in a young girl without any pre-existing risk factors.

Design/Methods: Case Report.

Results: Case report.

Conclusion: Infection in a mature teratoma is a relatively uncommon event. Despite the rarity, it should be considered in a female patient presenting with an abdomino-pelvic mass along with the abdominal pain and fever.

P-0310 | Mediastinal Germ Cell Tumour (GCT) – is Cure as Good as the Malignant Gct in Other Extra-Cranial Sites

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Background/Objectives: Mediastinal GCT is often a challenge to manage as they tend to present with life threatening complications. We described our experiences in a single paediatric center.

Design/Methods: Data on epidemiology aspects, clinical presentation, treatment and outcomes were collected from SCCR. A total of 10 cases were reviewed from May 2004 to April 2015.

Results: Mediastinal GCT accounts for 17.5% of 57 extra-cranial GCT during the 11 years period. The median age was 14 years (2 to 17.3 years) and male: female ratio was 9:1. All had advanced Stage 3/4 disease. Two patients had Klinefelter syndrome and one had multiple congenital abnormalities. The most common presentation was cough more than 2 weeks in 8 patients. 50% patients required HD/ICU for oxygen support and monitoring on admission; of these 2 had pericardial effusion.

Eight patients had significant raised alpha-fetoprotein and/or beta human chorionic gonadotropin, sufficient to make a diagnosis of malignant GCT. The other 2 had teratoma with seminoma underwent upfront surgery. All had curative chemotherapy treatment except for the child with multiple congenital abnormalities with global retardation. The chemotherapy regimens were Carboplatin/Cisplatin, Etoposide and Bleomycin. Five had neoadjuvant chemother-

apy followed by surgery. The upfront surgery was performed in 3; only one had complete resection with clear margins and the other 2 had residual tumors with phrenic nerve damage from surgery. These 3 patients received adjuvant chemotherapy. One patient received chemotherapy alone, relapsed one year after off treatment. This case was salvaged with myeloablative chemotherapy. None received radiotherapy.

The 5 yrs OS and DFS were 83.3% and 71.4% respectively. There was one death from second cancer.

Conclusion: MGCT is seen mainly in adolescents and often present with subtle symptoms like cough. Neoadjuvant chemotherapy is the best option to reduce morbidity of surgery in large tumour.

P-0311 | Ovarian Immature Teratoma in Childhood, Adolescence and Young Adulthood: A Single General Hospital Experience in Japan

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Background/Objectives: In adolescence and young adulthood (AYA), the potential for malignancy from ovarian immature teratoma (IT) has led to the standard use of chemotherapy even after complete resection of the primary tumour, but no chemotherapy is normally administered to children. We investigated the characteristics of ovarian IT in such generation.

Design/Methods: We reviewed the medical records 278 patients (range 0-29 years old) of extracranial germ cell tumors (GCT) treated from 1994 to 2015 at our institution.

Results: Of 278 extracranial GCT patients, only 7 patients (2.5%) had unilateral ovarian IT. Three patients (6, 9, 11 years old) were in childhood and 4 patients (18, 24, 26, 26 years old) were in AYA. One patient demonstrated that preoperative stage I disease in childhood and 3 in AYA. The rest of the patients were all stage III. All patients underwent primary salpingo-oophorectomy. The pathological analysis revealed Grade (G) 1: 1 case, G 2: 2 cases in childhood and G1: 1 case, G2 3 cases in AYA. Complete remission (CR) was achieved by surgery alone in the patients with Stage I in childhood and Stage I (G1) in AYA, and by surgery with 3 courses of adjuvant BEP chemotherapy in 2 cases of Stage I (G2) in AYA. One child with Stage III (G2) disease is still alive having "Gliomatosis Peritonei" at 6 years after surgery followed by JEB chemotherapy. One child with Stage III (G1) died due to "Growing teratoma syndrome" at 9 years after undergoing the 1st surgery and chemotherapy. In another Stage III (G1) patient in AYA, CR was accomplished after 3 courses of BEP treatment followed by surgery.

Conclusion: In order to obtain a good prognosis and reduce the incidence of any late effects due to chemotherapy, adjuvant chemotherapy may thus be omitted for AYA patients with stage I ovarian IT.

P-0312 | Pearls of Paediatric Pelvic Masses: Ovarian, Testicular, and Extragonadal Neoplasms

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Background/Objectives: Pediatric pelvic neoplasms have numerous etiologies and although the majority of these are benign, prompt evaluation is essential to diagnose and treat some of the more urgent pathologies. The diagnosis is typically not made with imaging studies alone, but with the incorporation of the clinical history, epidemiology, and key imaging findings. Therefore, it is essential for the astute radiologist to have a solid understanding of these and how they relate to each of the different etiologies. The goal of this presentation is to portray not only key imaging findings, but highlight essential associated characteristics of paediatric pelvic neoplasms to arrive at a succinct differential diagnosis that will guide the proper treatment plan. Neoplasms such as rhabdomyosarcomas, teratomas, and other germ cell tumors will be explored.

Design/Methods: The presentation will be divided into paediatric ovarian, testicular, and extragonadal neoplasms. The ovarian neoplasms will be subdivided into benign and malignant masses. The testicular and extragonadal neoplasms will be categorized by their cell of origin. The final portion of the presentation will contain a self-assessment quiz to test one's knowledge and further highlight key points.

Results: Pediatric pelvic neoplasms have unique characteristics on different imaging modalities and it is imperative to have proper knowledge of these to guide treatment. Each of the neoplasms have accompanying pearls regarding the clinical history, radiopathologic correlation, laboratory results, and physical exam. These will be expanded upon in the discussion of the individual pathologies.

Conclusion: The anatomy of the paediatric pelvis is unique and it is important to have an understanding of fundamental imaging findings as well as knowledge regarding the epidemiology, clinical history, and treatment. An astute radiologist will have extensive knowledge about each of these and how they correlate to the possible etiologies of paediatric pelvic neoplasms.

P-0313 | Analysis of Recurrent Sacrococcygeal Teratoma in Children: Clinical Features, Relapse Risks and Anorectal Functional Sequelae

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Background/Objectives: To determine the clinic features of patients with SCTs over the past 7 years, and to identify risk factors of recurrence SCTs and anorectal functional sequelae of these patients.

Design/Methods: A retrospective review of all patients of SCTs in our center between 2007 and 2013 was performed. We analyzed the recorded data on each patient concerning demographics, signs and symptoms, tumour markers, therapeutic methods, Altman classification, histology, complications, etc. Besides that, we learned patients' survival and made an evaluation of anorectal functional sequelae post-operationally through phone call.

Results: One hundred and five inpatients with a diagnosis of SCT were treated in our hospital during the study period, including 78 girls and 27 boys. The majority of tumors (46.7%) were type of Altman's classification. 104 cases underwent surgical resection, and 62.5% cases had a mature histopathology, the proportion of malignant teratomas rose with increasing age. 88 cases were followed up with a median duration of 51.2 months. 15 children developed recurrent SCTs with a median of 11.5 months postoperatively, most of them had an elevation of AFP levels. 4 recurrent children experienced second tumour relapse. We observed a statistically significant difference in overall survival rate through Kaplan–Meier method between relapsed (66.7%) and non-relapsed (94.4%). In univariate analysis, incomplete resection during the primary surgery and malignant histology were proven to increase risks of recurrence. 71 SCTs' patients completed the questionnaires for evaluating anorectal functional sequelae. 49.3% cases indicated to have at least one of the parameters reflecting bowel function (involuntary bowel movements, soiling, constipation) abnormal. For those recurrent SCTs patients, nearly half had unsmooth defecate with different severity.

Conclusion: Tumour recurrence affected the outcome of children with SCT, and in our research, incomplete resection and malignant histology were considered risk factors. Constipation was the main problem of anorectal functional sequelae for recurrent children.

P-0314 | Childhood Malignant Ovarian Germ Cell Tumors: A Single Institution Experience

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Background/Objectives: This study was to analyze the clinical characteristics and outcome of children with malignant ovarian germ cell tumors(MOGCTs), and to investigate the therapeutic strategy.

Design/Methods: All patients with MOGCTs in a single institution during the period January 2001–December 2012 were analyzed by the characteristics of patients, treatment and outcome.

Results: Eight-nine patients with MOGCTs were demonstrated with a median age 9.5 years (range, 0–15). Abdominal pain and abdominal distension were the most clinical presentations. Elevated AFP was observed in 78 cases (87.6%). Eighty-seven patients received surgery plus chemotherapy. The surgery procedures consisted of salpingo-oophorectomy plus omentectomy (n=39), salpingo-oophorectomy (n=39), oophorectomy (n=11). Five patients died: 3 from disease, 1 from leukopenic sepsis and 1 from disseminated varicella. The overall 5-year survival rate was 95.5% for all patients, 100% for stage I, 96.2% for stage II, 95% for stage III, 91.7% for stage IV and 71.4% for relapse patients, respectively. Forty-one out of forty-nine patients in puberty or reproductive age have regular menstrual cycles. Six patients had menostaxis, two patients required psychological input during the follow up period. Two patients delivered healthy infants without congenital defects.

Conclusion: The prognosis of malignant ovarian germ cell tumour is favorable. Surgery combined with platinum-based chemotherapy can improve curative efficacy and survival. Further investigation of novel and high dose chemotherapy regimens is needed for the patients with relapsed tumors. Sex hormone replacement therapy is not necessary for most patients received fertility-preserving surgery.

HISTIOCYTOSIS

P-0315 | Hemophagocytic Lymphohistiocytosis Syndrome : A Tertiary Care Centre Experience from South India

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Background/Objectives: HLH is an immune dysregulation phenomenon. It is been widely diagnosed owing to increasing awareness. The aim of this study is to identify the epidemiology, clinical and laboratory profile, treatment, underlying diseases and outcome in patients diagnosed with HLH at a paediatric tertiary care hospital.

Design/Methods: Prospective Longitudinal Observational study at Rainbow Children Hospital between August 2014 to January 2016.

Results: 60 children met the inclusion criteria & were diagnosed with HLH out of which 32 were males & 27 were females. 27 children (45.16%) were in age group from 31 days to 12 month. Most common clinical features were pallor (100%), fever (95%), organomegaly (93.2% with hepatosplenomegaly in 61% patients), CNS symptoms (42%) & rash (40.6%). Hyperferritinemia (98%), Anemia (96.6%), high LDH (96.5%), thrombocytopenia (88%), Haemophagocytosis in Bone-marrow (87.7%), Transaminitis (83%) and hypoalbuminemia (78%) were the predominant laboratory features. Infection (42/59) was the most common underlying disease associated with HLH with Dengue in 14 patients. Other causes were SLE (2), Organic acidemias (2 Methylmalonic acidemia & 1 Propionicacidemia), Post liver transplant B-cell lymphoma(1), Steven Johnson syndrome(1) with E. Coli sepsis. 3 patient had syndromic association – Chediak Higashi syndrome(2) & Griscelli syndrome(1). Out of 10 patients in whom genetic study for primary HLH was done 1 had MUNC mutation, 2 had Perforin mutation. 38 patients received dexamethasone, 14 patients received etoposide/cyclosporine, 1 patient underwent bone marrow transplant and 6 did not require any definitive treatment. Poor prognosis was

seen in 27% patient. On follow-up, 4 patients deteriorated, 3 were lost to follow-up and rest were well at the end of 6 month. CNS clinical features, platelet count <30000, Hb <7 gm/dl, peritoneal dialysis for renal failure, culture positivity and S. albumin <2.5 gm/dl were associated with poor prognosis.

Conclusion: Infection associated HLH has good prognosis if diagnosed and treated early. In resource limited countries genetic study in all patients may not be feasible. It should be done in patients diagnosed with HLH with <3 year age, CNS symptoms, consanguinity, family history of similar illness and no improvement after starting dexamethasone.

P-0316 | Reactivations and Sequela in Patients with Langerhans Cell Histiocytosis: Experience of a Tertiary Centre in Hong Kong

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Background/Objectives: Langerhans cell histiocytosis (LCH) is a rare disease with diverse clinical course. Despite improvement of survival outcome in the recent decades, reactivations and sequela of the disease remain a concern. This study aimed to provide information on reactivations and the long term outcome of local LCH patients.

Design/Methods: Medical records of the patients with diagnosis of LCH and being managed in our centre from year 1984 to 2014 were retrospectively reviewed. Data on the courses of illness, mortality, intervention, types and time of late events were collected and analysed.

Results: Seventy-one patients were included with a mean observation time of 11.8 years (median 10.3 years, range 0.9–31.3 years). Reactivation occurred in 24 patients (34%), with no statistically difference in incidence between patients who presented with single or multisystem disease. Reactivations were more common in patients presented with multifocal bone or central nervous system-risk lesions involvement, where reactivation occurred in 60% (n=12) and 69% (n=9) respectively. Most reactivations occurred in the first 2.5 years after diagnosis. One patient died after the first reactivation. Sequela related to LCH were present in 56% (n=39). Incidence of common sequelae as follows: Orthopaedic related 27%, pituitary dysfunction 18%, growth retardation 13%, cosmetic 10%, neurological 7% and hearing 7%. Reactivations were associated with higher rate of sequela, which occurred in 87% of patients (n=21/24) with reactivations compared to 38% (n=18/47) without, p<0.001. In particular, patients with reactivations had significantly higher incidence of diabetes insipidus, orthopaedic and neurological sequela.

Conclusion: Sequela were common after LCH, with reactivation as an important association. Neurological sequela could be particularly severe and debilitating. Vigilant long term follow up would be essential for optimizing patient outcome. Further studies on the treatment of reactivations and prevention of sequela are warranted.

P-0317 | LCH in Children of Northern Greece: 20 Years Experience

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Background/Objectives: Langerhans cell histiocytosis (LCH) represents a clonal proliferative disorder. Clinical presentation is heterogeneous as practically every organ or system may be involved.

The aim of this study was to evaluate retrospectively clinical characteristics and treatment outcome of children with LCH in Northern Greece.

Design/Methods: Clinical data from LCH cases that have been treated between 1985-2015 in our department were collected and studied retrospectively. LCH was confirmed histopathologically in all cases.

Results: Twenty six children with LCH (19 boys, 7 girls) with a median age of diagnosis of 5.8 years (range 6mo-16.5 ys) were found. Twenty of them had single-system disease (15 with single focal and 5 with multifocal) and 6 had multisystem disease (bones, lungs, pituitary gland, skin). Bones were most frequently affected: 25 out of 26 patients (pts) (18 of which had skull lytic lesions, 5 femoral and 5 iliac lesions). Central diabetes insipidus was observed in 3 pts, whereas lungs were involved in 2, and skin in 4. Most frequent symptoms were patients lower limb pain and secretory otitis, meanwhile in several cases LCH was accidentally diagnosed. Treatment comprised chemotherapy in 18 patients (LCH-I, LCH-II, LCH-III protocols), surgery in 11 pts, radiotherapy in 4 patients, while 1 patient didn't take any therapy. Relapse was observed in 7 pts, out of which 2 had multiple re-activations. Up to date 25 patients are alive (OS: 96.1%) and 1 died within a year from diagnosis (death was attributed to T-cell lymphoma).

Conclusion: LCH generally has a good prognosis, but unfortunately in some patients, especially with multi-system disease, can seriously influence life status and life expectancy.

P-0318 | Rosai-Dorfman Disease in Children, A Single Centre Experience

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Background/Objectives: Rosai-Dorfman disease (RDD) is a rare histiocytic disorder that usually presents with painless massive cervical lymphadenopathy. Extranodal involvement may occur in about 40% of patients. Pathologically, lymph nodes show massive accumulation of histiocytes and lymphocytes. The course of the disease is unpredictable but is usually self-limited. The disease may take chronic course with exacerbations and remissions. Treatment is indicated if there is vital organ compromise, otherwise watch and wait policy may be reasonable.

Design/Methods: Retrospective and descriptive review of paediatric patients diagnosed with RDD in our institution, from 2012 to 2015. Data regarding age, symptoms, nodal/extranodal involvement, treatment and outcome were collected.

Results: Five patients were identified. All were male, median age at diagnosis 5.3 years (range 2.4 – 11 years). Two patients had nodal involvement only, two had nodal and extranodal involvement (spleen). The remaining patient had extranodal disease only involving soft tissue in midline of frontal/labelar junction and extradural mass. One patient had constitutional symptoms. One patient was subsequently diagnosed to have autoimmune lymphoproliferative syndrome (ALPS) by genetic analysis and continues to be well. With a median of 16 months from diagnosis, three patients continue to have stable disease and required no treatment. One patient with extranodal disease had surgical resection of the lesion but developed a local recurrence and progressive disease. He was treated with a course of steroids with good response.

Conclusion: These cases treated at a single referral centre confirm what is published in the literature that RDD generally runs an indolent course. Surgery is indicated when there is vital organ dysfunction. Steroids and other agents can be used if there is disease progression or if surgery is not feasible. ALPS can present a diagnostic challenge.

P-0319 | Analysis of Prognostic Factors in Children with Hemophagocytic Lymphohistiocytosis: A Single Institution's Experience in Southern Taiwan

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Background/Objectives: Hemophagocytic lymphohistiocytosis (HLH) carries a high rate of mortality in children. Although an early diagnosis is crucial to decrease mortality, the treatments are often challenging.

Design/Methods: Children with HLH were retrospectively collected from March 2004 to April 2015 at our hospital. We reviewed medical records to analysis the related factors associated with survival.

Results: A total of 20 patients were included in the study, age ranging from 1.3 to 15 years at diagnosis. The median age of onset was 6.3 years. There were 8 boys and 12 girls. 95% (19/20) patients had fever at diagnosis. There were 16 patients had bicytopenia (80%). 8 patients had splenomegaly (40%). All patients had evidence of hemophagocytosis in bone marrow and hyperferritinemia. Their ferritin levels ranged from 563 to 146131ug/L (median: 15331ug/L). 7 patients had neurological symptoms/signs (35%). The most common causes were infections. 14 patients (70%) were diagnosed as infection-associated HLH, 20% rheumatic disease-associated HLH, 5% malignancy-associated HLH and other etiology in 5%. The treatment included intravenous immunoglobulin (IVIG) used in 3 patients (15%); IVIG + etoposide + corticosteroids in 1 patient (5%); IVIG + steroids in 3 patients (15%), HLH protocol was administered in 13 patients (65%). Patients with critical conditions required intensive care unit admission: 10/14 (71%) infection-associated, 3/4 (75%) rheumatic disease-associated and 1/1 (100%) malignancy-associated. One patient with infection-associated HLH (7%), and 2 patients with rheumatic disease-associated HLH (50%) died. There seemed to be better survival rate for patients who had fever less than 7 days than more than 7 days at diagnosis but without statistical significance. ($P=0.531$).

Conclusion: Children with HLH are at high risk for death. Early diagnosis and advanced treatment are required to improve the outcome in this life-threatening disease.

P-0320 | Clinical Features and Outcomes of 140 Childhood Hemophagocytic Lymphohistiocytosis

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Background/Objectives: To investigate the clinical features of hemophagocytic lymphohistiocytosis (HLH), to analysis the outcome of treatment in children.

Design/Methods: The clinical features at onset and outcome of treatment from 140 paediatric patients from January 2010 to December 2015 in our hospital were analyzed retrospectively. Genetic mutations were tested in 23 patients. PCR products of the coding exons included the adjacent intronic sequences for identification of splice-site variants.

Results: Among the 140 patients, 85 were males and 55 were females with a ratio of 1.6:1. The age of onset ranged from 1month to 15 years. 86 were less than 3 years (86/140, 61%). 3 were diagnosed familial HLH (FHL) within 23 cases. A total of 137 patients with secondary HLH (sHLH) were diagnosed, among which 110 cases were infection associated HLH including 33 EBV-HLH (33/110, 30%), 11 were associated with rheumatoid disorders and autoimmune diseases, 5 malignancies, 11 undetermined. 140 cases met inclusion criteria according to Histiocyte Society diagnostic guidelines HLH 2004. The most common clinical features included high fever, cytopenia, hepatosplenomegaly, and coagulopathy. 97.1% of patients showed an elevation of serum ferritin ($\geq 500\mu\text{g/L}$). 3 cases of FHL were treated with HLH 2004 protocol, all got remission and waiting for hematopoietic stem cell transplantation. Management for sHLH was mainly treated for underlying diseases and took into consideration using HLH 2004 protocol. EBV-HLH was treated initially with HLH 2004 protocol and the duration of the treatment depended on its response. 108 patients got remission (108/140, 77%) and 2 relapsed (2/140, 1.4%). The overall mortality rate was 22% (31/140).

Conclusion: HLH in paediatric patients has diversity of etiology. HLH has severe clinical feature and poor prognosis. Prompt diagnosis of HLH in children and identify the cause may be of great importance to treatment and prognosis.

P-0321 | Hemophagocytic Lymphohistiocytosis in Paediatric Malignancies- An Audit of 50 Consecutive Patients at a Tertiary Cancer Center

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Background/Objectives: Hemophagocytic lymphohistiocytosis (HLH) is an uncommon life-threatening inflammatory disorder and may be familial or secondary. Malignancies and their infectious complications frequently trigger secondary, or unmask familial HLH. Management guidelines for HLH were evolved excluding patients with malignancies. Best practices in this setting therefore remain undefined.

Design/Methods: Children below 15 years age with malignancy at a tertiary cancer center from Sept-2012 to Mar-2016, with fever and fulfilling modified criteria of HLH-2004 were analyzed retrospectively for demographics, disease characteristics and outcomes.

Results: Fifty children were analyzable. Males were predominant (M:F, 38:12). Fever, cytopenias and hyperferritinemia (Median: 48618 ng/dl) were universal. Other features were hypertriglyceridemia (82%), hypofibrinogenemia (16%), and bone-marrow hemophagocytosis (30%). Supportive criteria included elevated LDH (84%), transaminitis (85%), coagulopathy (48%), and cerebrospinal fluid pleocytosis (2/5 patients with neurological manifestations). Forty-five (90%) had hematolymphoid malignancies (ALL-30, AML-7, HD-6, NHL-2). Infectious agent was confirmed in 74% including viruses (62%, 15- Dengue, 8- CMV, 8- other viruses), and Bacterial (12%). Active malignancy was the trigger in 8%. Management was with dexamethasone alone (58%), dexamethasone+etoposide (19%) or complete HLH-2004 protocol (8%). Six patients died before specific therapy and 1 spontaneously improved. Anti-malignancy and supportive therapy were continued on merit. Mortality in the treatment groups was 29%, 37.5% and 67% respectively. Twenty-six (52%) patients were alive at a median follow-up of 4 months (1-42 months), 25 in remission. Death was attributable to HLH in 83% patients, most occurring within one month of diagnosis. Once in remission, 82% patients sustained it, while six relapsed. Of the latter, 5 died of HLH, 2 of which had Perforin deficiency. One patient achieved second remission.

Conclusion: HLH in paediatric malignancies may be indistinguishable from expected complications and is highly fatal. High index of suspicion aids correct diagnosis and management which involves deft adaptation of existing guidelines. Dexamethasone alone is an effective therapeutic option.

P-0322 | Paediatric Langerhans Cell Histiocytosis - Imaging Features and How the Radiologist Can Assist with Further Management

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Background/Objectives: Langerhans Cell Histiocytosis (LCH) is a rare histiocytic disorder, classically of the paediatric population but which may also affect adults. LCH affects up to 4.1 per million children each year in the UK and Ireland. Our goal in this presentation is to illustrate typical and atypical imaging features of LCH and discuss how these are relevant to further management.

Design/Methods: Our lady's children Hospital Crumlin (OLCHC) is the major tertiary referral centre for the evaluation and management of LCH in Ireland. Since 2005, sixty cases of LCH have presented or have been referred to OLCHC for further management.

Results: The average age of presentation was 4.9yrs old, with a range from 1 month to 14.5 years old, and a very slight male predilection. The majority of cases (80%, n=48) were unisystem, with approximately half of these cases (25%, n=15) were multifocal bone. The vast (90%, n=54) of all cases were biopsy proven. One fifth of all patients (n=12) presented with multisystem disease, with a younger average age (1.4 years old) than the overall cohort.

Conclusion: LCH is a rare histiocytic multisystem disorder predominantly affecting the paediatric population. Its typical and atypical features, with particular emphasis on the most clinically relevant radiological findings, are discussed.

P-0323 | Necrotising Palisaded Granulomatous Dermatitis in a Child with Acquired Hemophagocytic Lymphohistiocytosis – A Case Report

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Background/Objectives: Hemophagocytic Lymphohistiocytosis (HLH) is a potentially fatal hyper inflammatory condition caused by a highly stimulated but ineffective immune response. Various cutaneous manifestations have been described in association with HLH. Recognition and management of this rare disorder pose a unique challenge.

To describe a case with Epstein Barr virus (EBV) induced HLH with cutaneous granulomatous lesions.

Design/Methods: Case report.

Results: 2 year boy presented with fever of one month duration and hepatosplenomegaly. He had anemia, thrombocytopenia and leucocytosis with elevated serum LDH (1941 U/L), ferritin (>2000mcg/dl) and triglycerides (1345 mg/dl) and hypofibrinogenemia (150mg/dl). He had CSF pleocytosis and bone marrow evaluation revealed hemophagocytosis. Quantitative estimation of EBV DNA by RT – PCR was positive. Genomic workup for familial HLH was negative for PRF1, MUNC-13-4, STX11, and STXBP2. Natural Killer cell enumeration panel was normal. The patient was diagnosed with HLH with CNS involvement secondary to EBV infection and was treated with HLH 2004 protocol with etoposide, dexamethasone and cyclosporine.

Six months post completion of therapy, he developed multiple non tender, firm, nodular swellings over the hand and scalp. Recurrence of HLH was considered. Granuloma annulare and rheumatoid nodules were ruled out as a possibility. Biopsy of the skin lesions revealed necrotizing palisaded granulomas in a perivascular pattern with no evidence of hemophagocytosis, vasculitis or viral cytopathic changes. Immunohistochemistry showed CD1a and CD68 positivity highlighting the histiocytic population of the granulomas and negative for CD31 and S100. A diagnosis of necrotizing palisaded granuloma was made and he was treated with topical corticosteroids upon which the lesions completely resolved.

Conclusion: Palisaded necrotizing granulomas are an unusual presentation. Similar lesions were reported previously with *familial* HLH with MUNC-13-4 mutation but not in EBV associated HLH as in our case. Besides just the rarity of the disease, such unusual findings can often complicate the diagnosis of HLH.

LATE EFFECTS

P-0324 | Quality of Life among Cancer Diseased Children Survivors in a Developing Country: A Single Center Study in South Egypt

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Background/Objectives: Successful treatment of cancer has resulted in increased demands on survivors and had diverse effects on the Quality of life (QOL) of diseased children and their families. In this study we aimed to detect the QOL in survivors of childhood cancer in a cancer treatment center in south Egypt.

Design/Methods: A model of quality of life questionnaire containing aspects of physical, psychological, social, and spiritual well-being has been applied to illustrate the multidimensional needs of cancer survivors and the necessity of comprehensive care extending over the long term.

Results: A clear defective psychological and social support to the cancer survivors children and their families were detected.

Conclusion: Our data demonstrate the multidimensional needs of cancer survivors and the importance of comprehensive, multidisciplinary care. This may better be achieved by the cooperation between researchers, clinicians, and the true experts in that field.

P-0325 | Healthcare Burden among Young People with Cancer and Related Comorbidity: A Population Based Linked Cohort Analysis

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Background/Objectives: In 2012, the Children and Young People's (CYP) Health Outcomes forum emphasised the importance of improving young people's health. The burden of care for CYPs with cancer on healthcare systems is unknown, and this lack of data limits the ability to improve health-service. We used a specialist cancer register in CYP from the north of England linked to their hospital admissions data to analyse healthcare utilisation.

Design/Methods: 3,315 cases of cancer aged 0-29 years diagnosed between 1996-2009 and admitted between 1996-2011 in Yorkshire were identified. Hospitalisation and day rate ratios (HRR and DRR) were estimated using negative-binomial regression accounting for person-years of follow-up and other demographic characteristics. Median time to first admission after treatment completion was estimated by age and diagnostic group for cause-specific admissions coded according to ICD-10.

Results: Overall, admission rates decreased with increasing age at diagnosis (HRR=0.980%; CI: 0.975-0.984). Relapsed cases had double the admission of non-relapsed cases. Cases initially treated with chemotherapy alone had the highest HRR compared with other treatment. Cases with CNS tumours from more-deprived areas had significantly higher admission rates than those from less-deprived areas (24%, CI=6-45%). Females experienced significantly longer hospital-stays compared with males for leukaemia (DRR=19%; CI 10-42%). Cases with leukaemia and sarcoma had significantly longer hospital-stays among 0-14s vs 15-29s (DRR 2.27 and 1.03). Length of hospital-stay was significantly longer for the most deprived cases for CNS tumours (DRR 12%; CI 7-16%). Time to re-admission to hospital for majority of causes following completion of treatment was shorter for 0-14 year olds compared with 15-29s except for survivors of bone tumours.

Conclusion: Teenagers and young adults (TYA) with leukaemia and sarcoma stayed longer in hospital than children, but were less likely to be admitted in the first place. Children experienced cancer-related comorbidity earlier after completion of treatment compared to TYA.

P-0326 | Childhood Cancer and School Grade Performance in Adolescents

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Background/Objectives: It is important to study whether childhood cancer survivors experience learning problems during adolescence. We examined the association between childhood cancer and grades at age 15 in Denmark.

Design/Methods: We used nationwide Danish registries on school grades for all Danish children aged 15 in public schools during 2001-2014. We compared grades of childhood cancer survivors to all children who attended the same school at the same time. By applying a matched design we eliminated socio-demographic differences. Using regression models we estimated grade differences by subject and its correlation to cancer site and age at diagnosis. The available statistical precision allowed for an analysis of both rare cancer sites as well as the effect of age at diagnosis.

Results: The total sample size was 793,332 children. Mean age was 15.24 and 49.7% were girls. During the study period 1956 childhood cancer cases was observed, and 1320 had information on grades at age 15. We found significantly lower rank grades in all subjects for childhood cancer survivors overall compared to the background population (50 percentile). Most affected were survivors of CNS tumours (44 percentile), Neuroblastoma and Lymphoma (45 percentile) and Leukaemia (47 percentile), other malignant neoplasm (43 percentile) and Germ-cell tumours (48 percentile). Survivors from Retinoblastoma, Renal tumours, Hepatic

tumours, Bone tumours, Soft-tissue sarcomas and malignant epithelial tumour did not obtain lower grades. Learning problems was associated with young age at diagnosis for survivors of CNS tumours and Leukaemia.

Conclusion: The effect of childhood cancer on school grade performance in adolescents differed substantially between cancer sites and the largest effect was among survivors of CNS tumours and Leukaemia diagnosed at a young age. Increasing awareness children affected by cancer and special accommodations or services may help maximize the survivors learning potential.

P-0327 | Ovarian Cryopreservation (OCP) in Paediatric Oncology and Haematology: From Bench to Bedside

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Background/Objectives: Some long-term survivors of paediatric cancer or haematological diseases are at risk of developing premature ovarian failure (POF). OCP remains the only fertility preservation option in this population.

Design/Methods: Descriptive study. Clinical records of children undergoing OCP in our centre were analyzed. Study time period: October 2008 - December 2015.

Results: OCP was performed in 57 girls. Median age at the time of the OCP: 10.5 years (IQR 7.4 to 13.4). Underlying diseases: ALL (16), AML (8), MDS (5), Ewing sarcoma (7), Hodgkin disease (5), Soft tissue sarcoma (4), Germ cell tumour (3), Wilms tumour (2), Osteosarcoma (2), Sickle cell disease (2), Ovarian tumour (1), Disseminated medulloblastoma (1), Chronic granulomatous disease (1). Thirty-six patients (63.1%) underwent HSCT as part of their treatment. Total Body Irradiation and Busulfan based regimens were the most prevalent conditioning schedules (85%). Seven patients received pelvic radiotherapy: median dose of 34.9 Gy (IQR 19.8-50.4). Partial (90% cases) or entire laparoscopic ovariectomy was carried out without surgical complications. Oncological planned treatment was started without any delay. The tissue was successfully obtained at the same time as other surgical procedures in 69.7% of cases (60% venous central line insertion). Thirty-nine patients had previously received non-gonadotoxic chemotherapy; despite this fact normal count of primordial follicles was found in most samples (>90%). Current status: forty-three patients remain alive (complete remission), one patient is alive (progressive disease) and 13 patients died. Median follow-up: 1.9 years (IQR 0.5-3.9). Regarding gonadal function, although evaluable group is small (n=20), no ovarian activity after treatment was detected in 65% of patients.

Conclusion: In our series OCP was safely and efficiently carried out. Prior non-gonadotoxic chemotherapy may be considered if ovarian failure risk is high. The high rate of POF confirms the need to consider preserving fertility strategies even in very young patients.

P-0328 | Assessing Body Mass Index at Presentation, End of Treatment and in Aftercare within the Childhood Cancer Survivor Cohort. Would Earlier Intervention be of Benefit?

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Background/Objectives: Childhood cancer survivors are at increased risk of second Malignant Neoplasms (SMN's) and other chronic disease as a result of their treatment, which is further perpetuated if carrying excess weight (Blijdorp et al. 2012). In the general population obesity affects 60% of adults and 30% of children and is the second biggest preventable cause of cancer in the UK (CRUK, 2015). Research suggests that obese children are more likely to become obese adults (Aguilera et al. 2013). The aim of this study is to assess weight through treatment and beyond in an attempt to identify effective preventative strategies for survivors.

Design/Methods: A random sample of patients under regular follow up within the South West Aftercare (SWAftercare) service were evaluated for Body Mass Index (BMI) at point of diagnosis, End of Treatment (EoT) and at their most recent follow up appointment.

Results: Forty two patients were evaluated (26 male, 16 female). Their diagnoses included acute lymphoblastic leukaemia, central nervous system tumours and solid tumours. Nearly half (n=19) completed treatment with an unhealthy weight. Of this group 63% (n=12) went from a healthy weight at diagnosis to Overweight or Obese (OWO) at EoT and 37% (n=7) presented OWO and continued to be at EoT. Of these 19 patients 68% (n=13) continued to be OWO into Aftercare.

Conclusion: Some treatments can contribute to obesity through Hypothalamic Pituitary Axis damage. Although this is relevant, it does not explain the OWO patients who have not been exposed to obesity inducing treatments. Within SWAftercare, patients are offered weight management support, but this is too late to be addressing their unhealthy eating and physical activity behaviour. Earlier interventions around a preventative Multi-Disciplinary Team approach, ideally at the EoT, are recommended.

P-0329 | Assessing the Aftercare Burden of Paediatric Craniopharyngioma and the Need for Multi-Disciplinary Management: A UK-Based Single Centre Retrospective Observational Study

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Background/Objectives: Craniopharyngiomas are the most common childhood brain tumour and although benign, have potential for significant long-term morbidity and mortality. Although it is known that a multi-disciplinary team (MDT) approach is essential to aftercare

(UKCCSG Guidelines), we have no dedicated clinics for this group, and this study aims to address this unmet need and the implications for service development.

Design/Methods: A retrospective case note review was performed at 1 tertiary oncology centre. Notes review included assessment of presenting features and documented long-term morbidities including educational, social and medical issues. Three families were interviewed in depth about living with a child with a craniopharyngioma.

Results: Case notes of 17 patients diagnosed with craniopharyngioma between 1987-2015 were reviewed. Eight patients were treated with surgery and stereotactic radiotherapy, five with surgery and proton beam therapy and four with surgery alone. As expected, within this small cohort, 70.6% patients (n=12), across all treatment modalities suffered from panhypopituitarism, requiring quintuple hormonal replacement therapy. All patients suffered from additional morbidities requiring the input of more than 1 specialist from the MDT in addition to endocrine support. These non-endocrine morbidities differed depending upon treatment protocol. Traditionally reported factors such as tumour size and hydrocephalus at presentation had no correlation with post-treatment morbidity in this cohort.

Conclusion: The long term morbidity of craniopharyngioma presents unique challenges. Regardless of treatment modality, impact on quality of life is high and multiple attendances at hospital are required for follow-up. These patients would benefit from wellbeing support, a developing area in the aftercare of cancer patients, whilst addressing their medical, psychological and social needs. Despite this knowledge, no MDT clinic exists to cater for the supervision of these patients in the UK, and we hope to use this data and experience of pilot clinics to commission a service in the future.

P-0330 | Long Term Cardiac, Pulmonary and Thyroid Abnormalities in Survivors of Paediatric Hodgkin Lymphoma Treated with ABVD Regimen

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Background/Objectives: Pediatric Hodgkin lymphoma has excellent cure rates with available chemotherapy regimen. Long term toxicity is a major concern in these patients. ABVD has been mainstay of treatment in adult patients. Its use in paediatric patients is limited due the concern of long term toxicity. However this has not been adequately studied in this population.

Design/Methods: We evaluated 126 patients of Hodgkin lymphoma survivors treated with ABVD regimen in our institute with Multi Gated Acquisition Scan (MUGA) for left ventricular ejection fraction (LVEF), pulmonary function test (PFT) along with diffusion capacity of carbon monoxide (DLCO) and thyroid function tests to assess for cardiac, pulmonary and thyroid abnormalities.

Results: Median age at diagnosis was 11 years (range: 7-15 yr). One hundred and fourteen patients were male and nine were females. Based on modified Ann Arbor classification, 62 (49.2%) patients had early stage (IA, IB, IIA) and 63 (50.4%) had advanced stage (IIB-IV) disease. Median disease free interval of the cohort is 51 months (Range: 27-81 months). The median cumulative dose of doxorubicin received was 300 mg/m² (range: 200-400), bleomycin 110 mg/m² (range: 80-120). Eighty (64%) patients received radiotherapy to neck. One patient had mild decrease in LVEF (48%). FEV-1 was abnormal in 26(54.3%) patients with moderate decrease in 3 (3.7%) of them. DLCO was abnormal in 28(34.5%) patients and there was severe decrease in 2 (2.4%) patients. Thirty patients (37.5% of patients who received RT) had hypothyroidism; all of them had received radiotherapy to neck. Of them, 17 patients had subclinical hypothyroidism and 13 patients had clinical hypothyroidism. None of the patients with abnormal MUGA, FEV 1 and DLCO were symptomatic on follow-up.

Conclusion: Radiotherapy is associated with significant decrease in thyroid function. However, cardiotoxicity and severe pulmonary dysfunction was infrequent with ABVD regimen, and clinical cardio-pulmonary toxicity was not observed in any survivor.

P-0331 | Cognitive Behaviour Therapy in Childhood Cancer Survivors with Severe Cancer Related Fatigue

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Background/Objectives: Fatigue is a common and disabling late effect in cancer survivors and has a negative influence on quality of life. We retrospectively studied the effectiveness of cognitive behaviour therapy (CBT) in a cohort of childhood cancer survivors with cancer related fatigue, i.e. persistent (> 6 months) severe fatigue without a somatic or psychiatric explanation.

Design/Methods: Between 2009 - 2015 37 childhood cancer survivors (78% females; mean age 21 years, range 11-47) with cancer related fatigue were referred to our "Expert Centre Chronic Fatigue". The median age at cancer diagnosis was 11 years (0-17 years) and median follow-up time since cancer diagnosis was 10 years (3-34 years). Patients were offered CBT based on the treatment protocol used for adult cancer survivors. The primary outcome was fatigue severity (assessed by Checklist Individual Strength, fatigue severity subscale) while secondary outcomes were functional impairment (Sickness Impact Profile), psychological distress (Symptom Check List 90) and quality of life (EORTC QLQ-30, quality of life subscale). The assessment took place prior to and after CBT.

Results: By March 2016, 24 patients completed the CBT; 7 patients are still on CBT, 2 patients dropped out before completion of treatment and 4 patients decided not to start CBT. Of the 24 patients who completed CBT, 20 patients (83%) had a clinically significant improvement of fatigue (CIS fatigue < 35; p < 0.01, within treatment group Cohen's d: 2.53). Functional

impairment (p < 0.01) and quality of life (p < 0.05) improved significantly together with a decrease of psychological distress (p < 0.01).

Conclusion: In this pilot study severely fatigued childhood cancer survivors showed a clinically significant reduction in fatigue following CBT. Moreover: following CBT daily function and quality of life improved, and CBT reduced psychological distress. The efficacy should be further studied in a randomised controlled trial.

P-0332 | Late Renal Effects Related to the Abdominal Radiation of Paediatric Patients

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Background/Objectives: In an effort to understand late renal toxicity of paediatric patients undergoing abdominal radiation, we have studied clinical measures and kidney volumes up to three years.

Design/Methods: 100 paediatric patients undergoing abdominal radiation between 2010 and 2013 were included in this study, 50 treated with proton therapy and 50 with photon therapy. All patients were treated with normal fractionation. Clinical measures for renal function, including blood urea nitrogen (BUN), creatinine, and hemoglobin were recorded at the start of treatment and at one-year intervals. Kidney volumes for a small subset of 8 patients were contoured on follow up CT scans at one, two and three years. Correlations between measures for renal function and delivered dose to the kidneys were examined, as was the relationship between kidney volume and dose.

Results: The median patient age of the entire cohort at the time of irradiation was 7.8 yrs (range 1.1-19.2 yrs), and the median follow up time was 13.8 months (range 0.2-63.2 months). BUN, creatinine and hemoglobin values at one, two and three years were not correlated with total or ipsilateral mean dose. The median age of the patients in the smaller volume study was 4.2 yrs (range 2.6 -16.5 yrs). Changes in kidney volumes from baseline at one, two and three years were highly correlated with mean dose to the given kidney, with a dose > 14.5 Gy being associated with an average loss of 5.9 cc at 3 years and a dose < 14.5 being associated with an average gain of 23.4 cc.

Conclusion: In the present study, kidney dose was not associated with clinical measures for renal function, but this could be complicated by external factors, including the impact of chemotherapy. Higher mean kidney dose is associated with cessation of growth or loss of volume over time.

P-0333 | Second Malignant Neoplasms (SMN). Report from four Polish Centers

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Background/Objectives: Second malignant neoplasms (SMN) are the most serious complications of anticancer treatment. Since childhood malignancies have a cure rate of 80% and since there is a growing number of patients with SMN follow-up of survivors of childhood cancer is mandatory to detect SMN and the risk of such conditions. The aim of our study was to present already existing data on SMN collected from national database of SMN form 4 Polish centers.

Design/Methods: Gender, age, diagnosis, treatment of first disease, time from primary tumour to SMN, SMN type, treatment and outcome were analyzed by descriptive statistics.

Results: Seventy patients treated for first neoplasm between 1997-2012 were analyzed: 37 males; 33 females, median age at primary disease ranged from 2.5 to 17 years (median 5.5 years). 38 patients had a primary diagnosis of CNS tumour; 32 had other neoplasms: soft tissue sarcoma - 4; NHL - 4; HL - 3; Neuroblastoma - 3; Wilms tumour - 3; ALL - 3; PNET/Ewing - 3; retinoblastoma - 3; Osteosarcoma - 2; Hepatoblastoma - 2; GCT - 2. All patients were treated according to adequate protocols. Time from diagnosis of primary disease to SMN ranged from 3 months to 20 years (median- 6 years). The following SMNs were diagnosed: hematologic malignancies 35 pts (50.0%) (AML- 21, ALL-3, MDS-1, NHL-3, HL-1 pts), malignant brain tumors-19, osteosarcoma - 5, thyroid cancer - 4, and other - 13 (including: renal cell carcinoma, ovarian cancer, breast cancer, melanoma, leiomyosarcoma of the uterus, Wilms tumour). Out of 70 SMN patients 35 (50%) are alive from 1.5 to 28 years (median 8 years). One patient with ependymoma developed astrocytoma 15 years after the first diagnosis, and sarcoma as a third neoplasm 7 years later.

Conclusion: More data collected will enable to perform analysis of risk factors and to determine further direction of investigations.

P-0334 | Hearing Loss after Platinum Treatment is Irreversible at Long-Term Follow-Up in Non-Cranial Irradiated CCS, a DCOG Study

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Background/Objectives: Cisplatin and carboplatin are effective anti-neoplastic agents, but are also potentially highly ototoxic. To date, only scarce data is available on whether hearing impairment at discontinuation of treatment in platinum-treated children is reversible.

Design/Methods: In this study, we studied the reversibility of hearing impairment from discontinuation of treatment onwards since, to date, no long follow-up data from large well-documented cohorts are available as yet.

Results: We evaluated hearing loss in 168 patients treated with platinum (median total cumulative dose cisplatin: 480 mg/m², median total cumulative dose carboplatin: 2520 mg/m²) at discontinuation of treatment and during follow-up. Median follow-up time was 5.5 years (range: 1.0-28.8 years). At discontinuation of therapy, 61/168 patients showed hearing impairment according to Münster ≥ grade 2b. The results showed that none of the patients revealed significant improvement of hearing function (< grade 2b during long-term follow-up).

Conclusion: This indicates that hearing loss, defined by Münster classification, is irreversible and that audiological follow-up and clinical surveillance is required.

P-0335 | Accessibility to Mortgage and Insurance after Childhood Cancer

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Background/Objectives: In France, as in many western countries, insurance is required to obtain a mortgage. Individuals who want to be insured have to complete a health questionnaire, whose content varies according to the insurance company. Before 2016, French insurers could impose higher premiums or they could refuse to insure childhood cancer survivors, even if they had no chronic condition at the time of subscribing the contract. The purpose of this presentation was to describe the experience of survivors in accessing mortgage.

Design/Methods: A qualitative study was conducted in 2012 with French childhood cancer survivors participating in the Euro2K cohort, an international study assessing late effects. The qualitative sample was constructed using random selection. Of the 97 survivors contacted by telephone, 80 participated (82.5%). Face to face interviews covered the medical history of participants and the perceived impact of childhood cancer on their social well-being, including their experience in accessing mortgage. Interviews were tape recorded and transcribed. Content analysis was computer assisted.

Results: Participants were treated for solid tumors or lymphoma (age < 18). Time elapsed since diagnosis ranged from 27 years to 42 years (mean: 34). Twenty-eight survivors reported their experience in trying to obtain a loan or a mortgage. Of those, 8 survivors (29%) said that they had hidden their history of childhood cancer to the insurer because of negative expectations (premium, refusal, limits of coverage). Some of them were not aware of the legal consequences of their act. All of those who were asked to disclose their childhood cancer reported a feeling of injustice, whether they had problem in obtaining mortgage or not.

Conclusion: The face to face design of the study allowed for a thorough understanding of difficulties experienced by survivors, and highlighted risk-taking strategies. French survivors are now protected by the so-called "right to forgiveness", a law adopted in 2016.

P-0336 | Investigating What Resources There are for Patients and Families Post Cancer Treatment Who have Cognitive Behavioural Difficulty When Transitioning to Adult Care

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Background/Objectives: To create a safe pathway for patients with learning difficulty post cancer treatment when transferring to adult care, which gives carers and patients confidence in their future environment.

Design/Methods: I spoke to families about their concerns, used Ready Steady Go transition document to help prepare patients for adult services. I contacted regional hospitals to find out what services and alerts could be put in place such as hospital passports for these young adults. I discussed the types of Power of Attorney, how they can be obtained and implemented. I also investigated Acts such as The Mental Capacity Act and the Disability Rights Act and how these should be applied to our patients.

Results: Families had concerns as to who would care for their children in the future and where that care would be undertaken. They expressed sadness at having to face their own mortality but wanted to feel enabled to help their child plan for their future. They admitted needing signposting to information which would guide their decision making. Learning disability nurses are present in some but not all South West regional hospitals. Hospital passports are available in many forms both electronic and hard copy. These need to be completed and kept updated by the patient and their family.

Conclusion: Services are inequitable across the region at present. Patients with learning difficulty need a pack of information, which can be used with their families to prepare them for future admission to adult services. They need advice and encouragement to seek accurate information and to formalise decisions that they have to undertake, to implement their wishes for their future health, welfare and financial arrangements.

Pack to include websites, disability nurse contacts, hospital passports, details of types of Power of Attorney and information on the Mental Capacity Act and Disability Rights and Equality Act.

P-0337 | Assessment of the Thyroid Functions and Thyroid Lesions in Survivors of Hodgkin Lymphoma and Brain Tumour Who Received Radiotherapy to the Head and Neck Region

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Background/Objectives: Thyroid dysfunction and thyroid lesions can be seen after radiotherapy to the head and neck region. Here, we aimed to document thyroid dysfunction and thyroid lesions in children with Hodgkin lymphoma and brain tumors who received radiotherapy to the head and neck region.

Design/Methods: Study group consisted of 37 patients who were in complete remission at least one year after therapy in our department. Their demographic findings, treatment details including radiotherapy dosage, thyroid functions, (sT4, TSH), thyroid ultrasonography and fine needle aspiration biopsy results were recorded to the data form.

Results: In our study, seven children had subclinical hypothyroidism. Abnormalities of Thyroid ultrasonography were shown in seven children as well. Age under ten years, duration of follow-up, and radiotherapy dosage were effective factors on the development of hypothyroidism and abnormalities of thyroid ultrasonography.

Conclusion: In our study, seven children had subclinical hypothyroidism. Abnormalities of Thyroid ultrasonography were shown in seven children as well. Age under ten years, duration of follow-up, and radiotherapy dosage were effective factors on the development of hypothyroidism and abnormalities of thyroid ultrasonography.

P-0338 | Evaluation of Vitamin D Levels and Bone Mineral Density Measures in Survivors of Childhood Lymphoma and Solid Tumour

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Background/Objectives: As an increasing number of children with cancer are long term survivors, long term adverse effects of their primary cancer treatment become more important. Decreased bone mineral density (BMD) is one of the most common late effects. Vitamin D insufficiency has been also reported in children with cancer.

Design/Methods: The study included a total of 109 children (69 boys, 40 girls. Patients who were in remission for at least two years included. Demographic data at the diagnosis, gender, age, stage, therapy protocols were noted. Serum Ca, P, ALP, PTH and 25(OH)D values of patients were analyzed and bone mineral densities (BMD) were measured using dual x-ray energy absorption meter (DEXA).

Results: The mean ages of the patients at diagnosis and at the time of inclusion were 6.77±4.51 years (6 months-19 years), and 11.82±5.10 years (3-28 years), respectively. The mean follow-up period was 4.76±3.00 years (2-13 years). The mean follow-up period after cessation of the therapy was 3.56±2.76 years (2-12.5 years). Vitamin D levels were sufficient (>20 ng/ml) in 40 patients (%36.7), insufficient (15-20 ng/ml) in 34 patients (%31.2), deficient (<15 ng/ml) in 31 patients (%28.4). Overall%59.6 of the subjects was found to have 25(OH)D levels less than 20 ng/ml. There were no significant associations between 25(OH)D levels and diagnoses, gender, puberty, stage of the disease, RT, steroids, age of diagnosis, time of study, mean follow-up period and biochemical findings. The effect of sampling period on 25(OH)D levels, showed significantly lower rates during the winter period. Measurements of BMD by DEXA revealed that 41 patients had lower z-scores.

Conclusion: This study shows that bone health of children who survived after cancer therapy was significantly affected. Serum vitamin D results revealed increased frequency of vitamin D insufficiency in cancer survivors compared to healthy children population. Our study also showed increased rate of decreased BMDs.

P-0339 | Thyroid Gland Dysfunction after Allogeneic Hematopoietic Stem Cell Transplantation in Children and Adolescents

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Background/Objectives: To evaluate the frequency and type of thyroid dysfunction following allogeneic hematopoietic stem cell transplantation (HSCT) in children and adolescents transplanted at a single center.

Design/Methods: We performed a retrospective chart review of patients who received HSCT between 1994 and 2011 at the Children's University Hospital, Freiburg, Germany (n=265). Patients without thyroid disease prior to HSCT and a minimum follow-up of 1 year post HSCT were included in the study (n=161). Thyroid function was assessed by TSH and free T4 serum levels.

Results: Median age at HSCT and at last follow-up of the 101 males and 60 females was 10.1 (0.4-19.6) years and 15.9 (2.4-31.7) years, respectively. Median time from HSCT was 6.0 (1.3-15.5) years. Diagnoses included non-malignant disorders (n=52), myelodysplastic syndrome (n=64) and other hematologic malignancies (n=45). One hundred twenty patients had received myeloablative conditioning (MAC), including 34 who had been given TBI; 41 patients had

received reduced intensity conditioning (RIC). Twenty seven patients (16.8%) had developed thyroid dysfunction. Of the 18 males (66.7%) and 9 females (33.3%) 20 patients had elevated TSH only, while 7 patients had decreased free T4 levels. Thyroid dysfunction was significantly more common in patients who had received TBI (35.3% of patients) compared to those who did not (11.8%, $p = 0.003$). There was no statistically significant difference between patients with thyroid dysfunction who had received MAC (24/120, 20%) compared to those with RIC (3/41, 7%). All other investigated factors including patient's age, sex, diagnosis, and other transplantation's characteristics had not any significant impact on the risk of developing hypothyroidism.

Conclusion: Thyroid dysfunction is a frequent late effect in children following HSCT requiring diligent follow up. Despite of the recent methods of delivery and fractionation of TBI it is still a major risk factor for hypothyroidism after HSCT in children.

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P-0340 | Prevalence of Overweight, Obesity and Increased Abdominal Circumference in Childhood Cancer Survivors

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Background/Objectives: Childhood cancer survivors may present treatment-related complications such as endocrine alterations, obesity and metabolic syndrome, which are related to increased cardiovascular risk. The aim of the study is to assess the prevalence of overweight, obesity, and increased abdominal circumference (AC) in adult childhood cancer survivors.

Design/Methods: Retrospective analysis of patients attending the outpatient Nutrition Clinic of a Specialized Pediatric Oncology Center. All childhood cancer survivors that were out of treatment for at least two years and aging 18 years or more were included. Body mass index (BMI) and AC were classified according to the Brazilian Guidelines of Obesity.

Results: Eighty seven patients were (52% male) included. The most prevalent oncological diagnoses were: lymphomas (19%), osteosarcomas (16%) and Central Nervous System (CNS) tumors (16%). According to BMI, 50% of patients were eutrophic, 21% overweight and 28% obese. AC was increased in 38 (43.6%) of patients: 18 (47.5%) were men and 20 (52.5%) women.

Conclusion: A very high prevalence of overweight and obesity was observed among childhood cancer survivors, which may lead to long term effects on cardiovascular risk, specially in patients with increased AC. Close monitoring of health status and promotion of healthy lifestyle and nutritional habits will be key to reducing the risk of cardiovascular complication among this population.

P-0341 | Clinical Classification of Abnormal MRI after Treatment for Paediatric Acute Lymphoblastic Leukemia: Relationship to Neurocognitive Outcomes

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Background/Objectives: Approximately 50% of survivors of paediatric acute lymphoblastic leukaemia (ALL) experience one or more cognitive late-effect, yet most treating centres do not have access to neuropsychology services for this population. Predicting risk is therefore problematic and most referrals occur due to an adverse medical event or abnormal MRI scan. It is unclear if standard neuroimaging provides a viable marker for those at risk of cognitive morbidity, as such, a substantial group of survivors who may benefit from cognitive remediation may be overlooked. This study looked at the correspondence between clinical ratings of brain MRI scans and cognitive performance in children treated for ALL with chemotherapy-only.

Design/Methods: As part of a larger longitudinal study investigating neurological and neurocognitive outcomes following ALL treatment, MRI and neurocognitive data was available from the first assessment time-point (3 months after treatment) for 18 consecutive patients (56% male). Brain scans were categorised as normal or abnormal by a neuro-radiologist and cognitive outcomes (IQ, working memory, processing speed, verbal comprehension and perceptual reasoning) were classified as below average, average or above average using age-based norms.

Results: Three scans (17%) were rated 'abnormal' including white matter hyperintensities and low-lying cerebellar tonsils. The presence of abnormalities did not correspond with cognitive outcomes, with nine children with 'normal' appearing MRI scans demonstrating cognitive deficits on formal assessment.

Conclusion: The current study replicated previous findings that clinical report of neuropathology does not correlate with neurocognitive outcomes in ALL survivors. Clinical imaging reports reflect a brief overview of grossly abnormal anatomy, but are not sensitive enough to identify subtle brain damage or functional alterations that may correspond to cognitive morbidity. Studies using neuroimaging techniques sensitive to microstructural changes, such as diffusion tensor imaging, are required to assess the value of MRI scans in identifying patients who are vulnerable to developing cognitive late effects.

P-0342 | Genetic Risk Factors of Chemotherapy-Related Ototoxicity and Cardiotoxicity in Hepatoblastoma

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Background/Objectives: Cisplatin and anthracycline are the most widely used anticancer agents against hepatoblastoma (HB). The Japanese Study Group for Pediatric Liver Tumour (JPLT)-2 study (1999-2012) was to evaluate the efficacy of cisplatin/pirarubicin (CITA regimen) for HB. Avoidance of treatment-related ototoxicity, cardiotoxicity, and secondary malignancy effects is important to improve long-term outcomes for childhood HB.

Design/Methods: In JPLT-2 study, 385 HB children were eligible for inclusion. Among them, we evaluated late effects including ototoxicity, cardiotoxicity and secondary malignancy in 304 survived cases. And among these 304 patients, in 120 patients whose germline DNA samples were available under informed consent, genotyping was performed by using the Illumina Human Omni Express Exome-8 v.1.3 BeadChip (Illumina). A linkage disequilibrium (LD)-based single-nucleotide polymorphism (SNP) selection strategy was used to identify a minimal set of informative variants. Associations between SNPs and toxicities were assessed using logistic regression. Ototoxicity was determined by audiometry and/or auditory brainstem response. Cardiotoxicity was determined by standardized echocardiography.

Results: Among the 304 survived cases, 68 ototoxicity, 19 cardiotoxicity, and 11 secondary malignancies were determined. The dose of cisplatin and/or pirarubicin seemed to be correlated with their occurrence but not significantly. We identified inherited genetic variations in three SNPs including ACYP2 associated with ototoxicity and in two SNPs associated with cardiotoxicity. However, we did not find out the significant genetic variations in the cases with secondary malignancy.

Conclusion: The risk variant in these SNPs strongly predisposed these patients to hearing loss or cardiac failure using chemotherapy. These results point to new biology underlying the ototoxic/ cardiotoxic effects of platinum/anthracycline agents. We should pay biological assessment for next protocol avoiding the ototoxic/cardiotoxic effects of chemotherapeutic agents.

P-0343 | Japanese Childhood Cancer Survivors' Readiness for Care as Adults: A Cross-Sectional Survey using the Transition-Q Scales

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Background/Objectives: Childhood cancer survivors' (CCSs') readiness for adult care has not been evaluated in Japan. We conducted a cross-sectional survey of Japanese CCSs' readiness for long-term care as adults to examine transition barriers and facilitators in CCSs and compared the results to those of CCSs in Canada.

Design/Methods: Participants were selected from the Heart Link mutual-aid health insurance membership directory and the Childhood Cancer Frontiers Millefeuille. We conducted a cross-sectional survey (self-report questionnaire) via mail, using the TRANSITION-Q (Klassen et al. The development of scales to measure childhood cancer survivors' readiness for transition to long-term follow-up care as adults. Health expectations. 2015;18(6): 1941-55).

Results: In total, 268 questionnaires were collected by January 2016 (response rate: 42.5%). After confirming the reliability and validity of the TRANSITION-Q, we analyzed 243 questionnaires. After excluding questionnaires for CCSs aged <15 or >26 years, we compared TRANSITION-Q scores between Japanese and Canadian CCSs. Relative to that of Japanese CCSs, Canadian CCSs showed greater cancer-related worry for 4 items ($p < 0.001$) and preference for self-management in 3 items ($p < 0.001$). Japanese CCSs showed greater preference for self-management, relative to that of Canadian CCSs, in 5 items ($p < 0.001$). In the expectation scale, Japanese CCSs showed lower levels of expectation concerning adult care in 6 of 12 items ($p < 0.001$). Relative to that of Canadian CCSs, a significantly higher number of Japanese CCSs preferred to visit the same doctor for long-term care as adults ($p < 0.001$).

Conclusion: The results confirmed the reliability and validity of the TRANSITION-Q and showed that Japanese CCSs expressed fewer cancer concerns, but a higher number of Japanese CCSs preferred to visit the same doctor for long-term care as adults.

P-0344 | Barriers Regarding Survivorship Care in Childhood Cancer Survivors Who have not Received Recommended Follow-Up

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Background/Objectives: Despite the risk of long-term complications of therapy, only about 20-30% of childhood cancer survivors receive recommended follow-up for reasons that are poorly understood. The objective of this study was to assess barriers to receiving survivorship care in patients confirmed to never have attended a survivorship clinic visit.

Design/Methods: Eligibility included cancer at age <18 years in Connecticut during 2000-2012, ≥ 2 years off-therapy, currently cancer-free, fluent in English or Spanish, and no prior attendance at a survivorship clinic confirmed by the Connecticut Tumour Registry and medical records. Patients (or parents of minors) were administered a web-based survey asking about barriers to attending a survivorship clinic visit.

Results: Overall, 96 childhood cancer survivors (47% female; mean age at evaluation 15.9 \pm 6.1 years) were enrolled. Diagnoses included 49% leukaemia/lymphoma, 6% sarcoma, 8% brain tumors, 22% other solid tumors, and 15% other. Overall, 74% received chemotherapy and 36%

received radiation. Ninety-five percent of participants responded that at least one knowledge barrier was moderately to very important. For example, 79% indicated "I did not know that a specialty survivorship clinic was available," and 57% indicated "I did not think that I/my child was at an increased risk for any late complications." Seventy-seven percent cited at least one psychosocial barrier, e.g. 63% endorsed "I wanted to put my/my child's cancer in the past and move on," and 40% indicated "I did not want to know potential complications of my/my child's past cancer." Inconvenience related to travel distance (29%) and lack of insurance coverage (21%) were moderately or very important for only a minority of participants.

Conclusion: Our study suggests that knowledge and psychosocial concerns, including avoidance, were frequent barriers to following-up with survivorship care in long-term survivors. Logistical concerns were less commonly cited. Interventions to improve survivorship care must address these barriers.

P-0345 | Impact of Imatinib on the Linear Growth and Body Mass Index in Children with Chronic Myeloid Leukemia

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Background/Objectives: To study the effect of imatinib on height and body mass index (BMI) in children with chronic myeloid leukaemia (CML).

Design/Methods: Clinical records of 169 patients with CML below 18 years on Imatinib between 2008 and 2014 were collected retrospectively. Children in accelerated phase or blast crisis or who attained final height were excluded. Mean age at onset of puberty was taken as 12 years for both boys and girls. Height for age (HAZ) and BMI for age/gender ["z"-scores (BAZ)] were computed using WHO Anthroplus v1.0.4. HAZ and BAZ at baseline, 1st and 2nd time points were designated as HAZ1, HAZ2, HAZ3 and BAZ1, BAZ2, BAZ3 respectively. The median duration between baseline and 1st time point was 16 and 1st and 2nd time point was 11 months respectively. Mean "z"-scores across the groups were compared by repeated measures ANOVA and by gender and pubertal age with post hoc tests. dHAZ, the difference between HAZ1 and HAZ3 and dBAZ, the difference between BAZ1 and BAZ3 were calculated using WHO Anthroplus v 1.0.4. All tests were two-tailed and p<0.05 was considered statistically significant. Data analyses were performed using SPSS software v19.

Results: 137 patients were eligible for analysis. At the time of diagnosis, 38 were pre-pubertal and 99 were post pubertal. Overall means of HAZ1, HAZ2, HAZ3 were significantly affected before (p<0.0001) and after puberty (p<0.0001) and in both genders. Overall, means of BAZ1, BAZ2 and BAZ3 were significantly affected (p<0.005). Genderwise, BAZ1, BAZ2, BAZ3 were significantly affected after puberty both in boys (p<0.011) and girls (p<0.032) but not in prepuberty. dHAZ was significant for both genders irrespective of age group (z=-2.002, p<0.04) but not for dBAZ. When dHAZ was compared between pre and postpuberty it was significantly affected in boys (z=-3.748, p<0.0001) and girls (z=-5.021, p<0.0001). When dBAZ was compared between pre and post pubertal children, it was significantly affected in boys (z=-2.283, p<0.022) but not in girls (z=-1.366, p<0.172)

Conclusion: Our study showed significant growth deceleration in children with CML-CP on Imatinib, irrespective of gender or pubertal age, however, BMI was affected predominantly in pubertal children irrespective of gender.

P-0346 | Second Malignancies in Childhood Cancer Survivors

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Background/Objectives: The aim of this study is to assess the incidence and outcome of second malignancies (SM) in paediatric cancer survivors in a tertiary center in 25 years.

Design/Methods: 1500 childhood cancer survivors treated in the Istanbul University, Oncology Institute during 1990-2010 and followed up for at least 5 years from diagnosis were evaluated for second malignancies.

Results: 37 SM were identified in 34 survivors at a median of 7 years (1-17) from diagnosis (AML/MDS 3[1-8], solid tumors 9 [2-17] years). The primary diagnosis was sarcomas in 11 (5 rhabdomyosarcomas [RMS]), CNS tumour 6, retinoblastoma 4, ALL/MDS/lymphoma 8, neuroblastoma 3, nasopharyngeal sarcoma 1, disseminated 1. The SM were 12 sarcomas (8 osteosarcomas, 1 fibrosarcoma, 1 Ewing Sarcoma, 1 Kaposi sarcoma, 1 leiomyosarcoma), 8 AML/MDS, 4 thyroid cancer, 3 malignant nerve sheath tumors (MNST), 2 renal cell carcinomas (RCC), 2 breast cancers, 2 glioblastoma multiforme (GBM), 1 non Hodgkin lymphoma, 1 meningioma, 1 histiocytosis (LCH). Three patients developed two separate SM each. 19 patients had received radiotherapy: 12 developed solid tumors within the radiation field, 3 in proximity; 4 developed AML/MDS. 3 had prior HSCT. 16 survivors are alive at a median of 4 (1-18) years after SM, 14 with no evidence of disease (NED). 18 died at a median of 1(0.1-3)year. All with thyroid cancer, renal cell carcinoma, breast cancer; also 1 MNST, 1 LCH, 6 sarcomas are with NED, all were detected during regular surveillance.

Conclusion: The risk of SM in our series has increased with longer follow-up, (2.4 vs 1%, from 2011 to 2016), emphasizing the need for longer follow-up and regular surveillance which leads to early detection of SM, thus improved survival. Since, the risk of SM is associated with the cumulative dose of some chemotherapeutics, the radiation dose/field; using the most efficient and least toxic protocols is important.

P-0347 | Adaptive Behaviour as an Indicator of Psychosocial Status of Childhood Brain Tumours Survivors

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Background/Objectives: Physical, sensory and neuropsychological late effects associated with childhood brain tumors hardly affected psychological wellbeing, social functioning and life independence of survivors. Difficulties with operationalization of personal life satisfaction, tend to look for new approach to late effects of this growing population. The new way seems to be assessment of adaptive behaviour defined as the performance (not only ability) of daily activities required for personal and social sufficiency, and measured by the Vineland Adaptive Behavior Scales - expanded form (Vineland-II). Consists of 5 domains: communication, daily living skills, socialization, motor skills (gross and fine), maladaptive behaviour. Its covers the areas of late effects of childhood brain tumours.

Design/Methods: Psychological repeated testing and long-term observation was performed in 350 childhood brain tumour survivors treated with neurosurgery, chemotherapy and radiotherapy, to determine psychosocial late effects. Age at psychological diagnosis ranged from 6 to 26 years. The patients were examined using battery of neuropsychological methods and psychological interview. Analysis of medical history was also performed. From this group randomly selected 30 young adult survivors to assessment by the Vineland-II.

Results: In our sample patients present low scores in the all domains: communication, daily living skills, socialization, motor skills, with significantly low level of social contacts. Typical problems in this area: difficulties in appropriate expression of emotions, inadequate mimic and body language, problems with establish and maintain peers and personal relationships, low tolerance of frustration. An interesting problem emerging from research is the low level of changing motivation coexisting with dissatisfaction with life status.

Conclusion: The results of our study suggest that level of adaptive behaviour is a good indicator of psychosocial status this group of patients. Vineland-II is a useful and reliable tool to assess psychosocial late effects of cancer survivors as a group as well as a method to individual assessment.

P-0348 | Health Status of Childhood Cancer Survivors in Poland

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Background/Objectives: In the last 50 years improvement in survival of children diagnosed for cancer gave us the possibility to analyse late effects of the treatment. We evaluated the general health status and epidemiology of organ late effects in the cohort of Polish children and adolescents- cancer survivors.

Design/Methods: Analysis was performed in the cohort of 2,003 childhood cancer survivors, who were registered in national on-line database. In the registry the data on medical history of disease and treatment, physical examination and battery of other tests- biochemical, hormonal, immunological, radiological examinations and functional investigation were collected. The median age at the follow-up was 13.6 years, median time since diagnosis was 8.2 years. Accurate data were found in 1295 cases. Chemotherapy was applied in 447 cases (34.5%), only surgery- 12 cases (0.9%), chemotherapy and radiotherapy- 335 cases (25.9%), chemo-, radiotherapy and surgery- 396 cases (30.6%), bone marrow transplantation- 105 cases (8.1%).

Results: Normal function of all organs had 436 (21.7%) survivors, dysfunction of one or two organs- 532 (26.5%) and 1035 (48.2%)- abnormalities in three or more organs. In whole group, the symptoms of impaired cardiac function was most often observed- in 554 cases (27.7%). More than 20% survivors complained for deteriorated function of urinary system (502), digestive system (416), immune system (417), dental problems/difficulty with chewing (470); growth disturbances and/or obesity was found in 379 cases, thyroid dysfunction in 367 cases. Procedures connected with bone marrow transplantation caused the most frequent deterioration of function of respiratory tract (p<0.02) and endocrinopathies, such as thyroid (p<0.0001), gonadal (p<0.0001) dysfunctions and growth disturbances (p<0.0001).

Conclusion: High incidence of adverse late effects in cancer survivors indicates the need of systematic monitoring of their health problem. Multidisciplinary surveillance for early detection of organ dysfunction is needed.

P-0349 | Evaluation of Late Cerebral Vascular Complications in Cranially Irradiated Paediatric Cancer Patients with Magnetic Resonance Angiography

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Background/Objectives: Magnetic resonance angiography (MRA) is employed in diagnosis and treatment of cardiac diseases, stroke and vascular disorders. Cranial radiotherapy can be used as a component of treatment in some types of cancer in practice of paediatric oncology. Narrowing can occur in large cerebral vessels by effect of radiation and stroke risk may emerge at young ages. In this study, we aimed early diagnosis of cerebral vascular complications in patients who have been treated with cranial radiotherapy as a component of their treatment.

Design/Methods: The patients who had taken cranial radiotherapy before the age of 18 and in remission for at least 1 year were included in the study. The patients who are on treatment, treated without cranial radiotherapy, pregnant or breastfeeding mothers and the patients with impaired renal functions or known allergy of contrast material were excluded.

Results: Cerebral MRA examination was made for 50 patients who were consistent with inclusion criteria between November 2013 and November 2015. Abnormalities in 6 patients (12%) were determined in cerebral MRA. Narrowing in left cerebral artery, truncated appearance in distal part of right cerebral artery, occlusions in cortical superficial branches of right middle cerebral artery, decrease in calibration of cortical branches of left middle cerebral artery, thinner left internal carotid artery with occlusion in left middle cerebral artery and its branches and hypoplasia in left posterior cerebral artery segment P1 were the angiographic abnormalities. All patients were asymptomatic and all of them are under neurologic and radiologic follow-up.

Conclusion: Cerebral MRA is a non-invasive method of follow-up for late cerebral vascular complications in surviving paediatric oncology patients who had been treated with cranial radiotherapy as part of their cancer treatment.

P-0350 | Survival and Late Effects of Childhood Cancer: A Single-Center Experience

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Background/Objectives: The aim of this report is to know the evolution of children diagnosed with cancer in our center and to analyze survivors' late effects.

Design/Methods: Cohort study which included patients aged 0-15 diagnosed with childhood cancer from 1990 to 2011. Age at diagnosis, gender, type of malignancy, treatment received, events appearance (recurrence or exitus) and number, time of onset, type, severity and likely cause of sequelae were recorded. The screening for detecting late effects was made according to treatment received. Kaplan Meier survival analysis was performed.

Results: Two hundred and ninety-seven patients were analyzed (59% were male), with an average age of 5.8±4.3 years. The most frequent diagnoses were leukaemias (30%), central nervous system malignancies (18.2%), lymphomas (11.8%) and neuroblastomas (11.8%), soft tissue sarcomas (5.4%), germinal tumors (5.4%), bone tumors (4.4%), renal tumors (4.4%), and others (10.2%). Required surgical treatment 50.6%, received chemotherapy 74%, radiotherapy 14.9% and 14.6% hematopoietic stem cell transplantation. Relapse was detected in 21%. The 5-year overall survival rate was 76.8%. Leading cause of death was mostly progressive disease (43.2%) and infectious disease (31.1%). Two hundred and twenty three patients were survivors, 37.9% presented any type of sequelae (38% severe), due to neoplasm (20%), surgery (56.5%), chemotherapy (17.6%) or radiotherapy (14%). The sequelae were endocrinologicals (40%), neurologicals (22.3%), renals (15.3%), musculoskeletal and aesthetics (both 9.4%). 53.5% developed a second neoplasm.

Conclusion: Survival rate is similar to that reported in other series. Percentage of severe sequelae is disturbing, due to the incapacity, continued health care needs and repercussion on the professional and personal projection of patients. Multidisciplinary teams promotion and continuous surveillance of childhood cancer survivors is needed to achieve the early detection of illness derived chronic problems and their treatment; as well as to implement programs to facilitate social insertion of these patients.

P-0351 | Adult Survivors of Childhood Cancers' Preferences for How and When to Receive Information about Late-Effects: A Population-Based Survey

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Background/Objectives: Survivors of childhood cancer need information about their risks of late effects to manage their health and communicate their special health care needs, yet many lack such knowledge. We investigated the preferences of adult survivors of childhood cancer for how and when such information should be provided.

Design/Methods: Norwegian survivors of childhood cancer (excluding CNS-tumours) diagnosed before the age of 18, between 1985-2009, and currently at least 18 of age (n=2018) were identified through the Norwegian Cancer Registry and mailed a survey regarding preferences for late effects information. The survey was based on a literature review and focus-groups with adult survivors of childhood malignant lymphomas.

Results: So far, 665 (31.6%) survivors have responded; mean age at diagnosis 11 years and current age 40 years. Data collection ends May 2016. Leukaemia (29%) and lymphoma (25%) were the most common diagnoses, 42% reported having received information about late effects. Oncologists were the preferred source of such information (85%). The most preferred information to receive was (on a 10-point scale: 10=very important): Possible physical late effects (mean=9.1); possible psychological late effects (mean=9.0); the cancer disease (mean=8.8) and lifestyle advice (mean=8.4). The top three preferred ways of receiving such information were: Allow time for the patient to ask questions after receiving information (mean=9.3); provide written, tailored information (mean=8.9), and check for the patient's understanding (mean=8.7). Receiving late effects information during routine follow-ups and when reaching young adulthood were ranked as "very important" by 72% and 54% of the survivors respectively.

Conclusion: Similar to previous research, the majority reported not having received information about late effects. Our results extend the limited knowledge of survivors' preferences for how and when to receive such information and could be useful for guiding clinical practice. Re-informing survivors once older should be considered.

P-0352 | Is there a Role for Cellular Senescence-Associated Genetic Determinants in Late Adverse Effects Prevalence in Survivors of a Childhood Cancer? Introducing the Petale Study

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Background/Objectives: Late adverse effects (LAE) will affect on average 75% of adult survivors of a childhood cancer. While several associations between specific drugs and LAE have been demonstrated (e.g.: anthracyclines and cardiotoxicity), there is an emerging idea that anti-cancer treatments could induce an accelerated aging-like process.

Objectives of this study are: 1) verify whether a subpopulation of adult survivors of childhood cancer suffers from clustered LAE, 2) verify if these patients are characterized by a distinct set of genetic polymorphisms with respect to cellular senescence-associated genes.

Design/Methods: The PETALE Study aims to assess extensively the prevalence of metabolic, cardiotoxicity, bone, neurocognitive and quality of life LAE in survivors of childhood acute lymphoblastic leukaemia (cALL). Whole-exome sequencing is completed for each participant. The main inclusion criteria are: having received a cALL diagnosis at our institution, having received treatment according to a standardized Dana-Farber Cancer Institute ALL protocol (87-01 to 2005-01), being ≥ 5 years post-diagnosis and relapse-free.

Results: We have already shown the role of polymorphisms on treatment-associated side-effects (Marcoux et al, *Ped Hematol/Oncol*, 2013) and the heterogeneity in increased expression of cellular senescence biomarkers in survivors of cALL (Marcoux et al, *Rad Oncol*, 2013). The PETALE Study currently includes 208 participants (recall rate: 89.1%). The study population is composed of young adults (mean age at study: 22.0 ± 6.5 years) having received in majority both chemotherapy and radiotherapy (62.8%) following a high-relapse risk treatment protocol (56.3%).

Conclusion: Based on our previous findings, we hypothesize that patients with polymorphisms associated to exacerbated cellular senescence are also more prone to multiple LAE. The PETALE Study integrated and comprehensive design will generate the data required to verify our model.

P-0353 | Full Cycle from Cancer Patient to Oncology Sister: A Personal Journey of 21 Cancer Free Years

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Background/Objectives: I am a cancer survivor. I want my story and experience to give a deeper understanding of the effect of chemotherapy and radiotherapy on a child. I hope to show that it is important to not only focus on the signs, symptoms and side-effects of the treatment, but also the emotional well-being of a child. Listening, believing and supporting a child makes a huge difference in their perspective of the reason for coming to the hospital and how they feel about getting chemotherapy. As a survivor I want to motivate and encourage fellow healthcare providers; we all know some days get tough, but you can make a huge difference every day.

Design/Methods: To tell my story: I was four years old; I still remember how I felt when I had cancer, the side-effects of chemotherapy and radiation. I had physical changes due to the cancer, and know how it was growing up being different. The late effects of the treatment I experience today, physical and emotional. To share my experience working in the oncology setting as a paediatric oncology survivor.

Results: Fellow healthcare providers will be encouraged and have a renewed sense of understanding and hope to go back and fight the battle with their patients. They need to remember to always encourage the children to not let cancer stop them from doing what they want.

Conclusion: My hope is to inspire staff of the paediatric oncology units' from my experience and to remind them that their patients need them to fight the battle with them. Do not give up; children are stronger than we think. I am now involved in oncology clinical trials and aim to give hope by getting access to treatment not always available and create opportunity for more survivors.

P-0354 | Negative Emotions Expressed During Follow-Up Consultations with Adolescent Survivors of Childhood Cancer are Often Associated with Late Effects

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Background/Objectives: Childhood cancer survivors face many challenges following treatment completion, including late effects. Whether negative emotions expressed by adolescent survivors during follow-up consultations reflect possible underlying late effects has to our knowledge not been explored.

Design/Methods: Video-recordings were made of 66 consecutively recruited follow-up consultations between 10 paediatric oncologists and 66 adolescents, aged 12-20 years, treated for leukaemia (72.7%), lymphoma (21.2%) or having received hematopoietic stem-cell transplantation for a benign disease (7.6%). Transcripts of the recordings were analyzed utterance by utterance according to two different sets of criteria, utterances about actual or potential late effects and utterances containing expressions of negative emotions.

Results: Of the 115 utterances coded as negative emotions, 49% were also coded as potential late effects. The most common types of late effect that were associated with negative emotions were fatigue (e.g. "I'm struggling with having no energy"), psychosocial distress (e.g. "When I touch this (scar from CVC) I become nauseous"), pain (e.g. "I'm wondering, for how long am I going to have this pain?"), and treatment-related alterations to physical appearance (body image, e.g. "Am I growing, is my height normal?").

Conclusion: Negative emotions expressed in the follow-up consultations were frequently related to concerns about actual or potential late effects among childhood cancer survivors. Eliciting and exploring patients' negative emotions as advocated within a patient-centered framework could provide clinically relevant information regarding late effect-related concerns as well as opportunities to provide emotional support.

P-0355 | Fertility in Childhood Cancer Survivors in India – Awareness, Advocacy and Patient Support Initiative

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Background/Objectives: Issues related to fertility in childhood cancer survivors in India have so far been neglected. Our objectives were to address this knowledge and service delivery gap.

Design/Methods: Step 1 – An educational and brainstorming stakeholder forum (survivors, parents, parent support groups, reproductive medicine specialist and paediatric oncologist) was held on 8th Nov 2013 in New Delhi.

Step 2 – Survivors and their parents completed a survey on fertility preservation counseling and options offered to them at diagnosis and end of treatment.

Step 3 – Conducted late-effects clinic focused on fertility from Dec 2013 to Mar 2014. Demographic, disease and treatment related information was captured. Status of fertility was established by clinical and laboratory evaluation.

Step 4 – Developed material for advocacy and increasing awareness.

Results: The stakeholder forum revealed a significant lack of awareness of issues related to fertility among childhood cancer survivors and their parents. This was confirmed in the subsequent survey where only three(14%) survivors were counseled about the risk of infertility. None were offered fertility preservation. Following end of treatment, sexuality and fertility issues had not been discussed.

Twenty-one survivors (71% male, median age 18 years, off treatment median seven years) were assessed in the late-effects clinic. Ten(48%) were at low-risk for infertility, nine(43%) at medium-risk and two (9%) at high-risk. Gonadal dysfunction was seen in three(14%) survivors: 0% low-risk, 11% medium-risk and 100% high-risk. Appropriate counseling and fertility preservation options were offered to these affected survivors.

The above results have been disseminated through print and social media to raise awareness. Cankids has created relevant information, education and communication material for patients and survivors.

Conclusion: A purposeful start has been made to understand the issues related to fertility in childhood cancer survivors in India. Concerted efforts with all stakeholders at a regional and national level would be the next logical step.

P-0356 | Educational Outcomes of Childhood Cancer Survivors: A Systematic Review

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Background/Objectives: Most childhood cancers are now treatable and most children diagnosed with cancer during childhood survive their illness. Therefore, it is increasingly important to examine the late and long-term effects of childhood cancer. One such effect could be on educational outcomes. This systematic review aims to determine whether the educational achievements of childhood cancer survivors are different compared to the healthy population.

Design/Methods: We searched SCOPUS, Web of Science, EBSCO, EMBASE, RIAN (the Irish Open Access database) and the Applied Social Sciences Index and Abstracts (ASSIA), from 2005 to 2015. We obtained English papers, reporting primary data on academic achievement of adults who are childhood cancer survivors, compared to a control group.

Results: Initially, 319 papers were identified and screened, with 11 meeting the inclusion criteria. The sample sizes of the studies included in the review ranged from n=56 to n=2,213. Nine of the studies included were from Europe, one was the USA, and one from Turkey. Eight of the papers focused on cancer patients from various types of cancers, one focused on survivors of leukaemia, one on survivors of cancer of the central nervous system and one on patients that underwent stem cell transplant.

Our Findings indicated that the academic achievements of cancer survivors across different types of cancer are heterogeneous, with some studies reporting less favorable outcomes for cancer survivors, others report similar outcomes, and another group of papers reported more favorable outcomes for cancer survivors.

Conclusion: The literature does not provide a clear pattern of the late-effect of cancer on education achievements. While this may suggest that there is no consistent difference between cancer survivors and healthy individual, it may be the result of a lack of a consistent measures that would capture achievement beyond level of education.

The study was funded by the Irish Cancer Society.

P-0357 | Moroccan Childhood Bone Tumour Survivors: Medical and Demographic Outcome

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Background/Objectives: Childhood cancer is curable but survivors are at risk of numerous late effects. Among children treated from cancer between 1978 and 2004 at the Children Hospital of Rabat, 1000 were considered cured, among them, 46 patients had bone tumors. The present study aims to establish a database of Moroccan childhood bone tumour survivors and to lay-out a strategy for long-term monitoring in order to improve their outcome.

Design/Methods: The study is transversal, exhaustive and descriptive. The data collected includes initial and current medical and demographic status. To reach the survivors, we used several means including phone, email, social networks, and postal mail. The questionnaire was completed by the survivors themselves, their parents or their physician.

Results: Although 46 patients were considered to be cured, only 17 questionnaires were gathered. Initially, the demographic data was as follows: 60% male, 78% over 10 years of age; 94% in school, 75% from urban areas, and 80% diagnosed between 1995 and 2004. The initial medical data showed that Ewing Sarcoma was more frequent than osteosarcoma, long bones more affected, especially the femur. All patients received chemotherapy, 38% radiotherapy, and 88% surgery, often conservative. Currently, the bone tumour survivors are aged from 20 to 44 years (72% from 20 to 30 years), educated (57% have a high school diploma or more), living with their parents (60%), unemployed (50%), single (70%) and only 23% are physically active. Medical findings show that all bone tumour survivors have physical issues, mostly orthopedic, from lameness to scoliosis. Two second cancers, a long term metastatic recurrence and 2 deaths were found.

Conclusion: This study on the Moroccan childhood bone tumour survivors, sometimes revealing grave medical issues, constitutes the first step of a long-term follow up strategy, including prevention, early diagnosis, and adequate treatment in order to improve survivors' outcomes.

P-0358 | Are the Childhood Cancer Survivors at Risk of Vitamin D Deficiency?

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Background/Objectives: Recent studies indicate that survivors of childhood cancers (CCS) have increased risk for vitamin D deficiency. Adequate replacement of vitamin D status might affect the quality of life of CCS. However, data on 25-hydroxyvitamin D (25(OH)D) status among CCS are limited.

The aim of the study was to evaluate the serum level of 25(OH)D in CCS depending on: age, gender, diagnosis, TSH and cholesterol level.

Design/Methods: The study group included 124 CCS (male:71, female:53), (mean age at the study- 13.37±4.26); treated due to: acute leukaemia (n=66;53.23%), lymphoma (n=13;10.48%) and solid tumors (n=45;36.29%). Mean time from diagnosis and mean age at diagnosis were 7.58±3.96 and 5.75±4.25 years, respectively. The results were compared with control group consisted of 60 healthy children. The 25(OH)D level was assessed using immunochemical method. The Mann-Whitney U test and t-Student test were used; The statistical significance was defined as p<0.05.

Results: Statistically significant difference in level of 25(OH)D between study and control groups was found (mean: 16.64±8.21 ng/ml vs. 20.84±10.23 ng/ml, p=0.013). Almost seventy percent of the patients (n=84) had vitamin D level below the range norm [20-60ng/ml]. The 25(OH)D status was similar in both sexes (male: 17.18±8.62 vs. female: 15.91±7.65 ng/ml, p=0.398). No statistical differences between level of 25(OH)D in patients with ALL (16.19±8.79 ng/ml), lymphoma (16.82±7.34 ng/ml) and solid tumors (17.25±7.69 ng/ml) were observed (p=0.801). Serum level of 25(OH)D in patients under 10 years old (mean:19.44±8.95 ng/ml) was statistically significant higher than in older (mean:15.23±7.23 ng/ml; p=0.026). There was no correlation in the level of vitamin D and TSH (r=-0.144) or cholesterol (r=-0.117).

Conclusion: We found high prevalence of 25(OH)D deficiency in CCS, especially older than 10 years. Half of the patients in the control group also had level below the range norm. Adequate supplementation of vitamin D seems to be important in CCS. Additional studies are still needed.

P-0359 | Prospective Analysis of Cerebrovascular Sequelae in Survivors of Paediatric Medulloblastoma

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Background/Objectives: Medulloblastoma is the most common malignant brain tumour in childhood. Treatment involves surgery, chemotherapy as well as radiotherapy to the primary site and craniospinal axis.

Considerable late effects in medulloblastoma survivors are cerebrovascular complications such as cerebral microbleeds (CMB) and cerebral cavernous malformations (CCM). Increasingly sensitive neuroimaging techniques like susceptibility-weighted magnetic resonance imaging (SWI) can reveal focal hemosiderin deposition representing abovementioned hemorrhagic or proliferative microangiopathies. The purpose of this study was to determine the prevalence of SWI lesions in a cohort of survivors of paediatric medulloblastoma.

Design/Methods: Twenty-six former medulloblastoma patients were enrolled in this prospective single center study and examined by craniospinal MRI including SWI sequences. CMB were identified as hypointense foci ≥2mm that did not correspond to vessels on consecutive slices. For each patient, lesions were counted by one neuroradiologist.

Results: All examined 26 medulloblastoma survivors (mean follow up age 24.2 years, range 4.58–53.75 years; mean follow-up time 15.6 years) were treated with a combination of surgery and radiochemotherapy. Two patients already underwent surgical resection of CCM.

Twenty-four (92%) were affected by SWI lesions ≥ 2 mm with a total lesion count of 366. Further analysis revealed a mean of 14 lesions per patient (median 7.5, range 0–71). Sixteen individuals (62%) presented with lesions > 4 mm suspicious for CCM. Longer follow-up time correlated significantly with higher total lesion count ($r=0.46$, $p>0.05$).

Conclusion: Though often asymptomatic, CMB and CCM occur frequently after treatment for childhood medulloblastoma. This study shows that small lesions –not seen on conventional MRI– can be detected using SWI. Although their clinical significance is poorly understood, as a sign of vascular damage, they may correspond to neurocognitive decline and lead to headache, seizures or focal neurologic deficits. Further studies are needed to standardize MRI sequence protocols and to improve quality of long-term follow-up of medulloblastoma survivors.

P-0360 | Evaluation of Vitamin D Levels in Paediatric Cancer Patients

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Background/Objectives: To determine pre and post-treatment (chemotherapy and /or radiotherapy) 25-hydroxy vitamin D [25(OH)D] levels in paediatric oncology patients, and the factors that may affect its levels.

Design/Methods: Consecutive 151 paediatric cancer patients who attended the Department of Pediatric Oncology between August 2013–January 2016 were included in the study. The patients were divided into two groups. The first group was composed of 49 patients who had both pre- and post-treatment 25(OH)D data, while the second group was composed of 102 patients who were in remission and had 25(OH)D samples taken only after the conclusion of therapy. In both groups serum vitamin D, parathormone (PTH) levels and calcium (Ca), phosphorus (P) and alkalene phosphatase (ALP) were determined. Factors related to vitamin D status such as age, sex, type of tumour, season of blood sampling, and methods of treatment were also determined.

Results: The median age of the first group and second group was 7 years(0.8–17) and 14 years(1–18) respectively. 25(OH)D deficiency at the time of diagnosis was noted in 53% of Group 1 patients.; it reached 73% at their follow-up measurement ($p<0.01$). There was no significant correlation between 25(OH)D levels and PTH and Ca, P, and alkalene phosphatase levels. In Group 2, 25(OH)D deficiency was 20%. Age, sex, treatment (radiotherapy, methotrexate, glucocorticoids) and body mass index were not correlated with 25OH)D levels. Sampling in the winter was associated with lower 25(OH)D levels.

Conclusion: Assessment and adequate replacement of vitamin D may be of particular value in paediatric cancer patients.

P-0361 | Ovarian Reserve Evaluation in Children and Adolescents after Stem Cell Transplantation in the National Cancer Program

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Background/Objectives: Increase in survival of the paediatric patients after stem cell transplantation (SCT), has allowed acknowledging the late effects of treatment. SCT produces a decrease in ovarian reserve and premature ovarian failure (POF) in almost 85% of the patients. The objectives were to know the function and post SCT ovarian reserve.

Design/Methods: A descriptive, observational and cross-sectional study post SCT in women treated in Hospital Luis Calvo Mackenna between 1999 and 2013. Approved by the Ethics Committee and had an informed consent. Exclusion criteria: death, less than a year after transplant, relapse, without ovaries, treatment with corticosteroids 3 months before. Clinical history, external physical and gynecological examination, gynecological hormone tests and abdominal ultrasound were performed. Primary ovarian failure was defined: Secondary or absence of pubertal development at age 13, primary amenorrhea associated with follicle stimulating hormone (FSH) > 40 mIU / ml and / or Antimüllerian hormone (AMH) < 0.3 ng / ml. Statistical analysis was bivariate and multivariate analysis.

Results: Fifty-nine patients lived, 51 met inclusion criteria, 41 evaluable (80%), four did not accept, six left the follow up. The median age was 14.8 years old (range 4–23 years). Ninthly three percent were oncological and myeloablative SCT. All patients that had a hormonal study had also diminished the ovarian reserve. Fifty percent had ovarian failure, 33% with hormone replacement. Two pregnancies, no abortion.

Conclusion: All patients had a decrease in ovarian reserve. Half had POF. It essential to evaluate by a gynecologist for hormone replacement and considering fertility preservation before SCT.

P-0362 | Gonadal and Sexual Dysfunction in Childhood Cancer Survivors

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Background/Objectives: Gonadal and sexual dysfunctions are significant complications in childhood cancer survivors. Few studies have addressed this issue, most of which focus on gonadal dysfunction. We evaluated the prevalence and risk factors for gonadal failure and semen abnormality among adolescent/young adult childhood cancer survivors. We also evaluated their sexual function.

Design/Methods: Subjects were childhood cancer survivors aged 15–29 years. More than 2 years should have passed after completion of therapy. Demographic and medical characteristics were obtained from the patients' medical records. Hormonal evaluation and semen analysis were performed. Sexual function was evaluated via questionnaire.

Results: The study included 105 survivors (57 male, 48 female). Thirteen female subjects (27.1%) needed sex hormone replacement. Five males (8.8%) were suspected with hypogonadism, but none of them was receiving sex hormone replacement. Of 27 semen samples, 14 showed azo- or oligospermia. Among adults, none were married and only 10 men (35.7%) and 8 women (34.3%) were in a romantic relationship at the time of the study. More than 10 percent of survivors had not experienced sex education.

Conclusion: The childhood cancer survivors in this study showed a high prevalence of gonadal/sexual dysfunction. Proper strategies for managing these complications to improve their quality of life, including proper sex education. Special concerns are required for management of male hypogonadism.

P-0363 | Musculoskeletal Sequelae of Childhood Solid Tumours Survivors, Treated with Intensive Chemotherapy, Surgery and Radiation Therapy

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Background/Objectives: Advances in diagnosis and treatment of childhood cancer have dramatically increased long-term survival and it is now evident that the disease and its treatment can significantly impair long-term health. Childhood solid tumours survivors are known to be at risk for the serious musculoskeletal late effects that may result in disability.

Design/Methods: One hundred and two children with solid tumours were treated between 1987 and 2014 years. The mean age at the time of orthopedic diagnosis was 13.25 ± 0.43 years (from 2 till 24 years). Common sites of primary disease include the thorax, abdomen, trunk and extremities. 31,0% patients had primary distant metastases. Treatment consisted of neoadjuvant chemotherapy, the radiotherapy and/or oncologic surgery and adjuvant chemotherapy. The most common late effects we had observed were: scoliosis - in 78,4% cases, muscular hypoplasia - 74,5%, osteopenia - 55,9%, limb-length discrepancy in spite of usage of growing endoprosthesis - 45,1%, poor joint movement - 66,7%, musculoskeletal deformity - 39,2%. 77,5% patients had from 1 till 5 late effects, 22,5% - 6 till 11. We have not observed serious Adverse Events, like Grade 4: life-threatening consequences and Grade 5: death related to Adverse Events. Among the children who developed the largest number of effects, children who received CT and radiotherapy were 17,4%, in the group with major surgery - 56,5%, CT, surgery and radiotherapy - 26,1%. This indicate, that some researchers reevaluate the role of radiation therapy in the development of musculoskeletal sequelae.

Results: Currently 90 patients are alive without disease, following up of 12 to 343 months. We have observed Grade 2 Adverse Events (CTCAE) in 43,3% cases. The lowest grade by MSTs we have observed in cases with distal leg localization - 51,4%.

Conclusion: We suggest that the usage an individual rehabilitation program can dramatically increase the quality of life.

P-0364 | Clinical Implimentation of a Pharmacogenetic Risk Prediction Model for Cisplatin Ototoxicity and Anthracycline Cardiotoxicity

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Background/Objectives: Anthracyclines and cisplatin are important medications in the treatment of childhood cancer, but their use is complicated by the risk of significant toxicities. Genomic variants have been discovered and replicated that can predict the likelihood of certain adverse reactions including cisplatin-induced ototoxicity and anthracycline-induced cardiotoxicity. A prospective study of returning pharmacogenomic results to oncologists has been implemented at our institution to help aid in risk/benefit profiling in patients who are to receive these agents.

Design/Methods: Clinical practice guidelines for the use of pharmacogenomic variants were developed and published in order to help guide physicians with how to use the information. Consent was obtained for all paediatric patients due to receive either anthracyclines or cisplatin. Saliva or blood was collect for DNA extraction and the genomic risk of toxicity was determined using a multi-gene panel. Results were returned to the treating oncologist within 48 hours.

Results: 135 subjects have been enrolled into the study. Significant changes in therapy were made by oncologists based on genomic risk results including the addition of cardioprotectants (dexrazoxane) or omission of anthracyclines in those at high risk of cardiac toxicity. We highlight two cases of high risk neuroblastoma that were found to be in the highest risk group for cardiac toxicity using our genomic risk model (89% risk). The first child was treated without anthracyclines and remains in remission two years post therapy with normal cardiac function.

In comparison, the second child was treated 10 years ago and required cardiac transplantation for heart failure and DNA obtained retrospectively revealed the same high risk genotype.

Conclusion: Implementation of pharmacogenomics into clinical practice is feasible and can be used to aid decision making for children with cancer. Ongoing quantitative and qualitative research is being performed to evaluate the effectiveness of this program and ongoing research will further refine our current model.

P-0365 | Second Neoplasm in Childhood/Adolescence Age. Experience in Institution. Hospital de Niños Ricardo Gutiérrez

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Background/Objectives: Second neoplasms (SN) are rare in cancer survivors. The aim of this study is to report patients treated for solid malignant tumors, which developed a SN in paediatric/adolescent age.

Design/Methods: Descriptive, retrospective study of patients (p) treated in Oncology Unit of Hospital de Niños Ricardo Gutiérrez, between 1986 and February 2016, which developed SN in paediatric/adolescence age.

Results: Three thousand and forty four patient with solid tumors were treated. Twenty two (0.72%) developed SN during childhood/adolescence. The first tumour diagnoses were: Rhabdomyosarcoma 5p, Hodgkin lymphoma 4p; Medulloblastoma 3p, Retinoblastoma (RB) 3p, Ewing sarcoma 2p, Wilms Tumour (WT) 1p, Chiasm glioma 1p, hepatoblastoma 1p, malignant peripheral nerve sheath tumour (MPNST) 1p, Pleuropulmonary blastoma 1p. Median age at diagnosis: 4.4 years (0.3-14). 21p received chemotherapy and 14p chemo and radiotherapy. All patients had complete remission. One developed SN intra-treatment of first tumour. Two patients had neurofibromatosis and one had hereditary RB. Mean time to SN diagnosis was 10.2 years (0.4-24.5). SN: leukaemias/lymphomas 7p (31.8%), Sarcomas 6p (27.3%), CNS tumors 4p (18.2%), other tumors 5p (extra-abdominal fibromatosis 2p, uterine fibroid 1p, cystadenoma 1p, WT 1p. Median age at diagnosis was 15.5 years (3.7-27.5). 17p (77.3%) had received alkylating agents and 5p (22.7%) Etoposide. 14p received RT: 7p (50%) developed second tumour in irradiated site. Thirteen p (59%) had complete remission. Eight (36.4%) died: Leukaemia 4p, osteosarcoma 2p, fibrosarcoma 1p, glioblastoma 1p. A patient with complete remission of 1^o and 2^o disease, presented a third tumour (glioblastoma) and died.

OS of SN was 63.6%.

Conclusion: The most frequent diagnoses of second tumour coincide with the literature, as well as the association with alkylating agents, etoposide and RT. Percentage of patients with SN in our study is lower than reported. This could be due to loss to follow up.

P-0366 | A Review of the Provision of Semen Cryopreservation in Adolescent Males Receiving Cancer Treatment

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Background/Objectives: Gonadal toxicity is an adverse side effect of chemotherapeutic alkylating agents and radiotherapy, with effects varying depending on the type of cancer diagnosed, which organs are involved and the treatment the patient may receive.

It is recommended that semen cryopreservation is universally available for all male patients who are commencing anticancer treatment.

The following is an audit detailing whether potential issues with future fertility were discussed and documented and whether semen cryopreservation was offered and if the patient availed of this service.

Design/Methods: This is a retrospective health care record (HCR) review of male patients diagnosed between 2011-2016 with either Hodgkin disease or a primary or relapsed Leukaemia receiving chemotherapy and/or radiotherapy and/or bone marrow transplant who may have been eligible for semen cryopreservation.

Results: A total of 41 patient charts were reviewed, with 19 (46%) patients diagnosed with Hodgkin disease and 22 (53%) patients diagnosed with primary or relapsed Leukaemia. Patients were aged between 13 -16 with a mean age of 14.15 years.

A total number of 22 (53%) patients were offered cryopreservation, with 16 (72%) males availing of this service. 8 (50%) patients produced satisfactory samples with 2 (12.5%) patients producing azoospermic samples and 1 (6.25%) patient producing a sample with asthenozoospermia. 4 (25%) patients were unable to produce samples and 1 (6.25%) patient cancelled their appointment.

Following discussion, 6 (27%) males and their parents/legal guardians did not wish to use this facility.

Conclusion: It is recommended that future fertility is discussed by a patient's physician at the time of diagnosis, with written documentation regarding the toxic effects of treatment and the process of semen cryopreservation being recorded. However factors including a lack of knowledge, finances, religion and ethics may influence whether a patient avails of this service and unfortunately even when the process is attempted, it is not always successful.

P-0367 | Neurological Outcome in Delayed Diagnosis of Spinal Cord Low Grade Gliomas

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Background/Objectives: Delayed diagnosis in spinal cord low grade gliomas (LGG) is common. Spinal cord LGG may have low mortality, but high neurological morbidity. Neurological outcome in spinal cord LGG with delayed diagnosis has not been well explored.

Design/Methods: We retrospectively examined neurological outcome in paediatric spinal cord LGG with delayed diagnosis from 1995-2015 in 14 patients (50% female; median [range] age at diagnosis= 8.8[2-17] years; time to last follow-up median [range]=10.7 [5.8-17.8] years). Neurological severity was measured at diagnosis and last follow-up using National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 4.03, Modified Rankin Scale (MRS) grade 0 (no symptoms) to 5 (severe disability), and Karnofsky Performance Score (KPS). Pre-diagnosis symptom interval (PSI) 0-6 months and \geq 6 months to first radiological diagnosis determined extent of delayed diagnosis.

Results: 14 patients had spinal cord (20% thoracic, 50% cervical/thoracic, 21% cervical) LGG (9 juvenile pilocytic astrocytoma, 2 ganglioglioma grade I, 1 oligodendroglioma grade II, 1 glioneuronal grade I, and 1 oligoastrocytoma grade II) with delayed diagnosis (43% PSI <6 months, 57% PSI \geq 6 months). All patients had upfront surgery (gross total resection [3], subtotal resection [9], and biopsy [2]); and adjuvant chemotherapy in 7 patients and radiation therapy in 6 patients. Overall median MRS from diagnosis (2) improved at follow-up (1.5) and median KPS from diagnosis (80) improved at follow-up (90) if PSI <6 months. Median MRS from diagnosis (1) worsened to follow-up (3) and median KPS worsened from diagnosis (90) to follow-up (80) if PSI \geq 6 months. Patients with PSI \geq 6 months had worse weakness, pyramidal tract symptoms, spasticity, bladder retention, bowel incontinence, and scoliosis with rod placement compared to those with PSI < 6 months.

Conclusion: Neurological outcomes worsen in spinal cord LGG with delayed diagnosis. Earlier diagnosis may improve neurological outcome.

P-0368 | Long-Term Renal Function and Hypertension in Adult Survivors of Childhood Sarcoma and Unilateral Non-Syndromic Renal Tumour

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Background/Objectives: To evaluate the prevalence of renal impairment and hypertension in adult survivors of childhood sarcoma (S) treated in a single centre (1980- 2010). Data were compared to those obtained in survivors nephrectomized for Unilateral non-Syndromic Renal Tumour (UnSRT).

Design/Methods: Renal function was assessed according to "Kidney Disease: Improving Global Outcomes (KDIGO)" guidelines by estimating Glomerular Filtration Rate (eGFR) and chronic kidney disease (CKD). Survivors were studied by chemistry, kidney ultrasound, urinalysis and blood pressure measurement. Previously studied UnSRT population consisted of 35 cases, 21F/14 M, mean age 25 yrs, mean follow-up 20 yrs (Pediatr Blood Cancer 2015).

Results: Out 42 adult survivors, 12 were lost or refused and 30 (10F/20M, mean age 27 yrs; mean follow-up 17 yrs) treated for S (21 RMS, 9 bone sarcoma) were enrolled. The mean eGFR was 110.6 ml/min/1.73mq (103.6 – 118.0 95% C.I.) in S group vs 99.7 ml/min/1.73mq (94.5 – 104.9 95% C.I.) in UnSRT group [p 0.01]. The prevalence of eGFR <90 ml/min/1.73mq was 10% (S) vs 22.9% (UnSRT) [ns]. The prevalence of CKD was 6.7% (S) vs 8.6% (UnSRT) [ns]. Hypertension was present in 13.3% (S) vs 2.9% (UnSRT) of the cases [ns]. Excluding cases with genitourinary RMS and with bone sarcoma treated with cisplatin and/or methotrexate, the mean eGFR was 112.2 ml/min/1.73mq (104.7 – 119.7 95% C.I.) vs 99.7 ml/min/1.73mq (94.5 – 104.9 95% C.I.) [p 0.04] and the prevalence of eGFR < 90 ml/min/1.73mq was 4.2% vs 22.9% [ns], of CKD 0% vs 8.6% [ns], of hypertension 8.3% vs 2.9% [ns].

Conclusion: After near two decades, the mean eGFR was statistically higher in adult sarcoma survivors than that in uninephrectomized adult renal tumour survivors, but the prevalence of CKD and hypertension is not statistically different between the two groups. Surprisingly, ifosfamide-treated sarcoma survivors had a good renal function.

P-0369 | Impact of Intravenous Methotrexate on Brain Development

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Background/Objectives: Acute lymphocytic leukaemia (ALL) is the most common form of childhood leukaemia. Although up to 90% of children survive, many are left with late effects, characterized by impaired cognitive ability.[1] Therapy begins at an early age, and involves treatment with many chemotherapy agents over a period of 2 to 3 years. There has been speculation that this intense regime contributes to the occurrence of late effects, and that genetics may influence an individual's susceptibility. The chemotherapy agent, methotrexate (MTX), is used at every stage of treatment for ALL - MTX disrupts the folate cycle, which involves many genes including the MTHFR gene.[2]

Design/Methods: We sought to determine if treatment with MTX at an infant stage of mouse development has consequences for the developing brain, measured by neuroanatomical volume changes seen in magnetic resonance imaging (MRI) through early adulthood. Furthermore, we have tested the hypothesis that mice deficient in the Mthfr gene are more sensitive to treatment with MTX. Wild type C57Bl/6 mice and mice heterozygous for the Mthfr gene (Mthfr+/-) were treated with intravenous MTX or saline at an infant equivalent age and followed throughout development with in vivo MRI, until they reached maturity.

Results: Mice treated with MTX exhibited significant brain volume loss immediately following treatment when compared to their saline-treated counterparts; gray matter was most severely

affected. The volume loss was recovered by adulthood, so that mice treated with saline or MTX had similar brain structure volumes at the final measurement. Mthfr^{-/-} mice were less severely affected by the MTX treatment than wild type mice, and did not experience volume loss after treatment.

Conclusion: Intravenous MTX treatment has a deleterious, genotype-dependent impact on brain volume that is resolved during subsequent development.

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P-0370 | Second Malignant Neoplasms in Children and Adolescents Treated for Haematological Malignancies and Solid Tumors: A Single Centre Experience of 15 Years

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Background/Objectives: The occurrence of second malignancies is not rare in children treated for primary tumors. The aim of this study is to investigate the incidence, characteristics and outcomes of second malignant neoplasms in children and adolescents treated for primary malignancies in a single centre over a 15 year period.

Design/Methods: This is a retrospective study of children and adolescents diagnosed with second malignant neoplasms after their primary diagnosis and treatment of haematological malignancies or solid tumors in the Paediatric Haematology Oncology Department, University Hospital Crete between 2000 and 2015. Medical records were reviewed and parameters including primary diagnosis, age at diagnosis, family history, age at diagnosis of second malignancy and overall survival were analyzed.

Results: Over a 15 year period, from a total of 239 cases with first diagnosis of neoplasia, 5 patients (5 boys, 0 girls) were diagnosed with second malignancies including cancer of the parotid gland, renal cell carcinoma, Hodgkin lymphoma, thyroid carcinoma and transitional liver cell carcinoma in children previously diagnosed and treated for acute myelogenous leukaemia, glioblastoma multiforme, B-ALL, Langerhans cell histiocytosis and myeloblastoma respectively. Mean age at diagnosis of second malignancy was 10 years and 4 months (range : 7 years and 10months to 14 years and 4 months). Five out of 5 patients had received chemotherapy for their primary diagnosis and 4/5 also received radiotherapy. Median time from primary diagnosis to second malignancy was 5 years (range: 3 to 10 years). Overall survival was 80% (4/5) at 12 months and 75% (3/4) at 5 years.

Conclusion: Children and adolescents who have received treatment for primary tumors are at an increased risk of developing subsequent malignant neoplasms and require close surveillance and long-term follow-up.

P-0371 | Late Effects and Non-Relapse Mortality of Long-Term Survivors Received Childhood Hematopoietic Stem Cell Transplantation

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Background/Objectives: Although survivors of childhood hematopoietic stem cell transplantation (HSCT) have increased in number recently, there have been few reports concerning their long-term prognosis. Our purpose is to evaluate late effects and non-relapse mortality of long-term survivors who received HSCT in childhood.

Design/Methods: We retrospectively analyzed 432 patients received HSCT, using medical records in a single-center, Kanagawa Children's Medical Center from January 1982 to September 2015. We assessed late effects and non-relapse mortality of 239 patients who survived for more than 2 years. Probabilities of non-relapse mortality and relapse were calculated by using cumulative incidence curves to accommodate competing risks.

Results: In 239 patients of 2-years survivors, median follow-up time was 9.1 years (range: 2.0-27.0) and median age at endpoint was 17.3 years (range: 4.8-40.0). Of 283 HSCTs, myeloablative conditioning regimen was 261 (92.2%) and non-myeloablative was 22 (7.8%). The frequency of late effects in 2-years survivors was as follows: endocrine complications 102(42.7%), chronic GVHD 55 (23.0%), musculoskeletal 31 (13.0%), neurosensory impairment 26 (10.9%), gastrointestinal 19 (7.9%), respiratory 19 (7.9%), otorhinolaryngological 15 (6.3%), secondary neoplasms 14 (5.9%), renal and/or urinary 19 (5.0%), cardiovascular 10 (4.2%). 39 of 239 long-term survivors had died, 29 of 39 died for recurrence, and 10 for non-relapse mortality. (2 multiple organ failure, 2 secondary neoplasm, 2 infection, 1 pneumothorax, 1 respiratory failure, 1 leukoencephalopathy, 1 accidental death). The cumulative incidence of non-relapse mortality at 10 and 25 years after HSCT were 3.7% (95% CI: 1.6-7.2%) and 18.3% (95% CI: 2.9-44.1%), respectively.

Conclusion: The cumulative incidence of non-relapse mortality has increased over more than 10 years after HSCT. The major cause of non-relapse mortality was organ dysfunction related to transplant-related toxicity. It is essential to follow up long-term survivors of paediatric HSCT in adulthood continuously.

P-0372 | Ifosfamide-Induced Tubular Dysfunction

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Background/Objectives: Ifosfamide (IF) and cyclophosphamide (CP) are highly effective alkylating cytostatic drugs. While both IF and its structural isomer CP have severe urotoxic

side effects, only IF is also a nephrotoxic drug, causing tubular damage resulting in Fanconi syndrome in some cases. Little information is available regarding the pathogenic mechanism of tubular damage by IF. This study is aimed at evaluating the incidence of late renal toxicity and Fanconi syndrome of ifosfamide.

Design/Methods: Of the 253 patients retrospectively investigated for renal function, serum and urine electrolytes, calcium phosphorus, magnesium, serum bicarbonate and urine pH during chemotherapy and after the cessation of treatment. There were 70 rhabdomyosarcoma, 22 other soft tissue sarcoma, 44 Ewing sarcoma, and 42 osteosarcoma patients and 72 patients with relapsed solid tumours. No patients had received cisplatin and/or carboplatin additionally.

Results: The median dose of ifosfamide was 54 g/m² (range, 20 to 120 g/m²). During chemotherapy, 109 of the patients had developed tubulopathy and only 29 had abnormal glomerular function rate.

Among the patients that developed tubulopathy; hypopotasemia was observed in 28%, hypophosphatemia in 9%; hypomagnesemia in 5%; and hypocalcemia in 5%. Interestingly none of the patients developed glycosuria; urine pH and serum bicarbonate levels were normal at all of them. Proteinuria was observed in only 1% and this was mild. Although this is called as Fanconi syndrome, it is interesting that there is no glycosuria, bicarbonatemia, and very seldom and mild proteinuria

Ifosfamide dose and interval from therapy to investigations were predictors of tubulopathy in univariate and multivariate analysis. In a multivariate analysis, length of interval since treatment had independent impacts on the risk of abnormal GFR and tubular dysfunction.

Conclusion: Tubulopathy is the main renal toxicity of ifosfamide. This tubulopathy is different from Fanconi syndrome.

P-0373 | Late Effects in Patients with Craniopharyngioma

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Background/Objectives: Craniopharyngiomas are benign epithelial intracranial neoplasms located in the sellar and suprasellar area of the skull. They affect both children and adults, and can be treated with several therapeutic modalities. Although overall survival seems encouraging, late effects due to tumour- and/or treatment are frequent and may significantly impair quality of life. Studies on late effects of craniopharyngioma predominantly assessed patients treated with neurosurgery and/or conventional external beam radiotherapy. Studies investigating other treatment options like ⁹⁰Yttrium brachytherapy are scarce. In this study, we describe late effects of craniopharyngioma in patients treated with various therapeutic modalities.

Design/Methods: We cross-sectionally describe our single-center cohort of 145 patients diagnosed with craniopharyngioma (73 aged < 18 years at diagnosis; 72 aged ≥ 18 years at diagnosis). Median follow-up since diagnosis is 14 years (interquartile range 6-24 years). Initial treatment consisted of complete surgical resection in 25 patients, incomplete surgical resection without postoperative radiotherapy in 47 patients, incomplete surgical resection with postoperative radiotherapy in 28 patients, ⁹⁰Yttrium brachytherapy in 21 patients, and cyst aspiration in 9 patients. Endocrinological, metabolic, and ophthalmological late effects, as well as presence of epilepsy at last follow-up visit were analyzed.

Results: At last follow-up assessment, presence of any pituitary hormone deficiency varied between 87.5-100% after complete surgical resection, incomplete surgical resection (with or without postoperative radiotherapy), ⁹⁰Yttrium brachytherapy, and cyst aspiration for craniopharyngioma treatment. Presence of panhypopituitarism varied between 37.5-64.0%, presence of a body mass index ≥ 2 SDS between 31.3-60.0%, presence of visual acuity disorders between 50.0-84.2%, presence of visual field defects between 54.2-94.4%, and presence of epilepsy between 14.3-38.1%.

Conclusion: Late effects are frequent after craniopharyngioma; irrespective of their initial therapeutic approach. Since pituitary hormone deficiencies are among the most important sequelae of craniopharyngioma, neuro-endocrinologists should play a pivotal role in the follow-up care of patients with craniopharyngioma.

P-0374 | The Influence of Physical Fitness on Health Outcomes among Survivors of Childhood Acute Lymphoblastic Leukemia

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Background/Objectives: Survivors of acute lymphoblastic leukaemia (ALL) are at risk of developing chronic illnesses that affect health status. However, little is known about the contribution of physical fitness to health outcomes among survivors. We aimed to measure the prevalence of adverse health status among survivors of ALL and identify components of physical fitness associated with health status.

Design/Methods: Participants included 365 adult survivors of ALL (mean age at evaluation of 28.6 ± 5.9 years) and 365 age-, sex-, and race-matched controls. Health status was assessed using the domains of general health, mental health, functional status and activity limitations. Fitness was evaluated by assessing flexibility (sit and reach test), muscular strength

and endurance (isokinetic knee extension [Newton-meters/kilogram] at 60° and 300°/s, respectively), resting heart rate and balance (sensory organization test). Generalized linear models were used to examine associations between fitness metrics and health status.

Results: Survivors were more likely to report poor general health (20.6% vs. 10.4%, risk ratio [RR]=2.0, 95% CI=1.4-2.9), poor mental health (28.0% vs. 14.5%, RR=1.9, 95% CI=1.4-2.6), functional impairments (10.5% vs. 4.1%, RR=2.5, 95% CI=1.4-4.6) and activity limitations (29.0% vs. 14.4%, RR=2.0, 95% CI=1.5-2.7) compared to controls. Survivors with knee extension strength (at 60°/s) more than 1.5 SD below the mean of the control population were more likely to report poor general health (RR=1.7, 95% CI=1.0-2.7), functional impairments (RR=3.0, 95% CI=1.5-6.3), and activity limitations (RR=1.5, 95% CI=1.0-2.2). The risk of poor general health (RR=1.7, 95% CI=1.1-2.5) and functional limitations (RR=2.0, 95% CI=1.1-3.9) was also increased among survivors with poor balance. Survivors who were physically active had a decreased risk of reporting poor mental health compared to survivors who were inactive (RR=0.6, 95% CI=0.3-0.9).

Conclusion: Adult survivors of ALL, particularly those with reduced muscular strength and poor balance, are at increased risk for adverse health status.

P-0375 | Childhood Cancer Survivorship: An Exploration of Awareness and Information Needs among Healthcare Professionals in Primary and Secondary Care in the United Kingdom

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Background/Objectives: The incidence rate of childhood cancer, coupled with the concept of increased survival, has established an ageing population who are a specific at-risk group. This group is susceptible to a range of late effects and require specialised healthcare.

Raised clinical suspicion and awareness regarding late effects amongst all healthcare professionals ideally would enable efficient monitoring and recognition of complications. However, it is recognized that the concept of late effects is somewhat unknown outside the paediatric oncology setting.

Design/Methods: This need to investigate health care professionals' awareness of late effects outside the paediatric oncology setting was identified by examining recent case histories where professionals failed to recognise links between the current problem and past childhood cancer treatment.

Questionnaires to both primary and secondary care practitioners were used to ascertain individuals' experience and understanding of late effects and how they would seek further information.

Results: In primary care, all practitioners had experience of caring for childhood cancer survivors, whilst in the secondary care study this was reduced to only 17%. Only one practitioner in secondary care was able to correctly identify recurrence or progression as the leading cause of mortality amongst survivors. Seventy-one percent of respondents noted that survivors may face a risk of recurrence, yet consensus regarding any other late effects varied (Cardiac 35%, Respiratory 17%, Infertility 29%).

Conclusion: The necessity and potential to improve patient care by increasing awareness of late effects amongst healthcare professionals has been identified by this initial study. A mnemonic known as CE-RISK has been developed with each letter representing a late effect-

C-cardiovascular, E-endocrine, R-relapse or secondary neoplasm, I-infertility, S-syndromes-metabolic, K-kidney function. Further work is in progress to co-create a patient held alert using CE-RISK that health professionals would also find beneficial.

P-0376 | Prospective Analysis of Cardiovascular Late Effects in Survivors of Paediatric Brain Tumors

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Background/Objectives: Brain tumors represent the most frequent solid tumors in childhood. Considering improved outcome a better understanding of long-term morbidity is needed.

The aim of this study was to evaluate cardiac function and to determine the prevalence of subclinical cardiovascular impairment in brain tumour survivors (BTS) using a clinical and echocardiographic approach.

Design/Methods: Forty-two BTS were enrolled in this prospective single center study. Electrocardiogram and transthoracic two-dimensional echocardiography including Doppler sonography were performed in all patients. Systolic left ventricular ejection fraction was calculated from enddiastolic and endsystolic volume using biplane Simpsons method. Assessment of diastolic left ventricular function was limited to peak mitral flow velocity, early diastolic velocity of the mitral annulus and the left atrial volume. In addition anthropometric data and blood pressure were determined.

Results: All examined BTS (mean follow-up age 21 years, range 4.8-54.0 years; mean follow-up time 13.2 years) were diagnosed as: Medulloblastoma (n=28), other malignant brain tumors (n=12) and benign brain tumors (n=2). Eight individuals (19%) showed impaired cardiac function. Seven BTS (16.6%) suffered from diastolic and two (4.8%) from systolic dysfunction. Mild valvular disorder respectively arterial hypertension was revealed in four BTS (9.5%). All diagnosed cardiovascular abnormalities were shown in BTS with malignant tumors treated with a combination of surgery, chemotherapy and craniospinal irradiation, none were treated with anthracyclines (mean follow-up time 21.4 years).

Conclusion: Even though it is believed that BTS have a lower risk for cardiovascular disease, in this study a remarkable part (31%) of former patients presented with previously unidentified subclinical signs of cardiac dysfunction and secondary morbidity.

Further studies are needed to define optimal cardiovascular long-term follow-up of childhood cancer survivors, especially with regard to subclinical disease and risk stratification.

LIVER TUMOURS

P-0377 | SIOP PODC Adapted Treatment Recommendations for Hepatoblastoma in Low-Middle Income Settings

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Background/Objectives: Hepatoblastoma is a rare, curable childhood cancer. Its treatment requires access to effective, simple chemotherapy and coordinated surgical care. Great progress has been made in high-income countries, with favourable outcomes, especially in localised disease. Like other cancers presenting in low-middle income countries (LMIC), barriers to cure include advanced disease at diagnosis, malnutrition, chronic infection, failure to complete therapy, minimal access to surgery and lack of evidence-based guidelines adapted to the varied treatment settings. The aim of this project was to create recommendations with the intention to simplify hepatoblastoma therapy, reduce toxicity and facilitate compliance, while adapting treatment to different settings based on available resources.

Design/Methods: A multidisciplinary SIOP-PODC Adapted Treatment Working Group with SIOPEL and COG representatives generated a guideline to support the care of children diagnosed with hepatoblastoma in LMIC. The guideline was created based on expert opinion, published evidence from LMIC and prior SIOPEL trial results.

Results: We present definitions of settings based on minimum resources needed for diagnosis and care. Recommendations for setting-adapted care include clinical evaluation at diagnosis, risk stratification, chemotherapy and supportive care guidelines, and surgical management. A focus is made on management of children with standard-risk disease curable in most LMIC countries, with single-agent cisplatin and timely surgical referral. Guidance is also provided for high-risk disease requiring advanced surgery and care.

Conclusion: Hepatoblastoma is a curable disease and our aim is to facilitate worldwide treatment of this disease through setting-based recommendations.

P-0378 | Characteristics and Outcome of Hepatoblastoma Patients: Experience of Children Cancer Hospital of Egypt

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Background/Objectives: To analyse the clinical characteristics and outcome of hepatoblastoma (HB) patients in Children Cancer Hospital of Egypt (57357 hospital) From 7/2007 to 6/2015.

Design/Methods: Analysis of clinical data of 124 patients from 140 (16 patients excluded) presented to Children Cancer Hospital of Egypt From 7/2007 to 6/2015.

Results: The mean age was 1.18 year (range: 0.05 year-16.14 years), male/female ratio was 1.5:1, complete remission (CR) was registered in 61(49.2%) patients while 16.9% (21 patients) had progressive disease (PR), 24.2% (30 patients) died, 7.3% (9 patients) had stable disease (SD), and 1.6% (2 patients) achieved partial remission (PR) and only one patient died before evaluation.

Eighty two patients that had underwent surgery, 61 patients achieved CR, 2 PR, 1 patient with stable disease, 9 progressed and 9 patient died while the 42 patients with no surgery, 8 had SD, 12 patients progressed, 21 died and one patient died before evaluation.

The overall survival (OS) in this study was 66.7% with event free survival (EFS) 45.7%. OS in non-metastatic was 75.25% with P-value= 0.001. while EFS in non-metastatic was 54.78% with P-value <0.001, the most significance was in the OS and EFS regarding surgery where patients who had underwent surgery achieved OS and EFS (80.74% and 68.63% respectively) with a p-value <0.001, OS was 100% in stage I, 74.72% in stage III and 23.94% in stage IV with P value 0.001 Also there was a significant correlation between the EFS with stage: EFS was 100% in stage I, 53.20% in stage III and 17.86% in stage IV with P value <0.001.

Conclusion: Due to the rarity of hepatoblastoma, national cooperation should be made for further research with special attention to Egypt because of the high incidence of hepatoblastoma.

Finally surgery is the main stay of treatment of hepatoblastoma and every effort must be made to achieve resectability of tumour by developing effective preoperative treatment.

P-0379 | Chemotherapy and Surgical Therapy for High- or Intermediate-Risk Hepatoblastoma

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Background/Objectives: The improvement in outcomes after hepatoblastoma treatment has been remarkable, but outcomes remain poor after treatment of advanced hepatoblastomas.

Design/Methods: Treatment and survival were retrospectively analyzed in 21 patients with high- or intermediate-risk hepatoblastomas treated in our institution from 2002 to 2014.

Results: For the 21 patients (17 boys, 4 girls), the median age at diagnosis was 21 months (range, 12–83 months). The median observation period was 48 months (range, 20–156 months). The numbers of patients in the PRETEXT II/III/IV stages were 3/2/16, respectively. The median AFP at onset was 800,000 ng/ml (range, 50,000–19,000,000 ng/ml). Twelve patients had lung metastases (57%), and 2 had tumour rupture (10%). The preoperative chemotherapy was cisplatin/pirarubicin (CITA) but was switched to another regimen (such as ifomide/pirarubicin/etoposide/carboplatin [ITEC] or cisplatin/fluorouracil/vincristine [C5V]) when efficacy was poor. Lung metastases disappeared in 5 patients after preoperative chemotherapy. Eight patients underwent hepatectomy, and 13 received liver transplantation for a primary liver tumour (1 patient with a post-hepatectomy recurrence in the liver underwent liver transplantation). We resected pulmonary metastases completely before liver transplantation. For hepatectomy cases, we resected the liver tumour followed by pulmonary metastasectomy. The recurrence sites were lungs (n=5), brain (n=1), and abdomen (n=2). A re-recurrence was documented in 4/5 patients with lung metastases, but all 4 cases survived after metastasectomy (lung, brain). However, 2 patients with intra-abdominal recurrences died. To date, 4 cases (80%) are disease-free, and 4 patients (20%) died (3 tumour deaths and 1 leukaemia death).

Conclusion: A high survival rate was obtained by performing either aggressive resection of primary tumors or liver transplantation and the complete resection of metastases by preoperative chemotherapy for intermediate- or high-risk hepatoblastoma. Further follow-up and more cases are necessary to validate these findings.

P-0380 | Living-Related Transplantation of a Liver in Children with Hepatoblastoma

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Background/Objectives: Malignant liver tumors make 1–2% of a number of all tumors of the child age, with yearly incidence of 1.5 cases per million of children aged up to 15 years.

Design/Methods: At the posthoc analysis as of from 2008 to 2014 in Ukraine at the stage of surgical treatment of hepatoblastomas in children 7 living-related transplantations of a liver were performed, among them: orthotopic transplantation of the lateral section of a liver from the live relative donor (mother) was executed to five patients at the stage of surgical treatment, to one patient - hepatectomy, total pancreatectomy, gastroduodenectomy, splenectomy, extended lymphadenectomy, esophagojejunostomy, mesocaval shunting, orthotopic transplantation of the left lateral section of the liver from the live relative donor (mother) with cava portal transposition, and the transplantation concerning recurrence of hepatoblastoma after left-sided expanded hepatectomy was executed to one patient.

Average age of children to whom the living-related transplantation of a liver was carried out made 2,7 years. Chemotherapy according to the clinical protocol SIOPEL 3 was carried out to all patients, group of high risk.

Results: The average time of the execution of the operation made 14,5 hours. In the postoperative period biloma of the resective surface of the graft developed in 1 patient, it was removed by way of ultrasound-controlled puncture. Complete remission of the disease was recorded in all 7 patients to whom living-related transplantation of the liver was executed. The five-year survival rate of patients with hepatoblastoma to whom transplantation of the liver was executed makes 100%, the five-year survival of the graft made 100%.

Conclusion: Executing the living-related transplantation of a liver in children with hepatoblastoma of a liver is a difficult stage of multimodality therapy demanding considerable material and technical support and it allows to achieve good remote results statistically authentically.

P-0381 | Outcome of Thorough Lung Metastasectomy in 16 Patients with Hepatoblastoma

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Background/Objectives: Distant metastasis is one of the most important prognostic factors in hepatoblastoma. Recently, improved outcomes of dose-dense chemotherapy were reported, but the problem of ototoxicity remains. From 2008, we started a program to resect every metastasis of the lung without dose-dense chemotherapy even if the lesions remain multiple, bilateral, recurrent or chemotherapy-resistant. We therefore present the outcome of our program.

Design/Methods: Retrospective chart reviews of 16 patients with hepatoblastoma associated with lung metastases were performed. Each metastatic lung lesion was removed by wedge resection through an open thoracotomy after hepatectomy or in the case of those 4 patients that had unresectable liver tumors, before liver transplantation. Metastatic lesions on every organ except the lung were resected locally. Intraoperative indocyanine green (ICG) fluorescence navigation was used in 12 patients to detect small non-palpable lesions.

Results: The age at diagnosis ranged from 1 to 12 years old. Ten out of 16 patients had no other distant metastases except the lung. The other 6 patients had metastases to the bone, heart, peritoneum, lymph nodes or transplanted liver, which were surgically resected. All patients underwent neoadjuvant and adjuvant chemotherapy. The number of resected metastatic lung lesions in each patient ranged from 4 to 101 with a total of 426 resected lesions. Diameter of the smallest lesion was 0.053mm, which was detected by ICG fluorescence navigation. Observation period ranged from 24 to 90 months. Fourteen out of 16 patients were alive and serum alpha-fetoprotein level was normalized in 12 patients at the end of follow-up. Two-year survival rate was estimated at 87% without serious problems in living patient's quality of life from surgical procedures.

Conclusion: Our results suggested thorough lung metastasectomy is strongly recommended because of excellent survival rate without serious degradation of QOL.

P-0382 | Carbon Nanotubes for Efficient Mitochondrial tumor Targeting

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Background/Objectives: Cancer is uncontrollable growth of cells which are devoid of apoptosis. We developed a novel strategy i.e. Ligand mediated tumour targeting via carrier systems. Multiwalled Carbon nanotubes (MWCNTs) were used as it directly enters into the cell without passing through endo-lysosomes, large inner volume, distinct inner and outer surfaces & have ability to enter the cell by spontaneous mechanism. Thus, proposed work envisages Rhodamine-123 conjugated Paclitaxel loaded functionalized-CNTs to provide enhanced cell permeation in order to enhance mitochondrial availability of Paclitaxel.

Design/Methods: The raw MWCNT were procured and purified, oxidized & then conjugated with rhodamine-123 by carbodimide method. The MWCNT's were characterized *in-vitro* for shape & size by Scanning (SEM) & Transmission Electron Microscopy (TEM), FTIR analysis, X-ray diffraction and zeta potential determined. Stability studies were performed at exaggerated conditions along with Hemolytic Toxicity Study. The Cell Cytotoxicity Study-MTT Assay was done using Hela cell lines. Mitochondrial localization was determined by CLSM study. The *in-vivo* part of the study comprised of determining the distribution of drug in various organs by fluorescence microscopy.

Results: The Rhodamine-123 conjugated MWCNTs were prepared and characterized. The CNTs showed high paclitaxel loading, sustained release, and excellent biocompatibility as evident by *in-vitro* drug release and low hemolytic toxicity. MTT assay against HeLa cell lines suggested the potential anticancer activity of the developed system. CLSM study suggested that mitochondrial specific localization of Rhodamine-123 conjugated MWCNTs in HeLa cells.

Conclusion: Thus, Rhodamine-123 conjugated Paclitaxel loaded *f*-CNTs system have potential to provide an enhanced cell permeation and mitochondrial localization for effective tumour chemotherapy.

P-0383 | Transarterial Chemoembolization for Paediatric Hepatoblastoma

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Background/Objectives: Hepatoblastoma (HB) is the most common paediatric liver tumour and complete resection is a pivotal factor for long-term survival. However 50% of children with newly diagnosed HB are unresectable at presentation; thus strategies to improve resectability are important. Pre-operative systemic chemotherapy is routinely used to achieve this goal, however not all tumors respond and some patients are too ill to receive systemic chemotherapy. Transarterial Chemoembolization (TACE) allows delivery of high concentration of targeted intra-arterial chemotherapy with minimal systemic toxicity and ischemic necrosis by vascular embolization. There is limited data on paediatric TACE for hepatoblastoma.

Design/Methods: Three paediatric patients with unresectable HB at Texas Children's Hospital followed by March 2014 and March 2016 who underwent TACE with doxorubicin and lipiodol followed by embolization with polyvinyl alcohol (PVA) particles were identified and are reported.

Results: Patient 1: 2-year old male with a stage 3 HB was unable to continue systemic chemotherapy due to adenoviremia and respiratory failure. A single session of TACE reduced the tumour dimensions by 85% thereby providing adequate resection margins from the middle hepatic vein and main portal vein.

Patient 2: 11-year old female with an unresectable HB due to proximity to main portal vein received two courses of systemic chemotherapy without tumour shrinkage. She received two cycles of TACE with 25% reduction in tumour dimensions providing adequate surgical margins from main portal vein for resection.

Patient 3: 5-month old female with a stage 3 HB in close proximity to the main portal vein had limited response to systemic chemotherapy and became critically ill. She received one session of TACE with 40% reduction in tumour size allowing for resection.

Conclusion: Our experience demonstrates that TACE is effective for select unresectable children with HB to bridge to successful resection.

P-0384 | Application of GD-EOB-DTPA in Differential Diagnosis of Liver Regeneration Nodules in Children after Cytostatic Therapy: First Experience

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Background/Objectives: To describe radiological patterns of multiple liver lesions in hepatospecific phase in children after cytostatic and immunosuppressive therapy to analyze their nature.

Design/Methods: Six children aged 10 to 17 with multiple liver lesions were included in retrospective study with the following diagnoses: Ewing sarcoma(n=1), vaginal rhabdomyosarcoma(n=1), neuroblastoma(n=1), nephroblastoma(n=1), dermatofibrosarcoma(n=1), Li-Fraumeni syndrome(n=1). 6 patients underwent chemotherapy, 2-high-dose chemotherapy, 1-radiation therapy on abdominal area. All children underwent MRI at 3T using body coil. Contrast agent Gd-EOB-DTPA was used at dose of 0.1ml/kg.

Results: Liver lesions appeared in the interval 2 to 14 years after special treatment. Most of the nodules accumulated contrast agent in hepatospecific phase (i.e. have hepatocyte nature). Among multiple hepatocyte-nature lesions in patient with Li-Fraumeni syndrome the 3rd tumour (PEComa) has been revealed. It had different pattern of contrast enhancement compared to other lesions in hepatospecific phase. Diagnoses were confirmed histologically for non-hepatocyte lesions, by dynamic control for hepatocyte lesions.

Conclusion: Multiple liver hepatocyte nature lesions in children may be assigned to hepatotoxic therapy and were described as regenerative nodules. However, we shouldn't forget about the possibility of appearance of new primary tumors in these patients. Hepatospecific contrast agent can explain nature of the liver lesions and provide the possibility to avoid biopsies in some cases.

P-0385 | The Outcome of Hepatoblastoma Treated at National Hospital of Paediatrics (NHP) in Vietnam

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Background/Objectives: Hepatoblastoma is the most common malignant tumors of liver in children. The aim of this study was to review the outcome of all children with hepatoblastoma treated at the National Hospital of Pediatrics (NHP) in Vietnam from 2010 to 2014.

Design/Methods: Retrospective review of all children (0-16 years) diagnosed hepatoblastoma from 1/1/2010 to 31/12/2014. Data included patient demographics, PRETEXT staging with CT scanning, histology, treatment and outcome.

Results: Fifty-four (37 males, 17 females) patients aged from 0-167 months (median 24.4) were identified. The PRETEXT distribution was I: 6 patients (11.1%); II: 23 patients (44.6%); III: 15 patients (27.8%); IV: 10 patients (18.5%); 4 patients with lungs metastasis.

Seven patients were performed surgery upfront with complete resection then completed chemotherapy (regimen standard risk of SIOPEL 3 protocol). The others 47 patients were treated with neoadjuvant chemotherapy according to SIOPEL 3 protocol, among them 39 patients underwent hepatic resection (36 with complete resections, 2 with microscopic and 1 with macroscopic residue) and 8 patients remained unresectable. At a mean follow up of 37.7 months (0 to 73 months) 42 patients are still alive, 2 patients were lost of follow up, 10 patients died. The 3 years EFS and overall survival was 73.4% and 80.4% respectively.

Conclusion: Treatment of hepatoblastoma at NHP in Vietnam has a good result. The future perspective is liver transplantation for patients with inoperable tumors.

P-0386 | Undifferentiated Embryonal Sarcoma of the Liver – A Diagnostic Dilemma

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Background/Objectives: Undifferentiated sarcoma of the liver (UESL) is a highly malignant tumour of mesenchymal origin, mostly occurring in children with peak incidence is between 5 – 10 years and is generally associated with a poor prognosis. The radiological appearance of UESL is varied and can often be mistaken for benign diseases like hydatid cysts.

Objective: To describe a case of UESL in a child.

Design/Methods: Case report.

Results: A four year old Indian male presented with a one month history of fever, abdominal pain and jaundice. On examination he had hepatomegaly. Serum total and direct bilirubin was elevated with normal liver enzymes. Ultrasound abdomen showed hepatomegaly with complex cystic mass in right lobe. CT abdomen showed a multi-loculated thick walled well defined cystic lesion in the right lobe of liver with irregular septations and patchy hyperdensities within consistent with a diagnosis of intra-hepatic hydatid cysts. He underwent right hepatectomy. However, the histopathology of the specimen showed UESL, with immunohistochemistry being positive for vimentin, CD 10 and CD 68. PET -CT scan did not show any metastasis. He received chemotherapy with alternating cycles of Vincristine/Doxorubicin/Cyclophosphamide and Ifosfamide/Etoposide. He is currently 1 year 10 months post therapy and doing well with no evidence of relapse.

Conclusion: UESL can be a diagnostic dilemma, especially in geographical areas which are endemic for hydatid cyst. This case highlights the importance of considering UESL as one of the differential diagnosis in any cystic lesion of the liver in the paediatric age group.

P-0387 | The Utility of 64-Multidetector Computed Tomography in the Diagnosis and Staging of Hepatoblastoma: Multi-Institutional Study in Upper Egypt

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Background/Objectives: Hepatoblastoma (HB) is the most common primary hepatic malignancy of childhood. The probability of cure for hepatoblastoma is strictly related to the feasibility of achieving a complete mass definition and resection. Imaging plays a pivotal role in the diagnosis and management of children with hepatoblastoma.

Objective: To assess the utility of 64 MDCT in the diagnosis and staging, as well as for follow up of hepatoblastoma in paediatric patients.

Design/Methods: A prospective study was done on patients diagnosed with hepatoblastoma, at four institutions in Upper Egypt, during the period from January 2011 to December 2013. Initial clinical, laboratory (including α -fetoprotein (AFP) measurement) & radiologic evaluation (including abdominal ultrasound, and MDCT for the chest and abdomen) was done, at the baseline for tumour staging, according to SIOPEL pretreatment extent of the diseases (PRETEXT), and later on for follow up assessment & management.

Results: The study included 17 children, 9 males and 8 females with histologically proved hepatoblastoma. Post-contrast MDCT abdomen revealed that 13 patients had a single focal lesion, two patients showed multiple foci in the Rt. Lobe, while two patients had diffuse lesions.

Conclusion: MDCT in children with HB accurately displays the extent of hepatic involvement by tumour, tumour staging as well as its proximity to the vascular structures that could help the surgeon to identify the tumour resectability and can be used in follow up after treatment.

P-0388 | SIOPEL Protocol for Hepatoblastoma in Children. Experience of a Latin-American Paediatric Oncology Center

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Background/Objectives: Review of the epidemiologic features and survival of patients with Hepatoblastoma treated with the SIOPEL protocol.

Design/Methods: Analysis of medical records from 18 patients treated between 2008-2015 with hepatoblastoma who received SIOPEL protocol and had criteria to be enrolled.

Results: Malignant tumors of the liver are rare during childhood. Hepatoblastoma is the most common liver cancer in children. In our Hospital they represent 3% of all paediatric malignancies. Despite treatment with chemotherapy and surgical resection, the prognosis in patients with advanced disease guarded.

During the past eight years we evaluated forty-two patients with hepatic tumors of them, eighteen patients with Hepatoblastoma were treated with the SIOPEL protocol. 67% were males (2:1). Thirteen patients were younger than three years, three 3-6 years old, and two patients older than six years of age. Seven patients (39%) were PRETEXT IV, nine patients (50%) were PRETEXT III and two patients (11%) PRETEXT II. Almost 30% of patients had metastatic disease at diagnosis. The EFS was 61%. Seven patients died (five older than 3 years of age): 3 with progressive disease, 1 with secondary malignant Schwannoma, 2 due to toxicity and 1 who was in remission, died with bronchial aspiration. Finally only two patients were unresectable and were not candidates for hepatic transplantation. The SIOPEL protocol was well tolerated regarding infectious complications.

Conclusion: A multidisciplinary team approach is a crucial element for the management of Hepatoblastoma. The SIOPEL protocol can be applied in countries with limited resources. Hepatic transplantation remains a limitation in our unresectable patients and a program should be implemented in order to improve survival

Key words: Hepatoblastoma, children, SIOPEL, toxicity.

P-0389 | Outcome of Living Donor Liver Transplantation for Unresectable Non-Fetal Hepatoblastoma with Extrahepatic Extension

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Background/Objectives: Liver transplantation (LT) is a sole and mandatory method to extirpate unresectable hepatoblastoma (UH). However, the outcome of LT combined with pre-/post-LT chemotherapy and surgical metastasectomy has been controversial for UH associated with extrahepatic extension. Herein, we analyzed our experience and compared it with the literature.

Design/Methods: Seven children with UH underwent living donor LT at our hospital between 2010 and 2015, four patients for primary LT (Group P) and three for rescue LT (Group R). All the primary lesions were of non-fetal type. Lung metastases existed at initial diagnosis in five patients (two in Group P, three in Group R), but resolved before LT with either chemotherapy or metastasectomy assisted with ICG navigation. Chemotherapy including irinotecan or sorafenib was done in six patients, beginning between 0.5 and 2 month after LT. Follow-up period after LT was 1.6 (0.5–5.3) years. Our data was compared with the Japanese nationwide survey of LT outcome for UH (Sakamoto, et al. *Liver Transpl* 2014, 20: 333-346).

Results: All the grafts survived and functioned normally despite biliary complications or adhesion ileus in three patients. Five patients survived at the end of the follow-up, with two patients being recurrence-free (one each in Group P and R). Five patients developed post-LT recurrences mainly in the lungs (three in Group P and two in Group R). Despite chemotherapy and metastasectomy, two patients in Group P died of recurrences, and the other three continued multidisciplinary treatment. Immunosuppressants were totally withdrawn in five patients with post-LT recurrences. Our outcome of overall survival and recurrence-free survival was comparable with that of non-fetal UH with extrahepatic involvements in the nationwide survey.

Conclusion: Even a combination of LT with pre-/post-LT chemotherapy and metastasectomy assisted with ICG navigation, though principled approach for UH, may have limited therapeutic effect on patients with non-fetal UH associated with extrahepatic extension.

P-0390 | Significance of Transcription Factor GATA4 and the BCL2 Protein Family in Doxorubicin-Induced Apoptosis of Human Hepatoblastoma Cells

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Background/Objectives: Doxorubicin is an essential drug in the treatment of hepatoblastoma, the most common type of paediatric liver cancer. The major adverse effect of this drug is cardiotoxicity, caused in part by downregulation of transcription factor GATA4 expression in cardiomyocytes leading in turn to downregulated levels of anti-apoptotic BCL2 protein family members and consequently to the apoptosis of the heart muscle cells. GATA4, implicated in the early liver bud development, is also highly expressed in malignant hepatoblastoma cells. Analogously to the fact that GATA4 protects cardiomyocytes from apoptosis, we hypothesized that high levels of GATA4 in hepatoblastoma cells might render these malignant cells resistant to the apoptotic effect of doxorubicin.

Design/Methods: A human hepatoblastoma cell line HUH6 was treated with GATA4 siRNA and/or doxorubicin, after which cell viability, apoptosis, and gene expression were measured.

Results: Doxorubicin treatment caused a significant decrease in the expression levels of GATA4 in HUH6 cells. Parallel to this, we observed a marked downregulation of anti-apoptotic BCL2 and upregulation of pro-apoptotic BID. Doxorubicin was noted to decrease cell viability and trigger apoptosis, and siRNA-mediated silencing of GATA4 prior to treatment enhanced these effects of doxorubicin in HUH6 cells.

Conclusion: Our results implied that high levels of transcription factor GATA4 in hepatoblastoma cells hinder the desirable therapeutic effects of doxorubicin, especially apoptosis, in these malignant cells. Based on current results and earlier findings in cardiomyocytes, GATA4 likely exerts its actions by regulating the balance of the anti- and pro-apoptotic BCL2 family members in the intrinsic apoptotic pathway. Although doxorubicin by itself somewhat decreases GATA4 levels and thus renders hepatoblastoma cells more vulnerable to doxorubicin action, finding of ways to further reduce high GATA4 levels in hepatoblastoma tissue could be advantageous to the treatment outcome.

P-0391 | NFE2L2 Contributes to Proliferation and Cisplatin Resistance in Hepatoblastoma Via the PI3K/AKT Pathway

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Background/Objectives: Although the prognosis for hepatoblastoma (HB) has improved with advances in treatment, significant challenges remain for patients with advanced, metastatic, or relapsed disease, as well as relatively older children. Recently, activating mutations in *NFE2L2* have been reported in both HB and HCC. These activating mutations and/or high expression of *NFE2L2* have been observed in paediatric liver tumors with high-risk features and poor outcome. We hypothesized that *NFE2L2* activation/overexpression contributes to an aggressive phenotype and investigated its role in HB cell proliferation and chemoresistance. We also investigated the interaction of *NFE2L2* with other oncogenic pathways known to be active in HB, including PI3K/AKT.

Design/Methods: The Hep293TT cell line established from a highly aggressive HB from a 5-year-old female was transfected with *NFE2L2* siRNA. Analyses of cell proliferation and cell cycle kinetics were conducted using cell viability assays (CellTiter-Glo Luminescence), propidium iodide staining, and FACS analysis. A comprehensive transcriptome analysis of Hep293TT cells was carried out by RNA-seq. Protein expression was determined by Western blotting.

Results: RNA-seq analysis revealed high expression of *NFE2L2* in Hep293TT cells with a 2.01-fold change relative to mean expression level from 14 other paediatric cancer cell lines. Genetic knockdown of *NFE2L2* by siRNA inhibited cell proliferation, induced cell cycle arrest, suppressed cell migration and colony formation, and enhanced Hep293TT cells sensitivity to cisplatin. Interestingly, enhanced sensitivity to cisplatin was associated with a significant reduction in phospho-, but not total-AKT levels, as well as a reduction in phospho-mTOR, suggesting that *NFE2L2* may be a potential target for overcoming cisplatin resistance in HB by inhibiting AKT and mTOR. *NFE2L2* knockdown also altered the expression of ~165 genes ($p < 0.01$).

Conclusion: Our results suggest that *NFE2L2* promotes HB cell survival, migration and chemoresistance in part through PI3K/AKT. Further studies are warranted to determine the potential role of *NFE2L2* as a target for HB therapy.

P-0392 | A New Perspective for Infantile Hepatic Hemangioma in the Age of Propranolol

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Background/Objectives: Propranolol was first used in 2008 in hemangioma. Effect and safety of drug have changed treatment in hemangioma. Infantile hepatic hemangioma (IHH) has a spectrum of conditions varying from simple lesions to lethal ones. In this entity, management varies from 'wait and see policy' to liver transplantation.

Design/Methods: This study included patients who had been diagnosed as IHH and treated with propranolol and prednisolone in Baskent University between July 2009–December 2015. These patients were cases consulted with liver lesions and patients screened by ultrasonography for multiple hemangiomas. Patients were hospitalised, routine laboratory evaluations were done. All were treated with standardized regimen of propranolol (2-3 mg/kg/day; and prednisolone 1.5-2.0 mg/kg/day for 7 days).

Results: Age range was between 1.1- 8 months (median 2.4 months) and eight of them were male (n=13). There were no dermal hemangiomas in 4 patients. Both USG and MRI were used for diagnosis in 8, only USG in 4, and USG+MRI+biopsy in one patient. Three of patients were diagnosed as focal; 2 as multifocal, and 8 as diffuse nodular type. Three of patients had treatment previously. First patient had been treated with methylprednisolone, interferon and vincristine. This case had been published [DOI: 10.1002/pcb.22691]. In another patient no response had been achieved with steroids. There was a uterine hemangioma leading to hemorrhage in this patient's mother. Last patient was diagnosed with congenital hypothyroidism. Treatment duration was between 2-11 months in 11 patients, (median: 7 months). In two patients, lesions were resistant. These patients had treatment for 22 months. In 9 patients complete response (% 69) had been achieved in median 4 months (2-11 months), and partial response was seen in 4 patients.

Conclusion: We recommend propranolol and prednisolone to patients with liver hemangiomas. In case of no response, further evaluation including biopsy should be done. Beta-blockers should be given around 8 months.

LYMPHOMAS

P-0393 | Prognostic Factors and Treatment Outcome of Paediatric Anaplastic Large Cell Lymphoma Treated at the Children Cancer Hospital Egypt

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Background/Objectives: Anaplastic large cell lymphoma (ALCL) belongs to the group of high-grade non-Hodgkin lymphomas. ALCL cells are characterized by the expression of the CD30/Ki-1 and more often by a T-cell phenotype. Frequently, ALCL is associated with the t(2;5)(p23;q35) chromosomal translocation, which gives rise to the fusion gene NPM-ALK.

The aim of the current study is to report the clinico-epidemiologic data, prognostic factors and treatment outcome of paediatric ALCL treated at the Children Cancer Hospital Egypt (CCH) during 8 years period.

Design/Methods: A retrospective study including all patients diagnosed and treated as ALCL from July 2007 till July 2014 at CCH. Diagnosis of ALCL was based on morphologic and immunohistochemical criteria.

Results: Forty-three patients were enrolled in our study, forming 5.4% of all NHL patients treated at CCH within this period. They were 26 males (60.5%), and 17 (39.5%) females. Median age was 11.7 years. The most common tumour primary site was generalized lymphadenopathy (62%). ALK status was available in 65% of the cohort (28 patients), of which 75% (21 patients) were positive. Bone marrow was free in all patients, while 5 patients (11.6%) had CNS involvement. Stage II and III were 37.2% each (16 patients). Post induction evaluation showed 25 (58%) patients in complete remission (CR), 15 (34.9%) partial remission (PR), 2 (4.7%) were progressive (PD), and 1 (2.4%) stationary disease (SD), while at the end of treatment 83.7% were in CR, 11.6% PD and 4.7% relapsed. At the end of the study period, 81.4% (36 patients) were alive, and (8 patients) 18.6% died. The mean FU period was 50 months (range 12-96). The 4 years OS and EFS is 80.9% and 71.1% respectively.

Conclusion: Summary and Conclusion:

Results of treatment of ALCL in our center are comparable to most of the reported studies. Salvage for relapsing and progressing patients is difficult, and the outcome is extremely poor.

P-0394 | Prognostic Factors and Treatment Outcome of Relapsing Mature B Cell Non Hodgkin Lymphoma Treated According to LMB96 Protocol at the Children Cancer Hospital Egypt

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Background/Objectives: Non-Hodgkin lymphoma (NHL) consists of a complex group of cancers arising mainly from B lymphocytes (85% of cases). NHL usually develops in lymph nodes (nodal lymphoma), but can arise in other tissues almost anywhere in the body (extranodal lymphoma). NHL has cure rate approximating 80%. Unfortunately, relapsed NHL has a dismal prognosis, and the customary treatment is highly toxic chemotherapy followed by hematopoietic stem cell transplantation (HSCT).

Aim: to analyze prognostic factors and treatment outcome of relapsing mature B cell NHL treated at the Children Cancer Hospital during according to LMB 96 protocol during 8 years period.

Design/Methods: A retrospective study including all patients under age of 18 years or less initially diagnosed as mature B cell NHL who relapsed following initial chemotherapy during the period from July 2007 to July 2014.

Results: Thirty patients relapsed out of 576 NHL (5.2%) treated during this period. Mean age 8.4 years (range 3-17). They were 19 males and 11 females. Pathology was Burkitt lymphoma in 53.3%, Burkitt leukaemia 33.3%, DLBCL in 6.6%, and PMLBL in 3.4%. Relapsing site was single organ in 56.7% and multiple organs in 43.3%. Relapsing patients were stage III in 60% and IV in 36.6%. Median time to relapse was 6.1 months (range 3.9-48). Seventy percent of the patients received salvage chemotherapy, while 30% had best supportive care following relapse. Salvage chemotherapy was ICE in 30%, R-ICE 30%. Eight patients underwent HSCT, of whom Finally, 22 patients (73.3%) died and 8 (26.6%) were alive. The 1 year OS and EFS was 50.3% and 33.1%, while the 2 years OS and EFS were 29% and 6.9% respectively.

Conclusion: Relapsing mature B cell NHL have dismal outcome. Late relapse and single organ at time of relapse offer a better chance for survival following high dose chemotherapy and Hematopoietic Stem cell transplant.

P-0395 | 25 Years Experience of a Single Center: Clinical Features and Treatment Outcomes in Advanced Stage Non-Hodgkin Lymphoma in Childhood

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Background/Objectives: Non-Hodgkin lymphomas (NHL) of childhood and adolescence are a heterogeneous group of malign diseases originating from the lymphoid cells. Survival rates in NHL have increased significantly in the last decades, which usually responds to the poly-chemotherapy, however advanced stage NHL results still are not curative. This study aims was to evaluate and compare the demographic data and treatment results of childrens with advanced stage of NHL treated and therapeutic efficacy of modified NHL German Berlin Frankfurt Munster (BFM) protocols in our center retrospectively.

Design/Methods: 103 children (72 male, 31 female) from January 1990 to January 2016, new diagnosed with advanced NHL were enrolled to the study. The patients were stratified by risk factors and treated either with a modified B-nonB NHL BFM-90 (before 2004) or BFM-95 (after 2004) protocols. (Until September 1993, lymphoblastic patients received LSA2, non lymphoblastic NHL patients received COMP) and the use of 1 or 3 g/m² of methotrexate instead of 5 g/m²/24 h was the only important modification in BFM-90 protocol.

Results: The median age 6 years (2.5-14.5 years) were treated in the center with median 183 months follow-up. Histopathologic subtypes were: 25 lymphoblastic, 6 anaplastic large cell, 1 follicular, 71 Burkitt/diffuz B cell. Seventy three patients (71%) in stage III, and 30(29%) in stage IV. Initial primary tumour location sites were abdomen (58%), head and neck (18%) and thorax (15%). The median LDH level at diagnosis was 790U/L (224-10300). Treatment results: 31 patients (15 progressive disease, 14 toxicity, 2 seconder neoplasm) died. Seven patients were follow-up. The 5-year overall survival (OS) for all patients was 72% and event-free survival (EFS) was 68% respectively. Five year OS was 100, 89, 73, 52% in stage I, II, III, and IV and EFS was 68, 65% in stage III and IV respectively. Survival rates were significantly higher in patients receiving modified BFM regimens, than in ones COMP and LSA2L2 (p=0.061 for OS, p=0.049 for EFS).

Conclusion: Survival rates in the whole group are in parallel with advances attained in the world in NHL.

P-0396 | Clinical Features and Treatment Results in Childhood Hodgkin Lymphoma

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Background/Objectives: Hodgkin lymphoma(HL) of childhood is characterized by progressive enlargement of the lymph nodes. Survival rates in HL have increased significantly in the last decades and cure rates are 100% in early-stage. The aim of this study was to evaluate the

demographic data of the children with HL in our center retrospectively and treatment results are compare the results of the literature.

Design/Methods: One hundred and thirteen patients from September 1990 to September 2015, previously untreated, diagnosed as Hodgkin lymphoma with biopsy were included in this study. The patients were treated with chemotherapy and involved field radiotherapy according to the stages. Patients were treated 2-4 cycles of ABVD (Adriamycine, bleomysine, vinblastine, decarbasine) in I, II A, B and IIIA and six cycles MOPP/ABV in IIIB and IVA, B.

Results: Male /female ratio was 82 /31 and age was 7 years (2.5-16 years). Patients were classified as 12(11%) in stage I, 58(52%) in stage II, 32(28%) in stage III, and 11(9%) in stage IV. B symtoms were detected in 36% of patients and bulky disease 34% of patients. The most common histologic type was mixed cellular type (62%). Five and 10 year overall survival were 92% and 88%, event- free survival were 84% and 81% respectively. According to stage, overall survival was 100% in patients with stage I, 96% for stage II, 78% for stage III, 78% for stage IV. There was significant relationship between stage and survival (p=0.02).

Conclusion: Survival rates improved over time by increasing support therapies.

P-0397 | Primary Extranodal Non-Hodgkin Lymphomas in Rare Locations: Thirty-Five Years Experience of Single Centre

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Background/Objectives: Approximately one-third of non-Hodgkin lymphomas (NHL) arise primarily from extranodal regions – most commonly intestines, waldeyer rings, sinonasal and mandibular-maxillofacial regions. Primary extranodal NHL in locations such as bones, skin and stomach is rarely seen. Here, we evaluated cases with primary extranodal NHL arising from these rare sites.

Design/Methods: 1270 NHL patients diagnosed between 1980 and 2015 were evaluated retrospectively. There were 71 patients with tumors in extranodal sites other than intestines, waldeyer rings, sinonasal and mandibular-maxillofacial regions. Patients' age and gender, tumour's location and histopathological subtype, treatment and survival rates were recorded.

Results: There were 51 males, 20 females with a median age of 108 months. Primary tumour location was skin in 21.1% of cases, epidural region in 19.7%, bone and soft tissue in 15.5%, CNS in 9.9%, stomach in 9.9%, gonads in 8.5%, lungs in 5.6%, kidney in 4.2%, ocular adnexa in 4.2% and parotid in 1.4%. Median time until diagnosis was 2 months. Longest median duration of symptoms was reported in ocular adnexial and skin lymphomas while the shortest were in epidural and gonadal lymphomas. Histopathological subtypes were mature B cell lymphoma in 30 patients, mature T cell in 14, lymphoblastic in 13, and unclassified in 14. The disease was in early stage in 46.5% of patients and advanced stage in 53.5%. Gonadal and skin lymphomas were more commonly presented with early stage disease. Median follow-up time was 45 months. Five-year overall and event free survival were 65.5% and 53.8%, respectively. Longest overall survival rates were found to be in ocular adnexa (100%) and gonads (83.7%) and shortest were in lung lymphoma (50%).

Conclusion: Primary extranodal lymphomas in rare locations comprised 5.5% of our NHL cases. Most of them were high grade mature B cell phenotype. Tumour location was found to be more important than histopathology in prognosis.

P-0398 | Implications of Progressive Transformation of Germinal Center in Children. Experience at a Single Tertiary Care Center

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Background/Objectives: Progressive Transformation of Germinal Center (PTCG) is a rare condition heralded by persistent enlargement of the lymph nodes. First reported by Lennert & Müller-Hermelink in 1975, it is an intriguing case of cervical lymphadenopathy as it mimics nodular lymphocyte predominant Hodgkin disease (NLPHD). It is more common in males than females with a ratio of 3:1. Being an idiopathic disorder, its implications in children are not well known.

Design/Methods: We performed a retrospective review of 4 patients diagnosed with PTGC at our institute in the last 2 years.

Results: Median age at diagnosis was 129.62 months (range 77.08-148.10) and the mean duration of follow-up was 7.29 months. Three patients were males (75%). Mean WBC count was 10.25(range 8-12). No one had a past or family history of malignancy. All patients presented with a history of cervical lymphadenopathy. Epstein Bar Virus (EBV) status was done for 2 patients and was negative. Fever, Sweating, and weight loss were not reported in any of the patient with one had hepatomegaly. All the four patients underwent excisional biopsy for confirmation of diagnosis. One patient (25%) transformed into nodular lymphocytic predominant Hodgkin lymphoma. There was no recurrence reported.

Conclusion: PTGC carries a small risk of transforming into subsequent HL. Patients undergo multiple biopsies and are put on long term follow-up for recurrences. There is a need to design an optimal surveillance strategy for these patients and the indications for repeated biopsies.

P-0399 | Mycophenolate Mofetil Treatment in Children with Autoimmune Lymphoproliferative Syndrome

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Background/Objectives: Autoimmune lymphoproliferative syndrome (ALPS) is characterized by immune dysregulation due to a defect in lymphocyte apoptosis. The clinical manifestations may be noted in multiple family members and include lymphadenopathy, splenomegaly, increased risk of lymphoma and autoimmune disease, which typically involve hematopoietic cell lines manifesting as multilineage cytopenias.

Design/Methods: We present eight children diagnosed ALPS who treated with MMF in our department. The first diagnoses of patients were immune thrombocytopenic purpura or autoimmune hemolytic anemia. Then other Autoimmune cytopenias (hemolytic anemia, thrombocytopenia, or neutropenia) developed. Elevated CD3+TCR $\alpha\beta$ +CD4-CD8- DNT cells ($\geq 1.5\%$ of total lymphocytes or 2.5% of CD3+ lymphocytes) with normal or elevated lymphocyte counts and elevated immunoglobulin G levels (polyclonal hypergammaglobulinemia) were determined. Somatic or germline mutations were not been studied.

Results: Four of our patients were men. Age at diagnosis were 2-10 year. Initial therapy involves high dose corticosteroids (30 mg/kg) or intravenous immune globulin (IVIG). Other steroid sparing agents that have been trialed in ALPS include rituximab, mycophenolate mofetil (MMF), sirolimus and pentostatin. MMF is a prodrug of mycophenolic acid, which is a reversible inhibitor of inosine monophosphate dehydrogenase (IMPDH) in purine (guanine) biosynthesis that is ultimately necessary for the growth of both T and B cells. Thus, suppressing T and B cells limits autoimmune destruction of healthy cells. MMF is usually given concomitantly with high dose IV corticosteroids initially, and then continued while tapering oral prednisone, with an overlap of at least 2 weeks in order to allow MMF to achieve therapeutic levels.

Conclusion: All patients were treated with MMF an average of 2 years. Cytopenias recovered. Risk of infection increased. There were no serious complications.

P-0400 | Cox-2 Expression as a Prognostic Factor in Paediatric Classical Hodgkin Lymphoma

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Background/Objectives: Cyclooxygenase-2 (COX-2) is an inflammatory enzyme and it was proved to have a role in tumour initiation, angiogenesis, proliferation, and inhibition of apoptosis. COX-2 expression increases in many cancers and it is proved to be a negative prognostic parameter.

Design/Methods: We investigated the prognostic value of COX-2 expression using immunostaining in a group of paediatric Classical Hodgkin lymphoma (CHL) patients (n=131), who presented during the period from January 2005 till June 2013, and whose data were retrieved from the medical record of the Pediatric Oncology department, National Cancer Institute, Cairo University, Egypt and were followed up till August 2015. We analyzed the relation of COX-2 expression to the most recognized clinical variables and its impact on outcome.

Results: COX-2 was expressed on Reed-Sternberg cells in 37.4% of the whole group. The frequency of expression was found to be more among patients with bulky disease in comparison to non-bulky and the same applies to other groups such as: B symptoms, high ESR, extranodal extension, and advanced stage without statistical significance. With a mean follow-up period of 54.4 months, 5-year overall survival and progression free survival was lower in COX-2+ve than that in COX-2 -ve patients but still without statistical significance.

The impact on prognosis was observed in male group of patients. With a worse 5-year OS (82.9%) in +ve compared to 100% in COX-2 -ve patients (P value: 0.045) and tendency for statistical significant 5-year PFS (75.7% Vs 90.2%) in +ve and -ve respectively (P value: 0.06).

Conclusion: COX-2 was expressed on Reed-Sternberg cells in 37.4% of paediatric CHL patients. It was found to be an unfavorable prognostic factor in males and might be a therapeutic target. However, further studies including larger numbers of HL patients are needed to investigate that COX-2 may be a major prognostic variable in paediatric HL.

P-0401 | Non-Metastatic Paediatric Abdominal Non-Hodgkin Lymphoma at South Egypt Cancer Institute A 10- Year Report

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Background/Objectives: Abdominal Non-Hodgkin lymphomas (NHL) are the most common extra nodal presentation of paediatric NHL, small and large intestines are the most frequent sites of involvement in the paediatric age group. In this study we aim to identify the clinical presentation of abdominal NHL, management and survival of patients with stage II, III NHL at Pediatric Department SECI.

Design/Methods: This study included ninety three paediatric patients with abdominal NHL treated over 10 years at Pediatric Department SECI Assiut University between January 2004 and December 2014. The data of every patient included: age, sex, presenting symptoms and signs, metastatic work up to determine extent of the disease at presentation and the type of resection performed, histopathological examination, details of chemotherapy and survival.

Results: The study included 63 boys and 30 girls with a median age of 6 years (range: 2.5-15). 30 patients (86%) presented with abdominal pain, 46patients (56%) presented with abdominal mass and distention, 28 patients (34%) presented with weight loss, and intestinal obstruction occurred in 12 patients (17%). The ileocecal region and abdominal lymph nodes were the commonest sites (78.5%, 21% respectively). Burkitt lymphoma was the commonest histological type in 79 patients (83%). Twenty patients (28.5%) stage II (group A) and 73 patients (71.5%) stage III (group B). Complete resection was done in 20 patients (28.5%), debulking in 12 patients (17%) and imaging guided biopsy in 61 patients (54%). All patients received systemic chemotherapy. The median follow up duration was 63 months (range 51-78 months). The parameters that significantly affect the overall survival were localized disease with complete resection and response to chemotherapy.

Conclusion: The extent of disease at presentation is the most important prognostic factor in NHL. Surgery plays an important role such as complete resection in localized disease and diagnostic biopsy. Chemotherapy is the cornerstone in the management of paediatric NHL.

P-0402 | Pattern and Treatment Outcome of Paediatric Non Hodgkin Lymphoma from a Tertiary Cancer Institute in South Egypt

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Background/Objectives: Lymphoma (Hodgkin and non-Hodgkin) is the third most common childhood malignancy, and non-Hodgkin lymphoma (NHL) accounts for 7% of cancers in children less than 20 years of age. The prognosis for childhood NHL improved significantly with the realization that the majority of cases (85%) were disseminated from the start. The assignment of risk-adjusted systemic therapy as specific treatment protocols is necessary for long term disease free survival.

This study aimed to describe the pattern of Pediatric NHL at the Pediatric Oncology Department of South Egypt cancer Institute (SECI), Assiut University to have an idea about the disease pattern and treatment outcome in our locality and compare it with previous reports from other parts of Egypt and worldwide.

Design/Methods: A retrospective analyses of diagnosed paediatric NHL cases in a 14-year period (January2001 –Januray2015) was performed.

Results: This study included 242 patients, their age ranged between 2.5-14 years and median was 6.8 years. The male to female ratio was 2.3:1. Seventy two percent had extranodal disease and 28% had nodal disease, 50% presented with abdominal mass, 22.5% had thoracic involvement, peripheral node enlargement in 12.5%, head and neck in 10%. Burkitt lymphoma (BL) was the most common NHL subtype (64%), lymphoblastic lymphoma, diffuse large B-cell lymphoma and anaplastic large-cell lymphoma, accounting for 24, 8 and 4% respectively. The majority of patients (50%) were stage III and (43%) were stage IV. Complete remission was achieved in 180 cases (75%). A total of 32 patients (13%) succumbed to the disease during the first few months and 30 patients (12%) relapsed. The mean follow-up duration \pm SD was 74.6 \pm 25.1 months (range, 13-108 months). The 5-year overall survival (OS) and event-free survival (EFS) rates were 88.7 and 75%, respectively.

Conclusion: Several prognostic factors affect on survival including the LDH level, stage of the disease, and early response to COP.

P-0403 | Fab/LMB96 Regimen for Newly Diagnosed Mature B-Cell Non-Hodgkin Lymphoma in Children: Hacettepe Results

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Background/Objectives: Outcome of Burkitt lymphoma has been increased to 90% for EFS and 93% for OS with LMB FAB regimen. In this study, demographic characteristics and outcome of 51 patients with mature B cell lymphoma was treated with FAB/LMB96 regimen were presented.

Design/Methods: Standard intensity arms were the only selected regimen for all risk groups. Clinical characteristics, response to treatment and outcome were evaluated.

Results: Median age of 41 boys and 10 girls was 8 years. Histopathological subgroups were Burkitt lymphoma in 46, diffuse large B cell lymphoma in 4 and follicular lymphoma in 1 patients. Eleven patients had bone marrow involvement and 4 patients had CNS involvement at diagnosis. There were 1, 34 and 16 patients in risk Groups A, B and C. Mean LDH levels were 813U/L and 1675U/L for Groups B and C. Patients followed up median 32.2 months. The patient with abdominal stage 2A was treated as risk Group A is still alive without evidence of disease for 60 months. The 4-y OS rates were 96.6% and 72.2% for Group B and Group C patients, and 4-y EFS rates were 82.2% and 56.3%, respectively. At the end of induction, responses were complete (CR) in 28, very good partial in 7, partial in 10, progressive or relapsed disease in 6 patients. At the end of induction none of the patients in Group C with CR experienced event and all are still following up with no evidence of relapse. In Group B patients with CR 2 years EFS and OS were 90% and 94%.

Conclusion: Our results confirm the previously published survival results of FAB/LMB96. The regimen is an effective regimen for mature B cell non-Hodgkin lymphoma. It is also very effective for patients with CNS involvement without radiotherapy. The most important prognostic factor is the CR after induction chemotherapy.

P-0404 | Paediatric Hodgkins Lymphoma: Presentation at a Tertiary Hospital in Ghana

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Background/Objectives: Hodgkin lymphoma (HL) is a primary solid tumour of the immune system with varied histopathologic subtypes. The epidemiology of HL suggests an infectious etiology with Epstein Barr Virus (EBV) in up to 40% of cases and this association is believed to be causal. HL is the fourth commonest cancer seen amongst the paediatric population in the Paediatric Oncology Unit of the Komfo Anokye Teaching Hospital (KATH). The purpose of this study therefore, is to review the demographic profile of paediatric patients with HL, the proportion of patients with B symptoms, histopathologic subtypes, anatomical nodal sites of involvement and stage at presentation.

Design/Methods: This is a retrospective study which reviewed the clinical and histopathological features of Hodgkin Lymphoma in paediatric patients at Komfo Anokye Teaching Hospital from January 2010 to December, 2015.

Results: A total of 16 patient records were reviewed with 62.5% males and 37.5% females. The median age was 11years (Range; 4years-15years). Nodular sclerosing classic Hodgkin lymphoma was the commonest subtype seen in (43.8%) and Mixed Cellularity Hodgkin

lymphoma (21.4%) was the rarest. Nodular predominant HL was seen in 5 (31.3%) of patients. Cervical lymphadenopathy (92.9%) was the commonest site of presentation with mediastinal involvement (7.1%) being the least. All the patients presented with fever and weight loss. Over half (57.1%) of the patients presented with night sweats. Majority of patients (62.5%) presented with stage 3 disease while five (31.3%) presented with stage 4 disease. Only 1 (6.2%) patient presented with a stage 2 disease.

Conclusion: Patients were predominantly males with majority presenting with Nodular sclerosing histopathological subtype, cervical lymphadenopathy and B symptoms. Most of the patients presented with advanced disease impacting on the survival.

P-0405 | Hodgkin Lymphoma in Children – A Retrospective Analysis of a Tertiary Center Experience

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Background/Objectives: Hodgkin Lymphoma (HL) is characterized by progressive enlargement of the lymph nodes and comprises 8.8% of all childhood cancers. The aim of this study is to evaluate the response to chemotherapy of children with HL treated in Oncology Clinic of Sf. Maria Emergency Hospital for Children, Iasi, Romania, between 2010 and 2014.

Design/Methods: This is a retrospective study of 27 files of children with HL treated from 2010 to 2014.

Results: 15 males, 12 females; rural areas – 20; year of diagnosis: 2010 – 2 cases, 2011 – 3 cases, 2012 – 11 cases, 2013 – 5 cases, 2014 – 6 cases. The median age at diagnosis – 9.11 years old for females, 12.4 years old for males. Stage: II – 13 (48.14%); III – 9 (33.33%); IV – 5 (18.51%). 17 children with A symptoms (62.96%), 10 children with B symptoms. Histology: nodular sclerosis – 10; mixed cellularity – 14; lymphocyte-depleted – 3. Chemotherapy: ABVD – 25 cases, COPP/ABV hybrid – 1 case, OEPA – 1 case. Radiotherapy – 2 cases. Response: complete remission – 18 (66.66%), partial remission – 6 (22.22%), lost in follow-up subjects on treatment – 3.

Conclusion: An increasing number of children diagnosed with advanced HL associated with lower socioeconomic status was noticed. Two third of the children had complete remission, all of them after ABVD course, probably being in A low stage at diagnosis. Chemoprotocols differed because of the local shortage of drugs.

P-0406 | Castleman's Disease in a Patient with Glycogen Storage Disease Type 1A

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Background/Objectives: Patients with glycogen storage disease type 1a (GSD-1a) may develop many different abdominal tumors. The majority of these tumors are hepatocellular adenomas, hepatoblastomas and hepatocellular carcinomas. The pathophysiology of these tumors is thought to be related to the underlying metabolic disorder and genetic mutation. Castleman's disease is a rare lymphoproliferative disorder and has never been reported in association to glycogen storage diseases.

Design/Methods: We report the case of a 15-year-old male with a known diagnosis of GSD-1a who was found to have a large adrenal mass with prominent periaortic and pericaval lymph nodes. Excisional biopsy revealed Castleman's disease, hyaline-vascular variant. We report this rare occurrence and review the literature of intrabdominal neoplasms in general and Castleman's disease in particular in this context.

Results: 15-year-old Hispanic male with a diagnosis of GSD-1a diagnosed at five months of age by liver biopsy. He and his non-identical twin brother had multiple episodes of hypoglycemia during the first six months of life. His brother died at one year of age due to complications of this disorder.

As a routine exam to assess for hepatosplenomegaly, an abdominal ultrasound revealed a paraspinal cystic mass posterior to the intrahepatic inferior vena cava measuring 4.4 × 3.4 × 2.5 cm. Abdominal computed tomography showed that the lesion was displacing the right adrenal gland inferiorly and that the attenuation and washout measurements were not characteristic of adenomas. Prominent periaortic and pericaval nodes were found demonstrating an enhancement pattern similar to the dominant mass. Peripheral nerve sheath tumour, ganglioneuroblastoma/ganglioneuroma, pheochromocytoma or adrenal cortical carcinoma were differential diagnoses. Labs were unremarkable. Excisional biopsy revealed Castleman's disease, hyaline-vascular variant. His postoperative course and follow up was uneventful.

Conclusion: Castleman's disease is a potential diagnosis of abdominal masses in children with glycogen storage disease type 1a. Further studies may delineate the relationship between these two disorders.

P-0407 | Blastomycosis in An Adolescent Patient with Hodgkin Lymphoma

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Background/Objectives: To describe the case of an adolescent female with Hodgkin lymphoma, who developed pulmonary lesions post chemotherapy, and was diagnosed with blastomycosis.

Design/Methods: Blastomycosis is a rare but potentially fatal infection caused by the thermally dimorphic fungus *Blastomyces dermatitidis*. It is presumed to be a soil organism and it exists as a mould at outdoor and room temperatures and a yeast at body temperature. Primary infection generally follows inhalation of conidia, asexual fungal spores that are shed at maturity. In contrast to most invasive fungal infections, such as those by *Aspergillus spp.*, that are more commonly encountered in oncology and transplant patients, blastomycosis is most commonly reported in immune competent patients. Here, we describe the case of a 17 year old girl, with classical Hodgkin Lymphoma (stage IIB), who was diagnosed with blastomycosis shortly following the completion of her chemotherapy course.

Results: The examination of transbronchial biopsy and broncho-alveolar lavage specimens resulted in the diagnosis of blastomycosis infection. Amphotericin B is generally prescribed for the treatment of blastomycosis in immunocompromised patients, but given the patient's satisfactory immune status and no further expected treatment induced immune suppression, we elected to begin treatment with a course of oral itraconazole and monitor closely. Symptoms resolved quickly. Radiotherapy was undertaken as planned. A computerized tomography (CT) chest 3 months later demonstrated interval improvement of the lung lesions. She is currently nine months post radiotherapy and is asymptomatic at the time of abstract submission.

Conclusion: This case report emphasizes the importance of considering an endemic mycotic infection, like blastomycosis, when faced with pulmonary lesions in a recently immunosuppressed patient, not just opportunistic fungal infections. This is a particularly important consideration if the patient resides in or has visited an endemic area. Tissue and culture diagnosis is vital, to out rule underlying malignancy cause and to appropriately direct therapy.

P-0408 | Cost Effectiveness of Treating Endemic Burkitt Lymphoma in Uganda

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Background/Objectives: Despite high cure rates achieved in high-income countries, outcomes for children with Burkitt lymphoma (BL) in most low- and middle-income countries (LMICs) remain suboptimal. Perceptions of high cost and resource intensity remain political barriers to the prioritization of BL and other childhood cancer treatment programs in many LMIC health systems. Little to no knowledge exists of the actual cost and cost-effectiveness of treating paediatric cancers in LMICs. To improve outcomes for children with BL, the Uganda Cancer Institute implemented a comprehensive BL treatment program in 2012. Drawing on centralized patient-level data, we undertook an economic evaluation of the program to ascertain the cost-effectiveness of BL therapy in a specific LIC setting.

Design/Methods: We compared the treatment of BL (local standard) to usual care (no care), in a cohort of 120 patients treated between 2012 and 2014. Costs included direct, indirect healthcare, and indirect patient costs. Our primary measure of effectiveness was overall survival (OS). Patient outcomes were determined through electronic chart abstraction. The cost per DALY averted was calculated using WHO-CHOICE methodology and compared to standard definitions of cost-effectiveness.

Results: The 2-year OS with treatment was 47%. Nine percent of patients abandoned therapy. The cost per DALY averted in the treatment group was US\$42.66. Cumulative estimate of national DALYs averted through treatment was 20,571 years, and total national costs of treatment were US\$877,670. The ratio of cost per DALY averted to per capita gross domestic product (GDP) was 0.2, reflecting a very cost-effective intervention.

Conclusion: This study demonstrates that treating BL with locally tailored protocols is very cost-effective relative to per capita GDP. Studies of this kind will furnish crucial evidence to assist policymakers prioritize the allocation of health system resources among NCDs, including childhood cancer.

P-0409 | Neoadjuvant Anti-IL-6 Siltuximab Improves Resectability in Castleman Disease: A Case Report

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Background/Objectives: Human herpes virus-8 (HHV-8)-negative or idiopathic unicentric Castleman disease (CD) is a rare disorder in children. Management of CD has been challenging due to limited understanding of etiology and pathogenesis and few treatment options. Siltuximab, a chimeric monoclonal antibody against IL-6, is safe and effective in idiopathic multicentric Castleman disease (iMCD).

Design/Methods: A PUBMED search was conducted for queries including "Castleman," "paediatric" and "Siltuximab." Relevant papers were selected for literature review.

Results: We report a rare case of an 8 year old female who presented with a 3 month history of cough and chest pain. Computed tomography of the chest, abdomen and pelvis showed a left paraspinal mass with large feeding vessels. Biopsy reported unicentric CD, hyaline-vascular variant. Due to the highly vascular nature of the tumour, she was not a candidate for up front surgery. She was treated with weekly rituximab and prednisone for 4 weeks. The tumour did not respond, which prompted review of the literature and PET-CT to evaluate metabolic activity of the tumour. She was started on siltuximab for a total of six doses: 2 to start, followed by 4 more after CT evaluation showed stable disease. Although the siltuximab did not significantly decrease tumour size, PET-CT after siltuximab showed interval calcification and FDG activity only slightly above that of blood pool (diffuse low level activity). This allowed opportunity for complete surgical resection. She tolerated therapy and surgery well.

Conclusion: CD is rare in children, and in conjunction with an unresectable tumour presents a treatment challenge. Although the size of the tumour was not significantly improved with Siltuximab, the PET-avidity nearly resolved, improving the surgical environment for resection. Siltuximab as a neo-adjuvant therapy should be highly considered in unresectable idiopathic unicentric CD.

P-0410 | Assessment of Clinical, Laboratory and Radiographic Findings That Help Detection of Relapses/Recurrences in Childhood Cancers

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Background/Objectives: In paediatric cancers, following completion of treatment, patients are visited in order to detect any relapse/recurrence or adverse effects caused by treatment. The appropriate frequency of follow-up visits and the importance of examinations for detecting relapse/recurrence are still the subject of debate.

Design/Methods: Five hundred-thirty three patients diagnosed with cancer and treated at the department of Pediatric Oncology between 2004 and 2012 were assessed. Demographic characteristics, follow-up visits after remission, date of relapse/recurrence, symptoms after remission, the exact date of onset of symptoms, physical examination findings, laboratory examination findings, imaging methods, follow-up frequency and survival of 63 patients in whom relapse/recurrence were detected at follow-ups after treatment were investigated.

Results: Sixty-three patients were followed-up due to relapse/recurrence. There were 14 patients with non-Hodgkin lymphoma, 12 patients with Hodgkin lymphoma, 10 patients with neuroblastoma, 7 patients with Wilms tumour and 20 patients with other types of cancer. Twenty-one patients were symptomatic and 40 (65.6%) were asymptomatic when relapses/recurrences were detected. Survival analysis following relapse/recurrence revealed a statistically significant difference in terms of general survival between symptomatic and asymptomatic diagnoses ($p < 0.05$). A statistically significant difference in survival rates was determined between the tumour groups ($p < 0.05$). Survival rates were better in patients in whom relapse/recurrence was determined after more than 24 months. Forty-six percent of patients with relapse/recurrence survived, and 44.4% died.

Conclusion: Relapses/recurrences were mostly detected while patients were asymptomatic. Radiographic imaging was also important for detection of relapses/recurrences. While patients with Wilms tumour were mainly asymptomatic on the day of relapse/recurrence detection, numbers of symptomatic and asymptomatic patients with non-Hodgkin lymphoma or Hodgkin lymphoma were almost equal. Type of tumour should also be considered while patients are being followed-up for relapse/recurrence detection.

P-0411 | Demographics and Outcome in Paediatric Non Hodgkin Lymphoma: Single Centre Experience at the Children Hospital, Lahore, Pakistan

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Background/Objectives: Objective of the study is to discuss demographics and outcome of children with non Hodgkin lymphoma (NHL).

Design/Methods: It's a retrospective study, looking at the demographics and outcome of children with biopsy proven NHL presenting to the Haematology and Oncology department of the Children's Hospital and Institute of Child Health, Lahore between January 2012 and December 2014. Data regarding age, gender, histological subtypes, stage and outcome were analyzed. MCP 843 Protocol was used for Burkitts, Burkitts like and Diffuse Large B cell lymphoma, While EURO-LB 02 Protocol used for T-cell and B precursor cell Lymphoblastic Lymphoma(LL).

Results: Total 91 patients were treated at CHL during the study period. Eighteen patients were excluded due to missing data. Out of the 73 patients studied, 57(80%) were male. Majority 36(50.7%) were between 5-10 years of age, 23(32.4%) were of 10-14 years old. The most common presentation was abdominal mass present in 32(45%), lymphadenopathy 27(36%), intussusception 5(7%), intestinal obstruction 1(1%), while obstructive uropathy, nasopharyngeal mass, gastric mass, primary bone lymphoma, pericardial effusion, jaw swelling, cheek swelling and paraspinal mass were present in one patient each. Regarding histological subtypes, 29(41%) had Burkitt Lymphoma (BL), 10(14%) B Cell NHL, 29(41%) Lymphoblastic Lymphoma (LL), 2(2.8%) Diffuse Large B cell lymphoma (DLBCL), 1(1.4%) Anaplastic Large cell lymphoma (ALCL), 2(2.8%) non-specific histology. Majority had advanced disease, stages III, 67(91%) and IV 6(8.4%). Total of 48(67.6%) patients have completed treatment and are well, 5(6.8%) left against medical advice, 16(22%) died, 4(5.4%) patients relapsed.

Conclusion: Burkitt lymphoma is the most common type of NHL seen and usually presents with an abdominal mass. High Mortality can be explained by advanced stage at presentation and delayed diagnosis. Prognosis can be improved by better supportive care and more parental/family awareness about early recognition of symptoms of cancer.

P-0412 | Retrospective Study of Paediatric Patients with Hydroa Vacciniforme Like Lymphoma (HVLL)

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Background/Objectives: HVLL is a lymphoproliferative disease, recognized by the WHO since 2008 that is frequent in specific populations like Peruvian, Mexican and Asian, it's a disease linked to Epstein Barr virus infection. Clinical and pathological characteristics of the disease are not well defined.

To describe the clinical spectrum and pathologic characteristics of paediatric Peruvian patients with HVLL.

Design/Methods: Descriptive and retrospective study, patients under 18 years were included between March 1992 and June 2011 at INEN, clinical data, pathologic studies, immunohistochemical methods, in situ hybridization for EBV (EBER) and molecular rearrangements for B cell and T cell receptors were done.

Results: Thirty three patients were evaluated, papular and vesicular lesions and facial edema were the most frequent clinical characteristics, face was involved in all patients, being a clinical marker of the disease. Diffuse lymphoid infiltration up to the dermis was seen in most patients with perivascular and periadnexial pattern. The immunohistochemical methods: CD3 was positive in the 29 cases evaluated, other T cell and cytotoxic markers were found in the majority of patients, all the 14 patients evaluated with EBER were positive. Of the 15 patients that were evaluated with expanded immunohistochemical methods and molecular assays we found that 5 had T cell phenotype and 7 had T/NK cell phenotype. Twenty nine patients received some kind of treatment; most of them are dead or lost for follow up with evidence of progressive disease.

Conclusion: Papular and vesicular lesions as facial edema are the most frequent clinical features of this disease, as well as face involvement. Immunohistochemical methods and molecular studies suggest a plasticity of neoplastic cells in the spectrum of T and T/NK cells. Prognosis of patients is dismal, new treatments are needed.

P-0413 | Clinical Characteristics and Treatment Outcome of Paediatric Hodgkin Lymphoma at Children Hospital Benghazi - Libya

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Background/Objectives: Lymphoma is the third most common childhood malignancy. However, little data is available on lymphoma in our developing country. The present work was performed to identify clinical characteristics and treatment outcome of paediatric Hodgkin lymphoma (HL) at our centre.

Design/Methods: A retrospective study on 57 patients diagnosed with HL between 1995 and 2014. Used chemotherapeutic regimens were ABVD, COPP. For stage IV BEACOPP (Bleomycin, Etoposid, Adriamycin, Cyclophosphamide, Vincristine, Procarbazine, Prednisolone) and VVAC (Vinblastine, Vp16, AraC, Cisplatin) were added, 32 patients received radiotherapy. Ann Arbor HL staging criteria was applied for staging. Rye system was used for histopathology examination. Treatment outcome was evaluated using Kaplan-Meier methods. Differences between outcomes were tested using Logrank test.

Results: There were 40 males and 17 females. Male to female ratio was 2.4:1. Median age was 8.7 years. Bulky disease and B symptoms found in 9 and 28 patients respectively. Stage distributions were 13, 12, 20, 12 patients in stage I, II, III, IV respectively, 56% patients presented at stage III and IV. Histopathologic subtypes were nodular sclerosis, mixed cellularity, lymphocytic predominance and lymphocytic depletion in 26, 19, 11, 1 respectively. 80% of death and 60% of relapse in mixed cellularity, 82.4% patients had complete remission, 8.8% relapsed and cured, 8.8% relapsed and died. Overall survival (OS) and event-free survival (EFS) rates were 91.2% and 82.5% respectively with median follow up of 5 years. OS rate 80% with bulky disease and 87% without ($P > 0.05$). OS rate was 89.3% with B symptoms and 93.1% without ($P > 0.05$). Histopathology, stage and relapse had effect on OS rate ($P < 0.05$, $P < 0.01$, $P < 0.05$) respectively.

Conclusion: Stage, histopathology and relapse are statistically significant predictor factors for OS rate. Our patients are presented with advanced more than early stages; further studies are required to find out causes.

P-0414 | Monocentric Experience about the Efficacy and Safety of Aprepitant for Prevention of Chemotherapy Induced Nausea and Vomiting in Paediatric Patients

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Background/Objectives: Chemotherapy-induced nausea and vomiting (CINV) are common side effects for cancer patients with a considerable impact on quality of life. Traditional regimens to prevent CINV commonly contain a combination of corticosteroid plus ondansetron. Nevertheless, CINV persist in 20-30% of patients and in 40% remains even after chemotherapy (delayed nausea and vomiting). The NK-1 receptor inhibitor aprepitant, in addition to usual anti-emetic therapy, seems to improve both acute and delayed nausea and vomiting in adults. Preliminary studies have shown good efficacy and tolerability also in adolescents but data in paediatric hemato-oncologic disease are limited. Here, we report our experience about the safety and the efficacy of aprepitant in children with Hodgkin Lymphoma (HL).

Design/Methods: Patients received aprepitant orally (125 mg on Day 1, 80 mg on Days 2 and 3) in association with ondansetron (4 mg/mq) and dexamethasone (0.5-2 mg/kg). The efficacy was evaluated through a questionnaire given to the patient in the next cycle, after obtaining informed consent.

Results: Thirteen patients aged between 11 and 16 years were enrolled between January 2015 and February 2016; twelve received a first line chemotherapies (COPP/ABV, ABVD), and one a fourth-line therapy (Bendamustine); mean number of cycle administered was 3.1 (range 1 to 6). Six patients reported nausea with a variable intensity from 2 to 6 (scale from 1 to 10); only two patients reported vomiting (2 and 4 episodes). All patients experienced a grade III-IV neutropenia and a slight increase in transaminases (CTCAE criteria, v 4.02: Sept. 15, 2009), effects likely related to chemotherapy; no other side effects were registered.

Conclusion: We obtained a complete response rate of 54% with a good toxicity profile. This results make us continue to use aprepitant, since the reduction of nausea and vomiting sensation represents a considerable advantage on quality of life.

P-0415 | Efficacy of Low-Dose Chemotherapy Plus Rituximab in Paediatric High Grade Post-Transplant Lymphoproliferative Disease

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Background/Objectives: Post-transplant lymphoproliferative disease (PTLD) is a major cause of morbidity/mortality following transplantation. Treatment varies from reduction of immunosuppression alone, rituximab and modified B-cell non-Hodgkin lymphoma (B-NHL) chemotherapy. Treatment is particularly challenging in this population due to increased toxicity. Low-dose chemotherapy has proven effective for children with EBV-positive, non-fulminant PTLD, with an overall response rate of 83% and overall survival of 73%. Our objective was to evaluate the efficacy of low-dose chemotherapy (cyclophosphamide, vincristine and prednisolone) with rituximab (R-COP) in paediatric high grade PTLD.

Design/Methods: Paediatric patients diagnosed with PTLD referred to our institution between 2001 and 2015 were reviewed retrospectively. Those with high grade PTLD who received R-COP as initial treatment if reduction in immunosuppression alone failed were selected.

Results: Seven patients were identified. Five were male, median age at diagnosis was 7.3 years (range 1.8-17.9). All were post solid organ transplant. Five had monomorphic disease, one polymorphic and one early lesions. All had high (one moderate) proliferation index (3 Burkitts, 2 Diffuse Large B-cell lymphoma). Extranodal disease was present in five. Four had stage-IV disease. Six were Epstein-Barr virus positive. All patients received R-COP as first-line chemotherapy; median number of cycles was 5 (range 2-8). Overall response rate was 5 (71%), with complete response rate of 3(43%). Two patients had a good partial response although one subsequently progressed. Three patients progressed after a median of 5 cycles (range 2-8). The patients with incomplete response/progression had further chemotherapy as per B-NHL-like guidelines. All are alive and remain in remission after a median follow-up of 72.6 months (5-133), although 2 were lost to follow-up.

Conclusion: In this small case series, low-dose chemotherapy regimen R-COP is effective and with durable responses in children with high-grade PTLD. Close monitoring and early intensification of treatment is recommended for patients who demonstrate an incomplete response/progression to R-COP.

P-0416 | Burkitt Lymphoma (BL): HIV/AIDS Prevalence and Outcome of Treatment in Cameroon

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Background/Objectives: Cameroon has approximately 20 million inhabitants, of whom \geq age 0 to 15 years, of whom 1% were HIV positive in 2013. Pregnant women in the Northwest (NW) and Southwest regions (SW) have a HIV prevalence of 4.6% to 6.8% and the mother to child transmission rate in 18 month old breastfed children in 2013 was 25%. All patient with BL were treated with standardized chemotherapy at Bango, Mbingo and Mutengene Baptist hospitals in the NW and SW. Our objective was to record the prevalence of HIV, and response to treatment in these patients.

Design/Methods: Our database is a POND registry for the period 2003 to 2013. We analyzed the number of HIV positive patients, the St Jude stage, whether antiretroviral (ARV) treatment was given, and the long term outcome.

Results: Of 979 patients treated, 717 (73%) were tested for HIV, and 11 (1.5%) were positive. The age ranged from two to 13 years (mean 7 years). One patient had stage IV, 8 patients stage III and 2 patients stage II disease. Eight patients received ARV, three of whom with stage III disease, are alive at 56, 72 and 76 months follow-up respectively. The CD4 count in 4 patients ranged from 30 to 559 cells/ μ l.

Conclusion: The prevalence of HIV (1.5%) was comparable to that of the general population (1%). HIV positive BL patients have a good chance of cure with chemotherapy and long term ARV treatment.

P-0417 | Treatment and Outcomes in Classical Hodgkin Lymphoma Post-Transplant Lymphoproliferative Disorder in Children

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Background/Objectives: Classical Hodgkin lymphoma post-transplant lymphoproliferative disorder (HL-PTLD) has been rarely reported in children, with limited data in the literature to guide treatment decision-making. We report our experience with paediatric patients diagnosed with HL-PTLD who were treated according to the risk-adapted, response-based HL treatment regimens from the Hodgkin Consortium.

Design/Methods: We conducted a retrospective review of children with post-transplant lymphoproliferative disorder (PTLD) treated at a single institution. Between 2007-2013, 5 paediatric patients were diagnosed with classical Hodgkin lymphoma PTLD (HL-PTLD) following solid organ transplant. Histopathology was centrally reviewed to ensure appropriate HL diagnosis and classification. Only patients with classical HL-PTLD were included in the analysis.

Results: Among the 5 patients with HL-PTLD, two had undergone kidney transplant, two had undergone heart transplant, and one had undergone liver transplant. Median time from solid organ transplant to PTLD diagnosis was 6.1 years (range 2.1 years to 8.9 years). All patients had mixed cellularity histology HL, and all tumors were EBV-positive. Stages of HL-PTLD

ranged from IIA to IVB. Patients were treated according to Hodgkin Consortium protocols HOD-05 or HOD-99, with combined modality therapy including Stanford V chemotherapy and involved field radiation therapy, according to protocol guidelines for HL stage and risk group. All patients had treatment delays (range 2-5), most commonly due to neutropenia and/or infectious complications, and 4/5 patients received chemotherapy dose modification due to toxicity. At a median of 4.1 years of follow-up (range 1.8-8.2 years), all patients remain in remission from HL-PTLD and all have preserved organ transplant function.

Conclusion: In the largest series of children with classical HL-PTLD reported to date, combined modality therapy with risk-adapted chemotherapy and radiation therapy, using treatment regimens that would be used for non-PTLD HL with appropriate dose modification for toxicity, was generally well-tolerated and provided excellent survival outcomes as well as freedom from graft failure.

P-0418 | The Clinical Features and Outcome of 16 Burkitt Lymphoma Cases with Testicular Involvement Without Radiation Therapy - A Single Center Study from Beijing

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Background/Objectives: To study the efficiency of HD-MTX therapy replace the role of radiotherapy among testicular lymphoma, we analyze the clinical features and outcome of Burkitt lymphoma with testicular involvement without radiation therapy.

Design/Methods: Retrospective analysis was conducted in 16 Burkitt lymphoma cases with testicular lymphoma between Jan 2009 and Dec 2014. We follow the BCH-NHL-2009 protocol, which is modified from FAB LMB 89 (HD-MTX 5 g/m², the chemo-dosage is stratified by risk group).

Results: During the study period, 16 patients were enrolled from Beijing children's hospital - a single center. All the patients were in stage IV, the median age was 6.65 years (range from 2.25 to 13.5 years). 8 cases had BM involvement (5/8 was Burkitt leukaemia); 9 cases had CNS involvement (1/9 was CNS leukaemia); 5 cases had bi-testicular involvement. The median follow up time is 19.75 months (range from 1 to 67 months); During the study period, 2 cases died for the relapse, the rest 14 cases were alive.

Conclusion: For the Burkitt lymphoma with testicular involvement, to reduce the radiotherapy toxicity, we remove it in the protocol, but use HD-MTX(5g/m²) to take place, the short term survival is good.

P-0419 | Treatment of Childhood Relapsed Hodgkin Lymphoma

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Background/Objectives: The survival of childhood Hodgkin Lymphoma has significantly increased with appropriate treatment. However, in cases with relapse, the cure rate is reported to be 50% despite high dose chemotherapy and autologous hematopoietic bone marrow transplantation (BMT).

Design/Methods: The six patients with relapse Hodgkin Lymphoma among 90 patients followed by Istanbul Medical Faculty, Division of Pediatric Haematology Oncology between dates of 1998-2016 were assessed retrospectively.

Results: The mean age of diagnosis is 11.8 \pm 2.3 years (9-15 years). All cases were male. Four of them were mixed cellular and 2 of them were nodular sclerosis type. Primary localization was cervical (5 patients), supraclavicular and mediastinum (1 patient). The staging were 4B (three patients), 4A (1 patient), 3B (1 patient) and 2A (1 patient). All patients were administered chemotherapy according to GPOH protocol and were undergone radiotherapy on involved area.

One of patients was late and others were early relapse. The mean relapse time was 9.8 \pm 14.9(1-40) months. The median follow-up duration was 33 (41.5 \pm 229) months. In three patients only one relapse occurred while refractory relapse occurred in one patient after first relapse and recurrent relapses occurred in two patients. The BMT (two autologous and one autologous + allogeneic) were performed to three patients after three course ICE chemotherapy. One patient with refractory to ICE and BEAM chemotherapy who undergone autologous and allogeneic BMT has died. To the other three patients were not undergone BMT due to late relapse, refractory disease and unwillingness of parents. Among these patients, the refractory one passed away. The general survival rate was 50%. No targeted treatment was used in any patients. The father of patient with late relapse was also diagnosed with Hodgkin Lymphoma.

Conclusion: Although the autologous BMT is treatment type with curative potential in patients with relapse Hodgkin Lymphoma, we need more results of combined targeted treatments.

P-0420 | Targeted Therapy with Brentuximab Vedotin as a Bridge to Bone Marrow Transplantation in Children with Relapsed Anaplastic Lymphoma

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Background/Objectives: Anaplastic large cell lymphoma (ALCL) is an aggressive T cell non-Hodgkin lymphoma with relapse rate of 25%-30%. ALCL may carry the t(2;5)(p23;q35), resulting in the fusion gene Nucleophosmin (*NPM-ALK*). Novel targeted immunotherapy with

the antibody–drug conjugate Brentuximab vedotin (BV) has emerged for relapsed ALCL in adults.

Design/Methods: We report the use of BV in two children with relapsed ALCL. After obtaining approval from regulatory authorities, BV was given at a 1.8 mg/kg every 3 weeks, until bone marrow transplantation (BMT). Follow up included evaluation of minimal residual disease (MRD) by RT-PCR for *NPM-ALK*.

Results: An 11-year-old girl with systemic *NPM-ALK*-positive ALCL entered remission with first line chemotherapy. Three months after treatment completion, she suffered a disseminated relapse. She re-entered remission with BV, of which she received 6 cycles. She underwent mega-therapy with autologous BMT rescue. Six months after transplantation, RT-PCR for *NPM-ALK* became positive, with neither clinical nor imaging evidence of relapse. BV was reinstated and after 5 cycles she entered molecular remission, which allowed her to undergo allogeneic BMT. She remains in clinical and molecular remission 8 months post BMT.

The second patient is a 10-year-old boy with systemic *NPM-ALK*-positive ALCL. He entered into remission with first-line chemotherapy. Ten months after treatment completion, relapse was documented, by positive MRD for *NPM-ALK* and PET-CT scan. He entered into remission after 3 cycles of BV and after 6 cycles he underwent mega-therapy with autologous BMT rescue. Treatment with BV was well tolerated in both patients.

Conclusion: The use of BV as a single-agent in relapsed ALCL in paediatric patients may induce remission and may be used as a bridge to either auto- or allo-BMT. Efficacy and toxicity profile in paediatric population seems to be similar to adults, but further studies are required to validate these initial reports.

P-0421 | Clinico-Biological Features and Outcome of Lymphoblastic Lymphoma in Children Treated at a Referral Centre in India

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Background/Objectives: This is a retrospective analysis of outcomes of Pediatric Lymphoblastic Lymphoma (LBL) treated at our centre using the Modified BFM protocol between 2001 and 2014. The objective is to study the clinico-biological features and outcomes of Pediatric Lymphoblastic Lymphoma treated with Modified BFM protocol chemotherapy.

Design/Methods: All newly diagnosed cases of LBL were treated with chemotherapy similar to BFM 90 protocol. During Interim Maintenance, 4 cycles of Medium dose Methotrexate (3000 mg/m²) was used.

Results: One hundred and three patients of LBL were registered and included in the study. Using Immuno-histochemistry, the patients were sub-typed into TLBL in 93% (n=96) and BLBL in 6.8%(n=7). The median age of diagnosis was 10 years (Range 1-18 years). M: F Ratio was 4.7:1. The most common presentation was anterior mediastinal mass (72%) (n=75). Others presented with Lymph nodal swelling or a soft tissue/bony mass. Fever and/or Weight Loss were present in 36% patients. Bone marrow on microscopy was involved in 9.7% (n=10) and CSF was involved in 0.97% (n=1) of patients. Six patients had increased Methotrexate levels with/ without deranged Creatinine levels with medium dose Methotrexate. The Progression Free Survival(PFS) and Overall Survival(OS) of the entire cohort was 85.3% and 79% respectively with a median follow up period of 40 months. Toxic deaths were noted in 8 patients (2 – Tumour Lysis Syndrome, 6 – Sepsis). There were 12 relapses, most of them (11/12) occurred within 18 months of the initial diagnosis.

Conclusion: Lymphoblastic Lymphoma in children commonly presents with anterior mediastinal mass with male predominance. TLBL is the commoner subtype. Medium dose Methotrexate can be safely administered with acceptable toxicity especially in centres where facility for Methotrexate levels is not available. LBL responds well to chemotherapy and has a good long term outcome.

P-0422 | CD20-Targeted Treatment of Children with Mature B-cell non-Hodgkin Lymphoma. Experiences of the Hungarian Paediatric Oncology Group

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Background/Objectives: CD20-targeted therapies have been successfully applied in adults with B-cell malignancies but have not been registered for paediatric use. The use of rituximab was reported first in paediatric cases of refractory and relapsed (R/R) B-cell NHL followed by publications reporting on clinical trials including children with de novo disease. No reports were published on the paediatric use of obinutuzumab. Here we summarize experiences of the Hungarian Paediatric Oncology Group (HPOG) with CD20-targeted treatment of children with mature B-cell NHL.

Design/Methods: Records of patients with mature B-cell NHL having received CD20-targeted therapy from two centers of the HPOG, the Department of Pediatrics of University of Debrecen and the 2nd Department of Pediatrics of Semmelweis University were retrospectively studied. Application of rituximab and obinutuzumab was approved by the National Institute of Pharmacy, Budapest, Hungary.

Results: Between 2005 and 2014, 17 patients (11 boys and 6 girls), age between 1 to 17 years (median 12 yrs) were included. Patients had diffuse large B-cell lymphoma (10), Burkitt lymphoma (3), juvenile follicular lymphoma (2), primary mediastinal B-cell lymphoma (1) and grey-zone lymphoma (1). Sixteen patients received rituximab and two received obinutuzumab (one patient received both drugs). Two patients received rituximab monotherapy. All other patients received combined chemo-immunotherapy. In eight patients rituximab was given first-line, four patients were switched to rituximab-containing regimens in course of initial treatment. In four cases, rituximab was given in R/R NHL. Obinutuzumab was applied in R/R patients. Three patients died, survival time was between 8 to 127+ months (median 40 mo). No major side-effects were noticed with rituximab, both patients receiving obinutuzumab developed tumour lysis syndrome.

Conclusion: Rituximab may become part of standard treatment in childhood NHL, clinical trials can define the paediatric use of obinutuzumab.

P-0423 | Primary Cutaneous Lymphoma: A Report of 15 Cases from Single Center

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Background/Objectives: Primary cutaneous lymphomas (PCL) comprise a heterogeneous group of non-Hodgkin lymphomas (NHL). The objective of this study was to report our institutional experience with skin lymphoma over a 35-year period.

Design/Methods: From 1980 to 2015, 1270 children with NHL were admitted to the Pediatric Oncology Department of Hacettepe University. Of these, fifteen children with primary skin lymphoma were evaluated retrospectively. Patients' age and gender, the tumour's location and histopathological subtype, treatment and survival rates were recorded.

Results: There were nine males, six females with a median age of 121 (11–204) months. One patient had ataxia teleangiectasia. Median duration of symptoms from onset to diagnosis was 6 (1-36) months. Presentation symptoms were skin lesions described as erythematous or red to violaceous, sometimes ulcerated patches, plaques, maculopapular eruption, nodule or tumour. Skin lesions were located on the face and scalp in seven patients, trunk or extremity in four and disseminated in four. Size of the lesions varied between 0.5-12 cm in dimension. According to the WHO classification, three patients had mature B cell lymphoma, one EBV-related lymphoproliferative disease, one anaplastic large cell lymphoma, one NK cell lymphoma, one panniculitis-like lymphoma, three peripheral T cell lymphoma, three mycosis fungoides. Patients were treated with various chemotherapeutic regimens including LMB, LMT protocols. Two patients died from disease progression, three died from treatment-related complications. Nine patients (60%) are alive and disease free at a median of 42 (18 to 172) months. Overall and event free survival were 65.5% and 53.7%. Disseminated types had shorter overall and event free survival rates (25%;25) than localized types (81.8%; 72.7%); (p:0.016 and p:0.013).

Conclusion: Primary cutaneous lymphoma constitutes 1.18% of our NHL cases. Unlike adults most of them had aggressive histopathology. The disseminated forms were found to have worse survival rates.

P-0424 | Primary Gonadal Lymphoma in Childhood

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Background/Objectives: To retrospectively evaluate the clinical characteristics, treatment regimens, and outcome of primary gonadal lymphoma cases in our institution.

Design/Methods: Six patients diagnosed with primary gonadal lymphoma, between January 1980 and January 2015 at Hacettepe University, Pediatric Oncology Department, were retrospectively evaluated according to their age at diagnosis, clinical and histopathological findings, stage, treatment strategies and response to treatment.

Results: There were five boys and one girl with a median age of 74 (12-152) months. Symptoms were testicular swelling in all 5 patients diagnosed with primary testicular lymphoma. Patient diagnosed with primary ovarian lymphoma was presented with inguinal swelling, fever, weight loss and night sweating. All patients were referred to our department after surgical intervention including high ligation and orchiectomy or salpingo-oophorectomy. Histopathological subtypes were Burkitt lymphoma in two patients, diffuse large B cell lymphoma in one, lymphoblastic lymphoma in one, and unclassified in the remaining two. None of the patients had central nervous system (CNS) or bone marrow infiltration. Three patients were defined as stage-I disease while the other 3 patients were defined as stage-II. Four patients (66.7%) were treated with LMB-B protocol and the other 2 patients (33.3%) with LSA2L2 protocol. The median follow-up time was 62.5 (5 – 188) months. Only one patient had central nervous system relapse at fourth month and left the treatment. Five years overall and event free survival rates were both 83.3%.

Conclusion: Testicular involvement by NHL is usually associated with disseminated disease. Its incidence less than 5% at initial diagnosis and 4% at relapse. Primary testicular NHL is extremely rare. The patients admitted with early stage disease. We found that the prognosis of primary gonadal lymphoma is good.

P-0425 | Cytokine and Cytotoxic Molecules Release Syndrome in Children with Advanced Stage Anaplastic Large Cell Lymphoma

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Background/Objectives: At the present time results of some paediatric protocols (NHL-BFM90-95, ALCL99, CCG5941, AIEOPLNH97) for treatment anaplastic large cell lymphoma (ALCL) were published but prognostic and diagnostic significance of Cytokine and cytotoxic molecules release syndrome (CCMRS) is unknown. CCMRS includes specific clinical features such as flu-like symptoms (febrile fever, myalgia, osalgia, arthralgia), skin rash, peripheral

edema, polyserositis, coagulopathy, hepatopathy and nephropathy, electrolyte disturbances, absence of focal infection.

The aim of this study was to determine distinctive molecular-biological features of ALCL in children with CCMRS, to estimate the significance of this syndrome for overall survival (OS), event-free survival (EFS) and progression-free survival (PFS).

Design/Methods: From 2003 to 2015 twenty paediatric patients with ALCL were included in modified-ALCL-BFM2003 trial. CCMRS was assessed in 7 children with STAT3 / p-STAT3tyr705 - positive tumour samples. K2 risk group – in 3 cases, K3 – in 4, stage II – in 2, stage III in 2, stage IV in 2. Cutoff values of 20% for CD3, 20% for STAT3, 30% for pSTAT3tyr705 were established. t(2;5)(p23;q35) was assessed by using dual color *NPM1-ALK* Fusion/Translocation FISH probe.

Results: CCMRS was revealed in 5 out of 7 children with STAT3/p-STAT3tyr705 - positive tumour samples. All of these samples were characterized by t(2;5)(p23;q35) +, ALK+, CD3+, perforin +, granzyme-B +. Advanced stages (III and IV), K3 risk group – in 4 out of 5 patients. Male/female ratio was 1.5/1 (3/2). Median age – 11.5 ± 0.6 years (range from 6 till 16). Using protocol modified-ALCL-BFM2003 we have achieved 100% level of OS, EFS, PFS in this group of patients, a median follow-up was 88.5 ± 14.9 months.

Conclusion: CCMRS is associated with advanced stages of disease, K3 risk group, IL6R/STAT3/p-STAT3tyr705 pathway activation, expression T-cell marker CD3, cytotoxic molecules and has not got any significance for OS, EFS, PFS. This study will be continued.

P-0426 | Post Transplant Lymphoproliferative Disorder (PTLD) in Paediatric Kidney Transplant Recipients has A Good Outcome

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Background/Objectives: PTLT is a rare but potentially lethal complication of immunosuppression following transplantation. Multiple sites, frank malignancy and brain localisation of PTLT confer poor prognosis.

Here, we report fifteen-year experience on outcomes of PTLT in paediatric kidney transplant recipients at a large UK transplant centre.

Design/Methods: We included patients younger than 18 years at time of kidney transplant, who developed PTLT between Jan 2000- Jan 2015. Demographics, site and histology of PTLT, EBV status, management and patient and graft outcomes were collected.

Results: Of 255 kidney transplant recipients 8 developed PTLT (0.03%). The median age at transplant was 4.22 years [range 2.13 – 12.97] and median time to diagnosis of PTLT was 4.02 years [range 0.45 – 10.7]. Median follow up was 7 yrs [range: 0.82 – 10.7].

One patient received cyclosporine A (transplanted before 2004) and all others received tacrolimus for maintenance immunosuppression with anti-proliferative agent and steroid. Four took tacrolimus at time of PTLT diagnosis. All cases of PTLT were associated with EBV.

Three patients had multiple sites of PTLT, two of which included cerebral PTLT. Two further patients had cerebral PTLT only. The diagnosis was confirmed histologically in 6 cases (75%).

Three patients were treated with cyclophosphamide, vincristine and prednisolone (COP) chemotherapy, one received rituximab in addition. One had rituximab, cytotoxic T cells and radiotherapy. Half were treated with reduction in immunosuppression only.

Patient survival at last follow up was 100%. One patient with multi-site, non-cerebral, PTLT, lost their graft from sirolimus related toxicity following a change in immunosuppression following PTLT. At last follow up, median estimated GFR was 44.8 ml/min/1.73m² [range 18-108].

Conclusion: We report low incidence and very good outcomes for graft and patient survival following PTLT in paediatric kidney transplant recipients. In particular, PTLT localised to the brain responded well to reduction in immunosuppression. Multicentre studies are needed to corroborate our findings.

P-0427 | Atypical Clinical Course of Large B-Cell Lymphomas in Children – Single Centre Experience

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Background/Objectives: Large B-cell lymphomas are rare non-Hodgkin lymphomas (NHL) in children with rather poor prognosis.

Design/Methods: There were 3 children diagnosed with this type of lymphoma in the Department of Pediatrics, Haematology, and Oncology of the Medical University of Gdansk in years 2012-2016. The histopathological diagnoses included: primary mediastinal large B-cell lymphoma (PMLBCL) and diffuse large B-cell lymphoma (DLBCL). In all of the patients other malignancies were suspected at the beginning.

Results: PMLBCL was diagnosed in a 14-year-old female patient who initially presented with large mediastinal tumour mass. The initial treatment was introduced according to the protocol for NHL lymphoblastic T-cell because of life-threatening condition. This diagnosis was made on the basis of immunophenotyping of pleural effusion. Because of lack of response to the treatment and progression of neoplastic disease, after „second look” the histopathological examination revealed PMLBCL. However, change of therapy and autologous stem cell transplantation did not bring any result and the patient died of progression of the disease.

The second 2.5-year-old male patient was diagnosed with DLBCL localised in the skin of the head. The patient was initially monitored for haemangioma, and because rapid tumour growth the biopsy was performed. Currently he remains in complete remission after completion of therapy.

The third patient was a 16-year old female with DLBCL of the tibia. At the beginning inflammatory process of the bone was suspected, however conservative treatment did not bring any result. After several months the biopsy of the tumour was performed and malignancy was diagnosed, suspecting Ewing sarcoma or osteosarcoma. Final immunohistopathological examination showed DLBCL. She continues the treatment.

All three patients were treated with Inter NHL B-cell 2010 with different effects.

Conclusion: Initial symptoms of large B-cell lymphomas may be non-characteristic and may lead to delay in introduction of proper treatment which makes the prognosis poor in rare NHL.

P-0428 | Anaplastic Large Cell Lymphoma: Is it Secondary or Concurrent with Castleman Disease?

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Background/Objectives: Anaplastic large cell lymphoma (ALCL) accounts for 1-2% of adult non Hodgkin lymphomas and represent 30% of childhood's lymphomas and 70% of paediatric large cell lymphomas. Castleman's disease (CD) may evolve or may be concomitantly present with lymphomas. Objective: To present a patient with ALCL who had had 2 other pathologic diagnoses including Castleman's disease before the diagnosis of ALCL.

Design/Methods: A 31-year-old male was referred for fever and an unilateral inguinal lymphadenopathy to the hospital of infectious disease on October 2015. Common infectious diseases were ruled out. Pathological examination of the biopsied lymph node showed a granulomatous pattern. Further investigations for sarcoidosis, fungal infections, collagen disease were negative but patient's follow-up of revealed slowly growing abdominal lymphadenopathy, persistent low grade fever, sweats and loss of appetite. Second pathological opinion of the same lymph node concluded for hyaline vascular (HV) subtype of multicentric CD. The patient received a CVP combination chemotherapy on December 2015. Three weeks later patient's evolution showed a rapid progressive deterioration consisting in severe back pain, cytokine release syndrome, generalized lymphadenopathy, anasarca, cutaneous and gastrointestinal involvement. The third pathological examination coupled with immunohistochemical stains of another 2 newly removed lymph nodes established the diagnosis of ALCL, anaplastic lymphoma kinase (ALK)- positive.

Results: After 4 cycles of dose-adjusted EPOCH a very good partial response to treatment was attained confirmed on imaging studies.

Conclusion: Histopathological findings could not confirm or exclude with certainty the supposition of secondary or concomitant ALCL to CD. The present case might be unique because systemic ALCL, ALK+ has not been reported previously in a setting of multicentric CD.

P-0429 | Paediatric Hodgkin Lymphoma: A Single Center Experience from the West Part of Turkey

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Background/Objectives: To evaluate the epidemiological, clinical, pathological characteristics and treatment outcome of Hodgkin Lymphoma (HL) cases treated in our institution.

Design/Methods: Between 1988-2016, ≤18y patients were reviewed retrospectively. Since 1989, we used standard COPP/ABVD based regimens, then in 1997 we started to use the GPOH 90/95 protocol. Low dose radiotherapy was administered in patients with CR after chemo; higher doses of radiotherapy was delivered to patients having residual disease or progressive disease.

Results: Seventyone patients were eligible out of 89. The median age was 13years, M/F:1.4. The major histological subtypes were nodular sclerosis (55%). B-symptoms were present in 37% of cases. Stage distribution was Stage I-II (n:40), stage III-IV (n:31). The number of involved lymph node regions was <3 in 52%, and ≥3 in 48% of cases. The most common nodal sites involved were cervical (82%), mediastinal (72%). Bulky disease was present in 48% of patients. At presentation 18% of children had extranodal disease. The number of chemotherapy courses were as follows: 2-4 courses for stage I-IIA, 4-6 courses for stage IIB-III, 6-8 courses for stage IIIB-IV. All patients except 5 cases (stageIB (n:1), stageIIA (n:1), stageIIISB (n:1), stageIVB (n:2)) were irradiated. Median follow-up time was 7.5years (3mos-21years). At 5-years EFS was 81%, 10-15 and 20-years EFS rates were 79%; 5-years OS 94%, 10-15 and 20-years OS rates 88%. The OS and EFS rates were not found different between Stage I-II and Stage III-IV disease; also between patients who received GPOH 90/95 and COPP-ABVD regimens.

Conclusion: The epidemiologic and clinical features of paediatric HL may show considerable differences even between the regions of a country. Similar OS and EFS rates were obtained with GPOH90/95 and COPP/ABVD based regimens. This finding supports usage of new and safe treatment regimens in HL. No prognostic factor could be determined owing to the limited patient number.

P-0430 | Factors Associated with Time to Diagnosis of Childhood and Adolescent Non-Hodgkin Lymphoma in Peru

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Background/Objectives: Time to diagnosis (TD) or “lag time” is the time between a patient’s first symptom recognition to a diagnosis of cancer. Delayed TD allows tumour progression and poor outcome in Non-Hodgkin Lymphoma (NHL) in some studies, although it remains controversial.

Objectives: The aim of this study was to define clinical and socio-demographic factors associated to TD, which includes “Parents delay” (PD) and “Medical delay” (MD) in children and adolescents diagnosed with NHL in Lima, Peru.

Design/Methods: A total of 46 patients younger than 18 years of age diagnosed with NHL between January 2012 and December 2015 were retrospectively evaluated. Clinical and demographic variables such as type of diagnosis, clinical stage, sex, age and parental characteristics were analyzed to evaluate their effects on TD, PD and MD.

Results: Thirty-three patients were included in the study. The median age was 10 years (range 3–17) and 68.5% were male. Histological subtypes were mature B-cell NHL in 40%, lymphoblastic NHL in 31.4%, T/NK lymphoma in 14.3%, anaplastic large cell lymphoma in 5.7% and hydro-vacciniforme-like lymphoma in 5.7%. Stage III and IV tumors were seen in 77.2% of cases. The TD ranged between 2 weeks and 17.5 months (median, 8 weeks), with a median of PD and MD of 2 and 6 weeks, respectively. Among histological subtype, we could not find significant differences in TD. Age, parental age or level of education, metastatic disease, clinical stage and sex did not affect significantly TD.

Conclusion: In our country, median TD was comparable to described in developing countries, where index of suspicion of childhood cancer remains low. It is necessary to establish strategies for optimizing early diagnosis based on associated factors.

P-0431 | Pretreatment Neutrophil to Lymphocyte Ratio Predicts Event Free and Overall Survival in Patients of Childhood T Cell Non-Hodgkin Lymphoma

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Background/Objectives: Non-Hodgkin lymphoma (NHL) is a systemic disease and inflammatory in nature. Inflammatory biomarkers have been established as prognostic marker in various malignancies. We have evaluated prognostic significance of pretreatment neutrophil to lymphocyte ratio (NLR) in T-NHL.

Design/Methods: This is a single institutional review of patients up to 18 years of age with diagnosis of T-NHL treated between June’03 and Jan’15. NRL ratio was calculated as ratio of absolute neutrophil to absolute lymphocyte count derived from baseline peripheral blood parameters. And was correlated with event-free-survival (EFS) and overall survival (OS). Data was censored on 31st Jan’2016. NRL was dichotomized as low and high, and high NRL was defined as value above median.

Results: Seventy-six T-NHL were treated with median age of 13 years (range:1-18) and male:female ratio of 58:18. Disease subtype was T-lymphoblastic lymphoma in 43 (57%), anaplastic large cell lymphoma in 19 (25%) and others in 14 (18%). Disease stage was early in 11 (14%) and advanced in 66 (86%). “B” symptoms were present in 34 (45%) patients. Median NLR was 2.23 (range:0.45-13.29). No baseline clinical parameters predicted NLR, after median follow-up of 42.8 months (range:0.67-145), 5-year EFS and OS was 68.6±5.6% and 76±5.8%, respectively. NLR emerged as the only independent prognostic factor affecting both EFS (hazard ratio-3.18, p=0.02 and OS (hazard ratio-5.02, p=0.01) in multivariate analysis with high NLR (>2.23) predicting inferior outcome.

Conclusion: Pretreatment NLR independently predicted both EFS and OS. NLR should be evaluated in a prospective study in T-NHL and should be included in prognostic model to tailor therapy if found to be prognostic.

P-0432 | Primary B Cell Central Nervous System Lymphoma in An Immunocompetent Adolescent Boy

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Background/Objectives: Primary central nervous system non-Hodgkin lymphoma (PCNSL) is a rare (< 5%) malignant lymphoma limited to the cranial-spinal axis in the absence of systemic lymphoma. PCNSL typically affects elderly patients and is rare in immunocompetent young adults. PCNSL is a highly radiosensitive and chemosensitive infiltrative tumour, so surgery is restricted only to diagnostic biopsy. There is no consensus regarding the optimal management strategy for patients with PCNSL. We report an adolescent immunocompetent boy who attained remission with chemotherapy alone.

Design/Methods: Seventeen year old, developmentally normal, boy presented with signs and symptoms of raised intracranial pressure. Neuroimaging revealed a mass (5 × 4.2 × 4.6 cm) with extensive perilesional edema in left gangliocapsular, corona radiata and temporal lobe. Biopsy of the lesion was suggestive of B cell Lymphoma. CT thorax, CECT abdomen, CSF analysis and bone marrow biopsy ruled out metastatic disease. Retroviral serology was negative. He was treated as per LMB 96 protocol for CNS positive B cell NHL with high dose Methotrexate (8gms/m²).

Results: MRI brain after 3 cycles of chemotherapy revealed significant reduction in the size of the lesion (1 × 0.5 × 1 cms). Whole body PET CT after 4 cycles revealed disease in remission.

Conclusion: PCNSL is an uncommon tumour, and no phase III trial has been completed so far. Only radiotherapy limits the survival benefit, so combination of high dose methotrexate and radiotherapy is being used with varied outcomes. Because long-term survivors are at a higher risk for developing severe delayed cognitive dysfunctions, future treatment should improve efficacy while limiting the risk for neurotoxicity. Though the excellent response in our child

and the possible lower risks of neurotoxicity favours chemotherapy, as the sole treatment for PCNSL, larger population study is needed to standardize the optimum first line and salvage treatment for PCNSL.

P-0433 | Paediatric Non-Blastic Non-Hodgkins Lymphoma: A Perspective from India

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Background/Objectives: There is paucity of data on paediatric non-lymphoblastic non-hodgkins lymphoma (NHL) from developing countries. We conducted this study to study outcome and identify risk factors that can predict survival in paediatric non-lymphoblastic NHL at our centre.

Design/Methods: Patients < 18 years of age who were diagnosed with non-lymphoblastic NHL at our hospital from 1st January 2005 to 31st December 2014 were included. Data was collected retrospectively from case records.

Results: One hundred two patients with median age of 12 years (range: 1-18) were included in the study. There were 69/102 (68%) male and 33/102 (32%) female patients. The most common histological diagnosis was Burkitts Lymphoma (BL) in 59/102 (58%) patients followed by anaplastic large cell lymphoma (ALCL) in 28/102 (28%) and diffuse large B-cell lymphoma (DLBCL) in 12/102 (12%), T-cell lymphoma in 2/102 and primary mediastinal B-cell lymphoma in 1/102 patients. The LMB-89 protocol was the most common protocol used for treatment in 74/102 (72%) patients. The 2-year EFS for patients with BL, ALCL and DLBCL was 72%, 55.8% and 27.5% respectively (p=0.037). On univariate analysis factors that significantly predicted poor EFS included non-BL histological subtype, poor performance status, malnutrition and not achieving complete response on interim assessment.

Conclusion: Outcomes in non-lymphoblastic NHL from our centre are worse compared to data from the west. This is because a large proportion of patients present with advanced stage and in moribund condition. Patients with BL have better outcome compared to other subtypes.

P-0434 | Paediatric Hodgkin Lymphoma Treated at Cancer Institute, Chennai – Long Term Outcome

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Background/Objectives: Pediatric Hodgkin lymphoma (HL) is a highly curable malignancy. There is a paucity of data on outcome on paediatric HL from India. The present study was conducted to ascertain the outcomes of children with HL at our centre and to identify risk factors for disease relapse.

Design/Methods: We retrospectively analyzed the outcomes of 172 consecutive previously untreated patients with paediatric HL presenting at our centre from 2001 to 2010. Patients were treated with either ABVD or ABV/COPP chemotherapy.

Results: The median duration of follow-up of was 77 months. The median age of the patients was 10 years (range 2-18years), 127/172 (74%) patients were male. The extent of disease was Stage 1 and 2 in 59% of the patients. B symptoms was present in 32% of patients and 27% of patients had bulky disease. The most common histological subtype was mixed cellularity (45%) followed by nodular sclerosis (35%). The 5 year overall survival (OS) and progression free survival (PFS) of the entire cohort was 92.9% and 83.1% respectively. There were 32 events among 172 patients, of which 29/172 were due to relapse of disease or progression, 2/172 were deaths due to bleomycin toxicity and 1/172 patient died due to an accident. The mean and median duration of relapse was 22.49 months and 15.17 months respectively (range: 1.97-79.03 months). The 5 year OS for patients with stage I, II, III and IV was 96%, 94.7%, 84% and 69.8% respectively. On univariate analysis advanced stage, interim radiological response and presence of B symptoms significantly predicted inferior PFS and OS. On multivariate analysis only interim radiological response significantly predicted EFS (P<0.001) and OS (P<0.001).

Conclusion: Overall, our results are comparable to that observed in other centres in India and globally.

P-0435 | Relapsed Hodgkins Lymphoma: A Single Centre Experience from India

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Background/Objectives: Pediatric Hodgkins lymphoma (HL) has high cure rates; however, 15-20% of patients with paediatric HL will relapse. The present study was conducted to ascertain the outcomes of children with relapsed HL at our centre.

Design/Methods: We retrospectively analyzed the outcomes of 16 consecutive patients with relapsed paediatric HL treated at our centre between 2012 and 2015.

Results: The median duration of follow-up after relapse was 22.4 months. The median age of the patients was 14.5 years (range 3-18years), 13/16 (81%) patients were male. Among the 16 patients who received salvage chemotherapy, 8/16 had primary progressive disease (PPD) and 8/16 had disease relapse. The first line salvage chemotherapy regimens used included Dexamethasone, Ara-C and Cisplatin (DHAP) in 12/16 patients, Gemcitabine, Vinorelbine and Dexamethasone (GVD) in 3/16 patients and Ifosfamide, Carboplatin and Etoposide (ICE) in 1/16 patients. Complete response, partial response, stable disease and progressive disease after first line salvage chemotherapy was seen in 3/16, 7/16, 1/16 and 4/16 patients respectively. Second line salvage was given in 10/16 patients and the regimens used were GVD in 7/10, DHAP in 1/10, ICE in 1/10 and gemcitabine and Oxalipatin (GEMOX) in 1/10. The 2-year overall survival (OS) was 56.1%. Median Event Free Survival (EFS) after first line salvage and second line salvage was 4.8 months and 22.3 months respectively. Autologous transplantation was performed on 7/16 patients. The 2-year OS for patients with PPD and relapsed disease was

35% and 70% respectively ($P=0.25$). The 2-year OS for patients who underwent AHST was 41.7% compared to 51.9% for patients who did not undergo the procedure ($P=0.6$).

Conclusion: Patients with PPD had a worse outcome compared to patients who relapsed. Autologous transplantation did not improve OS. Our results are comparable to those reported from the western world.

P-0436 | Treatment of Paediatric B-Cell Non-Hodgkin Lymphoma in Croatia

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Background/Objectives: B-cell non-Hodgkin lymphoma (B-NHL) accounts for more than half of NHLs occurring in children and adolescents, comprising primarily of Burkitt lymphoma, Burkitt-like lymphoma and diffuse large B-cell lymphoma. The outcome of B-NHL has dramatically improved over the last decade with the introduction of short-term repeated intensive chemotherapy courses. The activity of rituximab in paediatric B-NHL lymphoma has not yet been determined. The aim of this nation-wide study was to evaluate and compare therapeutic efficacy of standard chemotherapy and the combination of rituximab and chemotherapy.

Design/Methods: Patients younger than age 19 years with newly diagnosed CD20+ B-NHL were eligible. The diagnosis of specific entities of B-NHL was based on well-defined cytomorphological, immunohistochemical and cytogenetic findings. The patients were treated according to B-NHL BFM 95 and 04 protocols, or combination of intensive chemotherapy plus rituximab (375 mg/m² IV infusion 5 days prior to each cycle). Risk-adapted stratification of treatment intensity and duration was implemented.

Results: Thirty six children (28 boys and 8 girls, ratio 3.5:1) with a median age of 9.2 years (range: 2.5-18) were treated in 2 national centers from January 2007 to December 2013. Twenty one (58.3%) patients received rituximab. The complete remission was achieved in all children. The survival rates were 100% for stage I, 91.6% for stage II, 40% for stage III, and 66.6% for stage IV. Overall survival rate was 80.6%. Patients treated with rituximab had better survival comparing to those treated with chemotherapy only (85.7% versus 73.7%), but significant difference was demonstrated only for advanced stages (III and IV). Major adverse effect was prolonged B-cell depletion.

Conclusion: Our treatment results are comparable with those reported in other international trials. The definitive role of rituximab in the treatment of children and adolescents with B-NHL needs to be evaluated in prospective controlled clinical studies.

P-0437 | Post-Transplant Lymphoproliferative Disorder in Children with Solid Organ Transplantation: Retrospective Analysis of 43 Cases

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Background/Objectives: Post-transplant lymphoproliferative disorder (PTLD) is a very heterogeneous disease in children with unpredictable outcome.

Design/Methods: A 15 year (November 1998 to December 2013) single center retrospectively study of children 0-18 years of age diagnosed with PTLD post solid organ transplantation was conducted to identify risk factors, clinical presentation, pathology, treatment and survival.

Results: 43 cases of PTLD in 27 patients were assessable for analyses. The transplants included kidney (4), heart (15), liver (7) and multi-organ (2) with overall survival (OS) 100%, 86%, 44% and 0% respectively at 50 months ($p=0.005$). Median age at PTLD presentation was 61.7 (13.5-198) months. Median time from transplant to first episode of PTLD was 16.8 (2-183) months. EBV mismatch at time of transplant adversely affected the OS ($p=0.017$).

There was no significant difference in the number of immunosuppressive medications for the development of PTLD. 55% had B symptoms, 81% had stage III/IV. The majority had elevated EBV titers at diagnosis. The pathology was monomorphic in 21 patients versus polymorphic in 20 patients with no significant difference in OS. Cell population identified were B cell (35), T cell (1), B and T combined (4) and EBV associated smooth muscle tumour (2). EBV positive in tumour 77%. Treatment included 18 with reduction in immunosuppression (RIS), RIS +/- antiviral 15, Rituximab +/- RIS 4, Rituximab + chemotherapy 3 and chemotherapy 3. There were no differences in the OS between the subgroups ($p=0.238$). The OS was 69% with Progression Free Survival 53% with a median follow up of 37.6(0.2-180) months for the entire group.

Conclusion: PTLD in children can present with multiple events in one individual. The presence of EBV mismatch at the time of the transplant and the type of transplant adversely affects the outcome. Prospective studies are needed to better understand this disease.

P-0438 | Therapy Results of Non-Hodgkin Lymphoma in Children

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Background/Objectives: We aimed to evaluate the survival rate and prognostic factors in children with non-Hodgkin lymphoma (NHL).

Design/Methods: Hospital records of patients with NHL who had been treated with NHL-BFM 95 protocol between 1998-2014 have been screened. Data including the demographic and clinical features, histopathological diagnosis, stage and reason of death were retrospectively collected from patients' chart records and electronic patient inventory. Survival rate was detected by Kaplan-Meier method.

Results: Median age of the 139 patients with NHL was 8.7 years (range 0.9-17.5 years), and male/female ratio was 3.8. Localization of the mass was abdomen in 45%, mediastinum in 24%, cervical region in 15%, and tonsil and Waldeyer ring in 9%. Histopathological diagnosis was B cell lymphoma in 68%, lymphoblastic lymphoma in 28%, and anaplastic large cell lymphoma in 4%. 84% of the patients had stage 3, and 9.5% had stage 4 disease. Mean lactate dehydrogenase level was 810 ± 1020 IU/l. 1-year and 5-year overall survival rate was 87%, and 83% respectively. Survival rate was 100% in stage 1, 80% in stage 2, 84% in stage 3, and 70% in stage 4 disease ($p=0.4$). There was not any significant difference in survival according to the lymphoma type and tumour localization. The reason of mortality was progressive disease in 19 (82%) out of 23 patients, and infection in 4 (18%). The latest recurrence was at 14th month.

Conclusion: 5-year overall survival rate was 83% in the patient group mostly diagnosed in advanced stages and all of the patients without recurrences in 14 months were in remission.

P-0439 | Breast Lymphoma. Case Report and Literature Review

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Background/Objectives: Primary non-Hodgkin lymphoma of the breast is rare in paediatric patients. It represents 0.4 to 0.5% of all primary breast tumors in children. No characteristic clinical nor radiological findings exist. Thus, a high index of suspicion is required. Biopsy confirms the diagnosis.

Design/Methods: Case Report: A 15-year-old female presented with increased volume and turgidity on both breasts. A chest film reveals a widened mediastinum and bilateral pleural effusion. CT demonstrates a non-calcified anterior mediastinal mass with enlarged lymph nodes. Mammary glands show increased density. A PET scan lights up the angle of the mandible, pleura, anterior-superior mediastinum, and thoracic vertebrae, with hypermetabolism also in both ovaries and breasts (Stage IV).

Results: A biopsy of the mediastinal mass through a Chamberlain incision reports T-Cell lymphoblastic lymphoma with large cells, hyper-chromatic nuclei, CD-3 + and CD-9 +, TdT and CD-10 negative.

Follow-up PET-CT three months after diagnosis shows adequate response to chemotherapy.

Conclusion: Lymphoma affecting the breast in children is quite uncommon, lacking any clinical or radiological characteristics. Treatment is individualized for each case. Mastectomy is not indicated except in case of recurrence of primary breast lymphoma, or for local control of symptoms in large, ulcerated, bleeding lesions.

Although lymphoma is a systemic disease, some authors state it is more common for primary breast lymphoma to present with synchronous mediastinal lesions, than it is for mediastinal lymphoma to invade the mammary glands.

P-0440 | The Use of Brentuximab Vedotin for Relapsed and Refractory Hodgkin Lymphoma in Children – An International, Multicentre Case Series

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Background/Objectives: Hodgkin lymphoma (HL) is a highly curable malignancy, with 5-year overall survival rates of 83-90%. Relapsed or refractory disease occurs in 10-20%, with brentuximab vedotin (brentuximab), a CD30-targeted antibody-drug conjugate, showing impressive responses in adults.

Design/Methods: This was a retrospective case series of patients treated with brentuximab for relapsed/refractory HL in two international paediatric oncology centres from 2010 to 2015.

Results: We report on 8 patients with a median age of 16 years (range 9-17) diagnosed with relapsed/refractory HL. Median number of prior treatment lines was 2 (range 2-4), with three patients (38%) receiving radiotherapy, one (12%) receiving autologous and one (12%) receiving allogeneic transplantation. Brentuximab 1.8 mg/kg three-weekly was used, with a median of 3.5 cycles (range 2-5), as a single agent in 6 patients (75%) and in combination with Bendamustine in 2(25%). Overall response rate was 6(75%) and complete response rate was 3(38%), although 6(75%) of patients had a subsequent relapse. Most toxicities were mild, with grade 3 toxicity seen in three patients (38%), related to neutropaenia or infection. Seven patients (88%) proceeded to allogeneic transplantation, with the other receiving an autologous transplant. In two patients brentuximab was used subsequently for relapse post-allograft, with one very good partial response and one sepsis-related fatality. At a median follow-up of 10 months from brentuximab administration (range 2 months to 4 years), three patients (38%) are in complete remission, with one death (12%), two (25%) being investigated for suspected relapse, and two (25%) with stable disease.

Conclusion: There are no specific studies on brentuximab for children with relapsed/refractory HL, thus we have collaborated to increase the pool of knowledge for this rare subgroup. Our results correlate with adult tolerability data, but further studies are needed to assess the efficacy of brentuximab as salvage treatment and a bridge to allogeneic transplant in children.

P-0441 | Subcutaneous Panniculitis-Like T-Cell Lymphoma in a Four Year Old Child – A Case Report

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Background/Objectives: Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a rare malignancy characterized by deep-seated skin nodules or plaques mimicking panniculitis due to neoplastic lymphocytes infiltrating subcutaneous fatty tissue. SPTCL accounts for less than 1% of all non-Hodgkin lymphomas and is extremely rare in childhood. We present a case of SPTCL in a four year child.

Objectives: To describe a case of SPTCL in a child and its management.

Design/Methods: Case report.

Results: Four year old Indian boy presented with a two year history of multiple nodular, non tender skin lesions predominantly over the thighs. He had skin biopsy at another center and was diagnosed as Erythema Induratum/Nodusum for which he received anti-tubercular treatment for 6 months. He had progressive disease and a repeat skin biopsy was reported as Lupus Panniculitis for which he received steroids and azathioprine for 4 months with no improvement.

In our evaluation he was noted to have multiple non tender subcutaneous nodules over the thighs with no lymphadenopathy or organomegaly and normal blood counts and elevated lactate dehydrogenase. Skin biopsy showed atypical lymphocytes surrounding adipocytes suggestive of panniculitis. Immunohistochemistry was positive for CD3, CD8 and negative for CD4, CD20, CD56 and EBV – suggestive of SPTCL. PET CT scan revealed metabolically active diffuse subcutaneous fat stranding with focal hypermetabolism in involved skin regions and the draining lymph nodes with splenomegaly. He was started on chemotherapy with Cyclophosphamide, Doxorubicin, Vincristine and Prednisolone. PET CT scan done at the end of treatment showed complete resolution. The patient is now twelve months post completion of therapy and in complete remission.

Conclusion: Diagnosis of SPTCL is a challenge since it can mimic some benign skin and soft tissue conditions. Accurate diagnosis requires clinical and pathological expertise. Our case is unique for the young age at presentation, difficulty in diagnosis and successful outcome after treatment.

P-0442 | Uncommon Lymphoma in Paediatric Age: Mycosis Fungoides

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Background/Objectives: Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphoma (CTCL), which typically occurs in elderly individuals. Children and adolescents are rarely affected. Data on clinical features, treatment response, disease progression in children are limited. Blood eosinophilia is known as a poor prognostic factor in adult patients with CTCL. An indolent course of the disease is noticed in paediatric patients.

Design/Methods: Case report.

Results: A 13 year old girl presented with a 5 months history of intense pruritic, erythematous patches of variable size and shape on her neck, trunk, abdomen, upper and lower limbs. Clinically, an erythematous plaque was also observed in association with a cutaneous tumour on her abdomen, axillary and inguinal lymphadenopathy.

Four biopsy specimens (nodal, two skin lesions, cutaneous tumour) were obtained for histopathologic examination. The presence of dermal atypical lymphoid with "cerebriform" nuclei infiltrate, mild epidermotropism both in skin and in tumour biopsy specimens was suggestive for MF. Small plaque parapsoriasis was also present. Immunohistochemically, atypical T-cell lymphocytes stained positive for CD2, CD3, CD4, CD5, CD7, CD8 markers and negative for CD30 marker. Increased level of peripheral blood eosinophils and tissue eosinophilia were observed at the time of diagnosis.

The diagnosis of MF was based on the clinical features combined with histopathologic findings. According to the ISCL/EORTC revision to the staging of MF and Sezary Syndrome, the diagnosis was established at the tumour stage, IIB.

Emollients and moderate potency topical steroids, narrowband ultraviolet B (NB-UVB) and chemotherapy (cyclophosphamide, doxorubicin, vincristine, prednisone combination) were used as treatment of MF, with partial response.

Conclusion: We reported a rare case of MF associated with both peripheral blood and tissue eosinophilia. A long follow-up period is needed. Studies are required for prognostic implications of eosinophilia in juvenile-onset MF.

P-0443 | Bendamustine Monotherapy An Effective Salvage Therapy for Refractory/Relapsed Paediatric Hodgkin Lymphoma (HL): A Retrospective Analysis

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Background/Objectives: Despite success in treatment of paediatric HL, 20% have resistant/relapsed disease. High-dose chemotherapy with autologous stem cell transplantation (ASCT) has improved outcomes with limited availability in LMIC. Bendamustine has clinical activity against adult relapsed/refractory lymphomas. With no such paediatric data, we report the results of bendamustine monotherapy in children with refractory/relapsed HL.

Design/Methods: Retrospective analysis of children with relapsed/refractory HL, treated between January 2013 - August 2015 was performed. Patients ineligible for ASCT/relapsed after ASCT (1), received bendamustine 120 mg/m² as 30 minutes infusion on days 1 & 2 every 28 days with growth factor support. Total 6 cycles planned for each patient. Early (following 2 cycles) and best response post 6 cycles of bendamustine were evaluated by PET-CT scan.

Results: Twelve patients on bendamustine, 8 received at least 2 cycles and underwent response assessment. Male:female 7:1; median age- 13.5 years (5-15 years); histology-mixed cellularity -5(62%) & nodular sclerosis-3(38%). Patients received median of 3 prior treatments (range, 1- 5). Relapsed HL (5) and primary progressive disease (3). PET-CT response post 2 cycles of bendamustine demonstrated Complete Remission (CR)-4(50%), (Partial Remission (PR) - 4(50%) and Overall Response Rate (ORR) -100%. 1 patient with PR post 2 cycles underwent haploidentical allo-SCT and died of sepsis. 7 patients received 6 cycles of bendamustine, 6 (85%) - CR and remained in CR. 1 patient in PR was started on lenalidomide - celecoxib maintenance, died of sepsis post chicken pox at 7 months. One patient relapsed after 14 months. Mean OS and median EFS were 21.15(13-29) & 24.4 (18-39) months. Treatment was well tolerated with manageable toxicities.

Conclusion: Within the limits of an observational retrospective study, these data indicates that bendamustine shows its efficacy in patients with relapsed/refractory HL, without any significant toxicity. It produces durable responses in patients with relapsed/refractory HL and may be an effective bridge to further therapeutic interventions.

P-0444 | Staging, Response Assessment and Treatment Adaptation Based on FDG-PET Imaging in Paediatric Hodgkin Lymphoma

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Background/Objectives: The study assessed the role of FDG-PET in staging, interim assessment and end of treatment assessment in children and adolescents with Hodgkin lymphoma.

Design/Methods: Patients lesser than 18 years of age who were diagnosed with Hodgkin lymphoma and completed therapy from January 2013 to December 2015 were included. Data was collected retrospectively from case records.

Results: Forty nine patients with mean age of 11.4±3.9 years were included in the study. Early favourable (stage I and II with no unfavourable features), early unfavourable (stage I and II with bulky disease/ B symptoms) and advanced disease (stage III and IV) was present in 15 (30.6%), 7 (14.3%) and 27 (55.1%) patients, respectively. Among 36 patients who underwent staging FDG-PET at diagnosis, 7 (19.4%) patients were upstaged and 1 (2.8%) patient was downstaged by PET when compared to CT. All 3 patients who had marrow infiltration on trephine biopsy and additional 4 patients with normal trephine biopsy had marrow uptake on PET. All but one (14 of 15) patient with early stage favourable disease were treated with 4 cycles ABVD chemotherapy alone after documenting metabolic remission in PET. In addition, radiotherapy was avoided in two of 7 patients with early unfavourable disease; and 23 of 27 patients with advanced disease subsequent to PET remission. Progression/stable disease on interim PET was detected in 3 patients which enabled escalation of chemotherapy regimen and subsequent remission of disease. The 3 year event free survival (EFS) for the entire cohort was 91±5.2% and 3 year overall survival was 100%.

Conclusion: FDG-PET is an excellent staging modality in childhood Hodgkin lymphoma and eliminates the requirement of trephine biopsy. Radiotherapy can be safely avoided in patients who attain metabolic remission on interim PET, without compromising EFS. Further, interim PET facilitates early identification of patients requiring intensification of chemotherapy.

P-0445 | Clinical Characteristics and Treatment Response in Children with Hodgkin Disease: Single Center Experience

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Background/Objectives: Prognosis of Hodgkin disease (HD) in childhood has remarkably improved in the last decades and survival of patients depends on the disease staging and histological type at diagnosis. In the last decades combined chemo-radiotherapy has been the treatment modality preferred by most study groups. Aim of our study was to register clinical/laboratory data at diagnosis, treatment (chemotherapy/radiotherapy/stem cell transplantation; SCT) and survival rates (event free survival; EFS, overall survival; OS).

Design/Methods: We searched databases of the Department of Pediatrics of children diagnosed with HD at the AHEPA Hospital for patients registered from 1996 to 2015. Overall, 35 patients were recorded and treated according to either COPP/ABVD or EURONet-PHL-CI protocols with or without radiotherapy. Clinical staging was determined according to the Ann-Arbor Classification.

Results: Among 35 patients, 18 (51.4%) were male. Mean age at diagnosis was 11.6 years. B-symptoms were present in 13/35 (35.7%) of patients. None had bone marrow involvement. The majority of patients were classified as stage II (42.8%) and stage IV (31.4%). The most frequent histological type was nodular sclerosis (23 patients). The majority of patients underwent conventional chemotherapy (20 patients; 57.1%) while 12 patients received combination of chemo- and radiotherapy (34.2%). Only 3 patients (8.56%) underwent autologous SCT after treatment. OS and 5-EFS of patients were 94.2% and 80% respectively.

Conclusion: Our findings demonstrate systemic chemotherapy alone to be an effective treatment in childhood HD. As survival of patients depends on disease stage at diagnosis the prompt admission of patients with suspicion of HD is required.

P-0446 | A Paediatric Case of Primary Pulmonary Hodgkin Lymphoma: A Rare but Favourable Entity

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Background/Objectives: Primary pulmonary Hodgkin lymphoma (PPHL) is a very rare entity involving only the pulmonary parenchyma without any nodal infiltration. Patients, having infiltration with no response to non-specific antibacterial treatment, should be evaluated in terms of malignancy and since it has a good prognosis, early recognition is mandatory. We report here an adolescent with refractory chest pain who is diagnosed with PPHL.

Design/Methods: A 14-year-old previously healthy girl presented with two months of left-sided chest pain. There were no fever, night sweats and no weight loss. On physical examination, the only pathological finding was decreased breath sounds on the left upper lung zone during auscultation. Chest X-Ray revealed refractory parenchymal infiltration on the left upper lobe despite antibiotic therapy. Computed tomography (CT) showed opacities with irregular borders on the left upper lobe anterior and superior lingular segments. After excluding tuberculosis, a tru-cut biopsy was planned. Ultrasound guided tru-cut biopsy revealed CD15 and CD30 (+) classical type Hodgkin lymphoma.

Results: Positron emission tomography (PET)/CT imaging revealed tumoral activity localized at the left upper lobe paramediastinal area measured 8 cm at the widest part and at superior neighborhood millimeter sized nodular hypermetabolic lesions. According to Ann-Arbor staging system, the patient diagnosed with stage IIEA Hodgkin lymphoma. Four adriamisin-bleomycin-vinblastine-dacarbazine (ABVD) courses was planned. After 2 courses of ABVD regimen, chest-X-ray was almost normal with no infiltration. At the tumour board, since the lesion was just inferior to the breast tissue, radiotherapy was omitted in favor of 2 more ABVD courses. At the end of 6 courses of chemotherapy, PET-CT scan results were compatible with complete anatomic and metabolic remission.

Conclusion: PPHL is a rare type limited to the lung parenchyma without any other pulmonary lymph node involvement and extrapulmonary involvement. The lesion might be nodular or cavitary and it must be kept in mind in resistant lung lesions.

P-0447 | Is Quality of Life is Better in Cases of Abdominal Burkitt Lymphoma Presenting with Abdominal Mass Treated Initially with Surgery

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Background/Objectives: The aim of the study is to see the effect of resection of the intestinal lymphoma before chemotherapy in terms of quality of life and tolerance of chemotherapy.

Design/Methods: All the cases of primary intestinal lymphoma presented directly to paediatric surgery department in one unit or referred from department of haematology were included in the study. The patients presented in department of Paediatric surgery were initially treated with resection of the mass with post-operative chemotherapy (n=3 : group A) where those who were referred from haematology (n=4; Group) were treated initially with chemotherapy and were operated either due to intestinal obstruction or neutropenic enterocolitis. Patients were registered according to criteria developed by Dawson and colleagues; The tolerance was assessed in terms of, total number of days of admission (excluding the days of chemotherapy) episodes of neutropenia, omission of the chemotherapy cycle, episodes of abdominal discomfort requiring admission and required bowel rest.

Results: Three cases included in group A and four in Group-B. Only one patient in group A required omission/delay of the chemotherapy cycle once whereas more than 50% cases of Group B required either omission or delay of the chemotherapy cycle. 75% cases in Group B required emergency laparotomy due to intestinal obstruction before completion of the chemotherapy. The recurrent admission during chemotherapy due to low total leucocyte count, abdominal distention and features of neutropenic enterocolitis were seen in 75% cases in group B and 33% cases of group A Overall growth and tolerance to chemotherapy was better in group A.

Conclusion: Quality of life of the patients of intestinal Burkitts lymphoma is better in those patients who had resection of the mass prior to radiotherapy rather than those who are subjected to surgery during or after chemotherapy regimen; though a detailed study is needed to reach a definitive result.

P-0448 | Burkitt Lymphoma Presenting as Intussusception; Our Experience

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Background/Objectives: Intussusception is invagination of a bowel segment, usually proximal, into distal bowel segment. It is a common cause of bowel obstruction in children with a peak incidence at age 3 - 9 months. Primary Non-Hodgkin Lymphoma presenting as ileocolic intussusception in paediatric age group is a very rare clinical entity. We present six cases of Burkitt lymphoma which presented as intussusception, highlighting the differing presentations of these children and their outcome.

Design/Methods: A retrospective review of all patients treated for non Hodgkins lymphoma presented at one paediatric surgery unit, from January 2010 to Dec 2015 was conducted and the results were analyzed.

Results: A total of 10 cases of primary non Hodgkins lymphoma of GIT were managed in during study period. 80% presented with acute intestinal obstruction, 60% had intussusception. Those presented with intussusception, 34% had intestinal perforation at time of exploration. In 67% cases lesion was in distal ileum whereas in 33% it was in large bowel. All were managed with complete macroscopic resection of the lesion with stoma. Continuity of the bowel was maintained after completion of the chemotherapy. Wound dehiscence observed in one case with no mortality in the patients presented with intussusception but two presented with obstruction due to luminal compromise were succumbed to death in follow up.

Conclusion: Prompt diagnosis and early intervention is the key in management of intussusception in such cases. Providing stoma after resection of mass followed by chemotherapy provides good result.

P-0449 | Hodgkin Lymphoma, Epstein-Barr Virus, and HIV in Malawi: Longitudinal Results from the Kamuzu Central Hospital Lymphoma Study

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Background/Objectives: Classical Hodgkin lymphoma (cHL) is associated with Epstein-Barr virus (EBV) and HIV. However, detailed prospective cHL descriptions are lacking from sub-Saharan Africa where both viruses are prevalent, especially in the current antiretroviral therapy (ART) era.

Design/Methods: We describe a prospective cohort of patients with cHL at a national teaching hospital in Malawi between June 2013 and December 2015. Chemotherapy and supportive care are standardized (ABVD for adults; modified ABVE-PC without etoposide for children).

Results: Thirty-three patients were confirmed to have cHL after consensus review by US and Malawian pathologists. Median age was 15.5 years (range 2-51) with 24 (72%) being male, and 18 (55%) being children <18 years. No children and 5/15 adults (33%) were HIV+, compared with 10% HIV prevalence in the general Malawi adult population. All HIV+ patients were on ART at cHL diagnosis for a median 15 months (range 2-137), with median CD4 count 138/ μ L (range 23-329) and 4 (80%) having undetectable HIV RNA. For the cohort overall, 18 (55%) had stage III/IV disease, 27 (82%) B symptoms, and 23 (70%) symptoms >6 months. Thirteen (39%) were receiving empiric treatment for tuberculosis lymphadenitis prior to cHL diagnosis, and 17 (52%) had significant performance status impairment. Anemia and elevated lactate dehydrogenase were common with median hemoglobin 8.9 g/dL (range 4.7-17.1) and LDH 359 IU/L (range 161-894). EBV-encoded RNA in situ hybridization was positive in 17/23 (74%) tumour specimens assessed, including 13/19 (68%) HIV- and 4/4 (100%) HIV+. As of March 31, 2016, there was no loss to follow-up after a median 11 months (range 5-26) among 26 patients still alive. Estimated Kaplan-Meier 12-month overall survival was 80% (95% confidence interval 56-91%).

Conclusion: cHL is common among adolescents and young adults in Malawi, typically associated with EBV and often HIV. Despite advanced disease and impaired performance status, 12-month overall survival was good.

P-0450 | The Value of 18FDG-PET/CT in Detecting Bone Marrow Involvement in Childhood Cancers

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Background/Objectives: The aim of this study was to assess the utility of F-18-fluoro-2-deoxy-d-glucose (F-18-FDG) positron emission tomography/computed tomography (PET/CT) in assessing bone marrow involvement (BMI) compared to bone marrow biopsy (BMB) in initial staging of Hodgkin lymphoma (HL), Non-hodgkin lymphoma (NHL), Neuroblastoma (NB) and Ewing Sarcoma (ES) in paediatric patients.

Design/Methods: Fifty-one patients (35 male, 16 female, mean age 9.07 years, range 2-18 years) with newly diagnosed HL, NHL, NB and ES between July 2014 and February 2016, evaluated with BMB and F-18-FDG PET/CT before chemotherapy were included in this study. There were 23 NHL, 11 HL, 12 NB, and 5 ES patients. We reviewed and compared their F-18-FDG PET/CT and BMB results retrospectively.

Results: Of the 51 patients, 20 patients had bone marrow involvement on F-18-FDG PET/CT while 31 of them did not have. BMB was positive in 11 and negative in 8 of these 20 patients. In 31 patients negative on F-18-FDG PET/CT, BMB was negative in 24 patients and positive in 1 patient. In 8 patients, BMB specimens were considered to be insufficient for evaluation.

Conclusion: Our study demonstrated that F-18-FDG PET/CT was useful in evaluation of bone marrow involvement in childhood HL, NHL, NB and ES at initial staging.

P-0451 | Hodgkin Lymphoma Single Centre Experience: Akdeniz University Paediatric Haematology Oncology

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Background/Objectives: Hodgkin lymphoma is a form of cancer involving the lymphatic and reticuloendothelial system and comprises approximately 10% of all paediatric cancers in Turkey. The age distribution and histopathology differ according to countries. The purpose of this study to evaluate the outcome of Hodgkin lymphoma in our center to identify the clinical properties and treatment response.

Design/Methods: This study is the retrospective analysis of 69 Hodgkin lymphoma patients treated at Akdeniz University Hospital, Division of Pediatric Haematology and Oncology, between January 1997 – December 2015.

Results: This study involves totally 69 Hodgkin lymphoma patients. There were 34 girls and 35 boys with a median age of 13 (range 3-18) at diagnosis. Twenty-one patients (30.4%) had B symptoms. Majority of the patients (60%) were 10-18 years old. The number of patients with stage I,II,III and IV were 7, 32, 15 and 15 respectively. Nodular sclerosis was the most common histological subtype (56.5%) followed by mixed cellular (30.5%), lymphocyte rich (10%) and nodular lymphocyte predominant (3%). ABVD, COPP and COPP/ABV were administered for 37 (53.7%), 15 (21.7%) and 17 (24.6%) patients respectively. Forty-six patients (66.6%) were treated with combined modality treatment including involved-field radiotherapy. Of the 7 patients with relapse, four were stage II and the other three were stage IV. Ten year overall survival (OS) and event free survival (EFS) were 97.6±2.4% and 89.7±4.1%, respectively. Patients treated with ABVD protocol had better EFS when compared with patients treated with COPP protocol (97.6±2.4% vs 68.4±1.3%, log-rank=0.014).

Conclusion: Interestingly, nodular sclerosis type is the most common histological type contrary to the previous data from our country and other developing countries. Better EFS with ABVD protocol is a motivating result to use this less toxic protocol. In recent years, success of therapy increases also in developing countries and approaches the level of developed countries.

P-0452 | Clinicopathological Features and Prognosis of Children with Non-Hodgkin Lymphoma

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Background/Objectives: To explore the clinicopathological features and prognosis for childhood non-Hodgkin lymphoma (NHL).

Design/Methods: From Jan, 2009 to Oct,2014, 56 children newly diagnosed with NHL were included in the study. The average age was (6.73±3.12) years old. Clinical staging was confirmed by the World Health Organization classification of tumors and St. Jude system. All statistical analyses were carried out using SPSS software version 19.0.

Results: 29 patients achieved complete remission (CR) after one course of treatment, 53 patients after two courses of treatment, 3 patients were failed to achieve CR and died of progression of disease, 6 patients had relapse and 2 patients died of serious infection. According to pathological type, 25 patients were diagnosed as Burkitt lymphoma, 13 were anaplastic large cell lymphoma, 5 were diffuse large B-cell lymphoma and 13 were progenitor cell or metrocyte lymphoma. According to clinical stages, 6 patients were divided into stage II, 25 into stage III, 25 into stage IV and no patient into stage I. The 5-year event-free survival (EFS) was 83.7±5%. The 5-year EFS of Burkitt lymphoma, anaplastic large cell lymphoma, large B-cell lymphoma and progenitor cell or metrocyte lymphoma were 96±3.9%, 58.3±14.2%, 80±17.9% and 84.6±10%, retrospectively. And there was no significant difference between Burkitt lymphoma and anaplastic large cell lymphoma (P=0.004). Also there was no significant difference between patients suffer from anaplastic large cell lymphoma with positive ALK gene and negative ALK gene. The 5-year EFS of stage II patients, stage III patients, stage IV patients were 100%, 79.6±8.1% and 83.8 ±7.4%, respectively (P=0.309, P=0.681, P=0.245).

Conclusion: Pathological and cytological diagnosis for newly treated children with non-Hodgkin lymphoma was the key to the prognosis. The regimen of NHL in children was effective and resulted in high EFS, while children with anaplastic large cell lymphoma remained to be improved.

P-0453 | The Results of Short-Intensive Chemotherapy Protocols in Turkish Children with Advanced Stage Burkitt Lymphoma

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Background/Objectives: Malignant lymphomas are the second most common malignancies in Turkey and the majority of the cases present with advanced stage (III-IV). We report the treatment results of modified Pediatric Oncology Group (POG) protocols in children with Burkitt (BL) and B-cell non-Burkitt lymphomas (B-cell nonBL).

Design/Methods: Fifty seven patients (50 BL, 7 B-cell nonBL) who were diagnosed between June 1992 and March 2016, aged between 20 months - 16 years (median 7 years). According to St. Jude staging system 85.4% of these patients were classified an advanced stage. For stage II patients "Total Therapy B Protocol" was used. For CNS prophylaxis continuous ARA-C 4.3g/m²/48 h was given as infusion. For stage III and IV patients "POG 9317" protocol received. Stage III patients were given 4.3g/m²/48 h continuous infusion of ARA-C for CNS prophylaxis. Stage III patients who went into partial remission following the induction therapy received "POG 9317" intensification phase. Stage IV patients were received ARA-C 12g/m² (3g/m² over 3h × 4 doses, given at 12h interval). For patients in stage IV intensification phase given only one and consolidation phase was repeated twice.

Results: Early toxic deaths were seen only in 7 patients (12.3%). 6 patients (10.5%) were lost because of relapse and progressive disease within the first 6 months. All stage II patients and 49 out of 57 (85.9%) advanced stage (III-IV) patients are being followed off treatment between 5-295 months.

Conclusion: With the use of Total B Therapy and POG 9317 in B-cell lymphomas presenting with extensive disease, we achieved the major advantage of fewer metabolic complications provided by a smoother induction using fractionated CTX. It seems that in POG 9317 the presence of Ifosfamide and VP-16 (intensification phase) and high doses of ARA-C (12g/m²) enabled us to control BM and CNS involvement.

P-0454 | Posttransplantation Lymphoproliferative Disease in Children with Liver Transplantation: Baskent University Experience

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Background/Objectives: Due to acquired immunosuppression, post-transplantation lymphoproliferative disease has become a common neoplastic process during development of transplantation surgery. Both types of B-cell neoplasms due to EBV re-activation as well as T-cell neoplasms can be seen. Treatment of B-cell post-transplant lymphoproliferative disease is standardized but treatment of T-cell disease is still controversial.

Design/Methods: The first liver transplantation in Turkey had been performed in 1989 by Prof. Dr. Mehmet Haberal in Baskent University. Since then, 218 ortotopic liver transplantations had been performed under 18 years-old and posttransplantation lymphoproliferative disease was diagnosed in 7 children.

Results: PTLD was developed in children between ages of 11 months and 14 years, five of them were male and disease occurrence after liver transplantation was differed between 4-57 months. All of patients had been taking calcineurin inhibitors as major immunosuppressive agent. In 5 of patients, lymphoproliferative disease was of B-cell origin. In all of them EBV viral load was high and EBER was positive at neoplastic tissue. Two of cases with B-cell disease were in polyclonal lymphoproliferation phase and treated with rituximab. The other three cases were in lymphoma phase. In these cases, modified OEPA-C chemotherapy regimen for immunosuppressed patients had been used. For T-cell PTLD; modified OEPA-C and modified BFM-90 regimens had been started for each patient. Conformal radiotherapy was given to patient with T-cell-PTLD who partially responded to chemotherapy. One patient with B-cell PTLD underwent surgery for inflammatory myofibroblastic tumour which had been developed in lungs. A patient with T-cell disease died due to neutropenic sepsis in remission. Six patients have been followed-up in remission between 40-101 months.

Conclusion: This retrospective evaluation of PTLD cases after liver transplantation is a big series in Turkey with case number, treatment strategies, 86% overall and problem-free survival in a median follow-up of 59 months.

MYELOID LEUKEMIAS, MYELOYDYSPLASTIC AND MYELOPROLIFERATIVE SYNDROMES

P-0455 | Fatal Case of Congenital Acute Myeloid Leukemia with T(8;16)(P11;P13)

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Background/Objectives: Acute myeloid leukaemia (AML) with t(8;16)(p11;13) is a rare recurrent cytogenetic abnormality found in adult and paediatric leukaemia. This translocation leads to dysregulated gene expression from a fusion protein with MOZ (MYST3) and CBP (CREBBP) and presents as an M4 subtype. Because of case reports of spontaneous remission and concerns for side effects of chemotherapy in neonates, many reports have suggested close observation without chemotherapy.

Design/Methods: We report a case of congenital AML t(8;16)(p11;13) and compare it with other cases in the literature. A full term female noted to have blueberry muffin lesions at birth was diagnosed with AML M4 with t(8;16). FLT3, CEBPA and NPM mutations were negative. She was transferred to our institution at 6 weeks of age at which time there was resolution of the leukaemia cutis and bone marrow revealed no blasts but FISH was positive for t(8;16). She was monitored closely without chemotherapy. She relapsed at 3 months and was treated per COG AML protocol. She relapsed at 10 months of age and received allogeneic stem cell transplantation but died of resistant disease.

Results: There have been 4 additional case reports (including ours) since The International-Berlin-Frankfurt-Munster AML study group reviewed 17 congenital cases with t(8;16)(p11;13). Of the 11 treated with chemotherapy, data is available for 9 patients, of whom, 7 obtained complete remission and survived. Of 10 patients treated with conservative management, 5 remained in complete remission. Five went on to receive chemotherapy due to relapse. Of these, 3 died from chemotherapy or other complications.

Conclusion: Neonatal AML with t(8;16)(p11;13) has a 50% chance of relapse in patients treated with conservative management. Although survival with chemotherapy is improved to 75% in these patients, the side effects of aggressive treatment are concerning. We propose these patients may benefit from a milder chemotherapy regimen given at the time of diagnosis.

P-0456 | Achieving Improving Survival Rates of Acute Myeloid Leukemia in Developing Countries Using AML15 Protocol

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Background/Objectives: Acute myeloid leukaemia (AML) makes up to 20% of acute leukaemia incidences. Marked differences in survival rates of AML occur between developed and developing countries with exception of APML. Survival rates in developed countries, reach 63-65% while its around 25-53.8% in developing countries.

Design/Methods: The clinical characteristics of paediatric AML patients admitted into our hospital from January 2009 to December 2013 was studied. All patients were treated with AML15 protocol and mean follow-up was 30 months.

Results: There were 41 cases of AML. 4 were infants and 11 cases were >10 years old, both factors for unfavorable prognosis. Female to male ratio was 1.22. The most common presenting symptoms were fever with skin and mucosal bleeding (65.7%), and firm organomegaly (68%). 17 patients presented with severe anemia ($Hb < 5g/dl$), WBC counts were $< 5000/\mu L$ in 14 patients and $> 50,000/\mu L$ in 7 patients. In 28 patients, platelet counts were $< 50,000$ cells/ mm^3 . All cases had blasts in peripheral smear except for 4. Unusual presenting symptoms include extradural spinal cord compression ($n=1$), leukemic cutis ($n=1$), subcutaneous deposits ($n=2$), leukoencephalopathy, and raccoon eyes & DIC ($n=1$). Based on morphology and immunophenotyping, the most common AML subtype was M5 ($n=14$, 36.8%). Other subtypes diagnosed include M1 ($n=5$, 13.2%), M2 ($n=4$, 10.5%), M3/APML ($n=6$, 15.8%), M4 ($n=5$, 13.2%), and M7 ($n=5$, 13.2%). Cytogenetic analyses revealed 4 with t(8;21), 1 with t(X;3)[A1], 2 with inv(16), 2 with t(9;22), and 1 with MLL rearrangements. All 6 cases of APML were t(15;17) positive. 3 patients opted out of treatment. Among the remaining 35, 3 failed to achieve induction remission and 1 died during induction therapy. From those who achieved induction remission, 2 were lost to follow-up. In total, 29 patients completed treatment, 5 relapsed and 2 died from febrile neutropenia. The survival rate was 62.9%.

Conclusion: The survival rates of paediatric AML patients in our study are on par with that of developed countries. Risk-adapted chemotherapy with good supportive care improves survival rates in developing countries.

P-0457 | Acute Myeloid Leukemia in Children with Down Syndrome – Treatment Outcome in the Experience of Polish Paediatric Leukemia/Lymphoma Study Group from 1998 to 2015

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Background/Objectives: Children with Down syndrome (DS) are at higher risk of developing acute myeloid leukaemia (AML). They respond very well to chemotherapy with very high remission rate but are particularly susceptible to toxicities especially infectious complications. The aim of the study was analysis of the treatment outcome of AML in children with DS in Poland from 1998 to 2015.

Design/Methods: Total 47 patients with DS and AML treated in Poland in analyzed period were eligible for the study. 15 of them were treated with AML-PGPLBC98 protocol (1998-2004) and 32 with AML-BFM2004 Interim (2005-2015). Survival rates were calculated and reasons of failures were analyzed.

Results: Probabilities of 5-years overall survival (OS) and event free survival (EFS) were the same: 0.70 ± 0.07 for whole analyzed group, 0.53 ± 0.13 for AML-PGPLBC98 protocol and 0.78 ± 0.07 for AML-BFM2004 Interim ($p=1.02$). Probability of 5-years relapse free survival (RFS) was 0.97 ± 0.03 for whole analyzed group, 0.89 ± 0.10 for AML-PGPLBC98 protocol and 1.00 for AML-BFM2004 Interim. There was one relapse in the first analyzed period and none in the second period. There were 6 deaths from toxicities (5 because of infectious complications, 1 of generalized bleedings), including 2 early deaths before remission and 4 deaths in remission and 1 death because of disease progression after relapse in patients treated with AML-PGPLBC98. Among patients treated with AML-BFM2004 Interim 7 died of toxicities (6 because of infectious complications, 1 of cardiac tamponade), 3 of them before remission and 4 patients in remission.

Conclusion: Improvement of the treatment outcome of AML in children with DS was observed although differences between protocols were not statistically significant. The progress was achieved by modification of the protocol with reduction of chemotherapy intensity. Improvement of supportive treatment in patients with Down's syndrome should be also implemented.

P-0458 | Prognostic Relevance of Minimal Residual Disease Detection in Paediatric Acute Myeloid Leukemia

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Background/Objectives: In acute myeloid leukaemia (AML), sizable proportions of patients have no definitive prognostic factors that can be identified at diagnosis. The degree of response

to treatment can be a useful predictive parameter in these. The aim of our study was to assess the prognostic significance of minimal residual disease (MRD) in paediatric AML.

Design/Methods: Fifty one patients of de novo paediatric AML (excluding acute promyelocytic leukaemia) were enrolled in this prospective study during the period December 1, 2012 to May 13, 2014. Standard 3+7 induction was used, with Daunomycin, 60 mg/m²/day, and Ara-C at 100 mg/m²/day. Patients who were not in remission after a single induction received re-induction with either ADE protocol or a repeat 3+7. Five-colour flow cytometric analysis was performed in post induction bone marrow for MRD assessment.

Results: MRD estimation was performed in 49 patients who were in morphological remission post-induction. Survival characteristics were calculated taking the cut-off of significant residual leukemic blasts as 0.1%. At this cut-off, there were statistically significant differences in event free survival, disease free survival and overall survival ($p < 0.05$) between patients who were MRD positive (MRD $\geq 0.1\%$) vs MRD negative (MRD $< 0.1\%$). MRD also was successful in sub-classifying patients with good risk cytogenetics into better and poor survival. No statistically significant difference in survival was found in between the MRD positive and negative groups in the intermediate cytogenetics group.

Conclusion: Persistent minimal residual disease is an important predictor of poor survival in paediatric AML and can be expected to be an important decision-making tool in future.

P-0459 | Clinico-Epidemiological Aspects and Survival Analysis of Acute Myeloid Leukemia among Egyptian Children Over the Last 20 Years (A Single Center Experience)

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Background/Objectives: Different clinical and biological features at diagnosis have been useful for the prediction of the clinical outcome of paediatric AML. The 5 years overall survival of childhood AML has dramatically improved in the recent decades.

The Aim of the study was to evaluate the clinico-epidemiological aspects, the Overall and Event free survival of paediatric AML and their relations to different prognostic factors.

Design/Methods: All AML patients, diagnosed in the Pediatric Oncology Department Ain Shams University hospitals, over a period of 20 years were included. The clinical & epidemiological data of the patients were collected, and the EFS and OS were calculated.

Results: This study included 59 patients (mean age of 6.5 ± 4.6 years), with no gender difference. Most of cases had FAB M2 AML (35.6%). While, the least in frequency was FAB M5 subtype (1.7%), none were diagnosed with FAB M6 morphology. Patients with cytogenetically normal constituted (39%). Favorable cytogenetics was present in (18.6%) of our patients { 10 had t(8;21) and one with inv (16) } Five patients were Down syndrome, all had M7 FAB subtype. Forty eight patients (44.1%) were with 3+7 protocol, 9 with modified MRC 12 and only 2 cases had BMT. Calculated remission rates were (53.8%) and (44.4%) respectively. Twenty two patients had progressive disease. Eighteen cases had relapse. Early death was recorded in 4 cases only and late death in 11. Good risk was found in eleven cases, standard in 33, while poor risk was reported in 15 cases. The 5 years OS and EFS were 44.1% and 39% respectively.

Conclusion: Although, the OS and EFS rates of our AML patients increased over the period of 20 years, yet still low compared to international reports. Comprehensive and integrated supportive care as well as extended researches are required to further improve the disease outcome in our center.

P-0460 | Clinical and Biological Correlates of Selected Polycomb Complex Genes Expression in Brazilian Children with Acute Promyelocytic Leukemia

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Background/Objectives: Prognostic markers in paediatric promyelocytic leukaemia (APL), which is characterized by the presence of the PML/RARA oncoprotein, have not been established. White blood cell count and FLT3-ITD mutation appear to be associated with a poorer outcome. To date, clinical and biological correlates of the expression of genes involved in epigenetic regulation such as those from the polycomb group (PcG) have not been studied in paediatric APL.

Design/Methods: We compared the expression levels of four of the PcG genes (*EZH2*, *YY1*, *BM11* and *SUZ12*) according to selected clinical and biological characteristics in 30 Brazilian children with APL (male, 17; female, 13; median age 10y, range 1-16y).

Results: Thirteen (43.3%) APL cases had FLT3-ITD mutations. Bone marrow cells from healthy children (median age, 8.2 years, range 4-17 years) and 39 AML cases (9 FLT3-ITD cases) (median age 8y, range 4m-18y) were used for comparison. Expression levels of *YY1* and *EZH2* genes were both significantly higher in APL cases and WBC count $\geq 10 \times 10^9/L$ than in cases with $< 10 \times 10^9/L$ (*YY1*: 1.79 ± 18.84 vs 0.18 ± 0.30 ; $P=0.01$ and *EZH2*: 1.15 ± 1.63 vs. 0.32 ± 0.45 ; $P=0.03$). Similarly, expression levels of *YY1* and *EZH2* genes were significantly higher in APL when compared with AML (2.94 ± 8.19 vs. 1.53 ± 11.83 ; $P=0.0015$ and 0.30 ± 0.48 vs 0.18 ± 0.22 ; $P=0.0082$), respectively. In APL, the expression levels of *SUZ12* and *EZH2* genes were about 15-fold (*SUZ12*: 10.6 ± 7.3 vs 0.33 ± 0.56 $P=0.0049$) and 2-fold (*EZH2*: 0.723 ± 2.88 vs 0.14 ± 0.3 ; $P=0.01$) higher in cases with FLT3-ITD mutations than in those with FLT3 wild-type. The expression levels of *SUZ12* (3.8 ± 7.38 , $P=0.0049$), *EZH2*: (0.33 ± 0.56 , $P=0.001$) and *BM11* (1.33 ± 3.22 , $P=0.0049$) were significantly higher in APL cases and FLT3-ITD than in those of AML cases with FLT3-ITD.

Conclusion: Our study revealed a very high incidence of *FLT3-ITD* among Brazilian children with APL and suggests that expression PcG genes might be a useful prognostic maker in paediatric APL.

P-0461 | Granulocytic Sarcomas in Children Can Present Like Solid Tumors; Experience of EGE University from Turkey

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Background/Objectives: Granulocytic sarcoma (GS) is an extramedullary malignant tumour composed of immature myeloid cells. They generally occur in skin, head and neck (orbit), bone, and least likely in intestine, abdomen, and central nervous system. GS is often associated with acute myeloid leukaemia (AML). The incidence of GS in patients with AML is 4-5% and they can occur during the course of AML or before bone marrow involvement happens, or AML may develop months later. According to tumour location, patients present with different symptoms.

Design/Methods: In this study, different and rare clinical symptoms, survival, and follow-up of 8 cases diagnosed as GS with or without AML in the last 10 years were retrospectively evaluated.

Results: The median age of patients (5 female, 3 male) at diagnosis was 79.5 months (6-190 months). Areas of involvement of GS included soft tissue in 6 patients (head and neck 2 patients, trunk 1 patient, intra-abdominopelvic 2 patients with pressure findings, skin 1 patient) and the other 2 patients had bone lesions.

At the diagnosis of GS in 4 patients AML (two M2, one M1, one M4) was determined. Seven patients were treated according to BFM-AML 2004 protocol and local radiotherapy was applied to them. Relapse occurred in 3 patients; in two AML was not present at diagnosis (Relapse time 12th and 44th months with AML). Bone marrow transplantation was performed to 2 patients who had relapses. The median follow-up time after diagnosis was 44 months (13-120 months). One patient died after bone marrow relapse. The others are being followed up in remission.

Conclusion: In children, GS usually accompanies AML. Frequently they consist of myelomonocytic and myelocytic cells as in our patients. Also they can occur like solid tumors and present pressure findings. In conclusion, GS appears as tumors with variable locations and prognosis.

P-0462 | Therapy for Childhood Acute Myeloid Leukaemia Based on the UKMRC AML Protocol - Experience and Outcome Over 12 years from a Tertiary Referral Centre in India

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Background/Objectives: Acute myeloid leukaemia (AML) has relatively poor prognosis. Optimal supportive care forms the backbone of treatment as children usually succumb to infections during therapy. Data from India about paediatric AML experiences is scarce. We present data on paediatric AML treated with UKMRC AML protocol at a tertiary referral centre in India.

Design/Methods: We conducted a retrospective analysis of 52 children diagnosed with AML by bone marrow morphology and flow cytometry over the past 12 years. Children with AML-M3 were excluded. Treatment was based on UKMRC AML protocol including 2 cycles of cytarabine, daunorubicin and etoposide for induction followed by 2 cycles of high-dose cytarabine (3g/m²BD on day 1, 3 & 5) during consolidation. Risk stratification was done at the end of induction based on remission status and cytogenetics. High risk children were offered allogeneic haematopoietic stem cell transplantation (HSCT) upfront. Remission at the end of induction, relapse rate, event-free survival, number of patients undergoing HSCT and overall survival were studied.

Results: Of the 52 children, 40 were diagnosed at our centre, 10 were treated partially elsewhere and 2 had secondary AML. Of the 40 children diagnosed at our centre, 22 had normal cytogenetics. DFS was 38% with chemotherapy alone and 54% for chemotherapy with HSCT. Three children succumbed to sepsis during induction and 27% relapsed after completing therapy. HSCT after first relapse was successful in 4/6 children. **Eleven required HSCT for high risk cytogenetics, persistent disease and non-achievement of remission after 2 induction cycles and relapse.** Survival rate post-HSCT was 54%.

Conclusion: Optimal high dose chemotherapy remains the backbone to provide cure, improve quality and decrease relapse in childhood AML. HSCT is advantageous due to graft versus leukaemia effect and also in relapsed disease, 60% of these children can be salvaged. Along with adequate supportive care, we can achieve cure comparable to developed nations.

P-0463 | Rare Clonal Blood Disorders in Childhood – Single Center Experience

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Background/Objectives: Myeloproliferative disorders (MPD) and paroxysmal nocturnal hemoglobinuria (PNH) are rare blood clonal disorders with characteristic onset in elderly patients and very rare in childhood.

Design/Methods: This study represents retrospective analyses of 6 patients with MPDs and PNH, diagnosed from 2010 to 2015, in Mother and Child Health Care Institute.

Results: The diagnosis of polycythemia vera (PV) and PNH was established in one and essential thrombocythemia (ET) and chronic myeloid leukaemia (CML) in two patients. Patients' age ranged from 10 to 18 years. The follow up period to diagnosis ranged from several days (in patients with CML and ET), up to 5 years in PNH patient. The majority of patients were without any symptoms at presentation, except one girl with CML who presented with fever and bone ach. Mild splenomegaly was noticed in PV and marked hepatosplenomegaly in CML. Patient with PNH had slow development of clinical course starting with thrombocytopenia, followed with progressive hemolytic anemia and hemoglobinuria. Maximal leucocyte count was detected in patient with CML (435x10⁹/l), hemoglobin count in PV (Hgb 181.7g/l) and platelet count was elevated in ET (1353-3018x10⁹/l), but also in patients with PV and CML. LDH was elevated in patients with CML (2018-8810IU/l) and PNH (maximal registered value 8934IU/l). BCR/ABL fusion gene was detected in both CML patients and JAK-2(V617F) mutation in two patients with ET and PV. PNH was diagnosed upon positive HAM test and flow cytometry (99%PNH+ neutrophils). The treatment depended upon the diagnosis. Hydroxyurea was introduced in patients with ET and CML, but was replaced with Imatinib in CML patients. Patient with PV currently is treated with Aspirin. PNH patient was treated symptomatically, until recently when the treatment with eculisumab was started.

Conclusion: MPD and PNH are not static disorders due to time-dependent clonal dominance, and their clinical phenotype is subjected to change over time.

P-0464 | Down Syndrome Associated Acute Leukemia of Childhood in Georgia: 10-Year Follow-Up

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Background/Objectives: Children with Down syndrome (DS) have a 10 to 15-fold higher risk of developing B-cell acute lymphoblastic leukaemia (DS-ALL) and acute myeloid leukaemia (DS-AML). Despite higher treatment related toxicities, risk-based therapy for Down syndrome related childhood acute leukaemia has been widely appreciated across many clinical trials.

Design/Methods: Clinical records of 7 children with Down syndrome associated acute leukaemia, admitted over the last 10 years were retrospectively analyzed. The patients were treated at M. Iashvili Children's Central Hospital, department of haematology /oncology,- the only facility in Georgia providing care for children with hematological malignancies.

Results: 7 children (6 Males and 1 Female) with Down syndrome have been admitted since the January of 2005. Median age of the patients was 27 months (range: 18-32 months), three of them were diagnosed DS-AML and four presented with DS-ALL.

Considering an overall number of 390 new cases of acute childhood leukaemia (ALL-307 and AML-83 cases) admitted at the hospital since 2005, Down syndrome associated acute leukaemia accounted for approximately 1.8% of all cases. Despite widely appreciated higher risk of developing acute megakaryocytic leukaemia (AML-M7) in children with Down syndrome, none of the analyzed DS-AML cases showed AML-M7 morphology or phenotype. All DS-ALL patients were diagnosed as Common ALL.

DS-AML patients were treated with AML-BFM-2004 and DS-ALL cases with ALL-IC-BFM 2004 protocol. All DS-ALL patients had good treatment response and have been staying disease free. One of the DS-AML patients experienced an induction failure and another developed bone marrow relapse after 135 days of induction, both patients died of the disease.

Conclusion: The 10-year incidence of Down syndrome associated acute leukaemia of childhood in Georgia is comparable to reported rates from other countries, although according to our data, the cases of DS-ALL outnumbered DS-AML patients and we also observed a trend of higher event free survival of DS-ALL patients comparing to DS-AML.

P-0465 | Fever of Unknown Origin and Idiopathic Myelofibrosis in a 17 Years Old Boy with Unusual Subsets of Bone Marrow T Cells: A Diagnostic Dilemma

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Background/Objectives: Idiopathic myelofibrosis (IM) is a rare disease mostly affecting adults. It is extremely unusual in children, the cases of paediatric idiopathic myelofibrosis (PIM) are secondary to malignancy, chronic renal failure and infections.

Design/Methods: A case report of seventeen years old boy with Fever of unknown origin and myelofibrosis.

Results: 17-years old boy admitted to our department with seven days history of fever, headache and acute pain in the right ear and orbital area. The boy gradually developed general fatigue, along with weight loss and night sweats.

Complete blood count on admission demonstrated: low white blood cells, anemia, thrombocytopenia and relative lymphocytosis. Biochemistry lab tests showed significantly elevated LDH, tests were negative on infectious agents. Bone marrow sample was hypocellular, with relative lymphocytosis-77%, and 6% of myeloid blasts.

Flow cytometry identified two CD45-positive populations of T-cells with variable expression of CD4,CD8,CD2,CD99 and CD5 receptors.

X ray showed a tumour in the right maxillary sinus, morphology of tissue proved inflammation, and no malignant cells were identified, CT scans revealed multiple periaortic and paracaval lymphadenopathy, no imaging signs of lymphoma were found.

The patient was treated with broad spectrum antibiotics and antipyretic agents. On follow up no major improvement of symptoms of generalized arthralgia, bone pain and persistent fever was observed.

Trephine biopsy exposed fibrotic phase of myelofibrosis, with excessive amount of collagen and reticulin fibers, osteosclerosis and dilatation of bone marrow sinusoids with few megakaryocyte aggregates.

Considering the investigation results, short course of chemotherapy with low dose ARA-C and intravenous corticosteroid was initiated. During treatment course the patient developed life threatening circulatory failure and died of disease progression.

Conclusion: PIM poses a significant diagnostic challenge. Unusual presentation of the disease with persistent fever of unknown origin, as well as lack of advanced diagnostics makes it difficult to draw the right diagnostic and treatment decisions in the setting of limited resources.

P-0466 | Significant Improvement of Treatment Outcome Over 2 Decades in Children with Acute Myeloid Leukemia (AML): Experiences in Southwestern Province of Korea

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Background/Objectives: The outcome of children with AML has improved significantly, reaching to 62% of 5-year survival in recent US report. For Korean patients, less than 10% survival was reported before 1990. This retrospective study aimed to witness the epidemiology and therapeutic improvement of outcomes in the Southwestern province of Korea over 2 decades during which the gross domestic product per capita increased 240% to \$27,300.

Design/Methods: This study included 116 children with AML diagnosed from 1996 to 2015. Over the time period the number of children < 19 years old decreased from 1.1 million to 0.7 million. The patients were subdivided into 2 time frames: Earlier cases (1996-2005; n=66) vs. Later cases (2006-2015; n=50). Patients' demographics, evolution of treatment strategies, survival outcomes, and results after hematopoietic stem cell transplantations (HSCTs) were compared between the 2 subgroups.

Results: Annual cases of AML have decreased with contraction of childhood population. AML M3 (n=19) accounted for 16% of cases. Prognostic groups based on cytogenetics were: favorable, 19.0%; intermediate, 69.8%; and adverse, 5.2%, respectively. The Kaplan-Meier (K-M) 5-year estimated overall survival of all cases was 56.0%, while those of earlier cases and later cases were 40.9% and 76.0%, respectively. Sixty-two patients underwent HSCTs. All autotransplants were performed for earlier cases, while more unrelated donor transplants were for later cases. The K-M 5-year survival for transplanted patients were 56.5% (48.6% for earlier cases and 67.7% for later cases). According to stem cell sources, matched sibling donor fared the best outcome of 81.2%, followed by unrelated bone marrow/peripheral blood (73.3%), umbilical cord blood (51.2%), and autologous blood (33.3%).

Conclusion: The outcome of Korean children with AML has improved significantly over 2 decades with better supportive care with economic development, selection of unrelated donors based on DNA typing, and tailored treatment based on prognostic groups.

P-0467 | Successful Management of Breakthrough Disseminated Trichosporon Asahii Infection in a Child with Acute Myeloid Leukaemia (AML)

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Background/Objectives: Life threatening fungal infections is seen during the treatment of AML. The commonly seen fungus are candida, aspergillus and mucor. Trichosporon Asahii is a normal commensal but can cause serious invasive infection in immunocompromised state. It carries high mortality. Here we present a successful management of such infection from a developing country.

Design/Methods: A 14 yrs old girl with AML-M2 type developed prolonged neutropenic sepsis during the induction. She was on Itraconazole prophylaxis. She has had localised staphylococcal cellulitis which resolved with sensitive antibiotics. However she continued to have fever spikes. The repeat blood culture grew trichosporon asahii. The further work up with Computerised Tomography (CT) of chest revealed granulomatous lesions on the right upper lobe of lung, ultrasound abdomen showed multiple micro abscesses in both liver and spleen. The echocardiogram was normal. The central venous access device was removed. Intravenous liposomal amphotericin B was added. Oral voriconazole was added after stopping itraconazole.

Results: Intravenous amphotericin (1.5mg/kg) was given for total 14 days and oral voriconazole continued throughout her treatment. She stopped spiking fever 12 days later. Subsequent blood cultures were negative. Ultrasound abdomen done 6 weeks later showed reduction in number and size of micro abscesses. Chest CT showed resolution of the granulomatous lesions. She has successfully completed the treatment for AML as per AML -15 protocol and as per the schedule. She has not received any colony stimulating factor. She has been on voriconazole through out of her treatment. The literature review showed just 2 reports in children with AML and trichosporon infection, one of which died whilst receiving treatment.

Conclusion: Fungal infections can be fatal. Breakthrough infections on itraconazole or posaconazole prophylaxis need to be acted swiftly adding broad spectrum antifungals. Disseminated trichosporon infection can be successfully treated by adding amphotericin B and voriconazole without compromising AML treatment.

P-0468 | DNMT3A Mutation in Chinese Childhood Acute Myeloid Leukemia

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Background/Objectives: DNMT3A mutation has been found in approximately 20% of adult AML patients and in 0~1.4% childhood AML. The prognosis of adult patients with DNMT3A mutation is worse, however, the prognosis of DNMT3A mutation in childhood AML is still dismal. Here, we tried to determine the incidence and prognostic significance of DNMT3A mutation in Chinese childhood AML.

Design/Methods: We detected the mutation in DNMT3A exon 23 by PCR and direct sequencing in 342 children with AML (range: 0~16 years old, M1:3, M2:142, M3:76, M4:43, M5:33, M6:11, M7:29, unclassified: five patients) from January in 2005 to June in 2013, treated on

BCH-2003AML protocol. Details regarding the clinical characteristics, fusion gene, and other molecular characteristics (*FLT3-ITD*, *NPM1*, *C-KIT* and *WT1*) of the study cohort were analyzed.

Results: DNMT3A mutations were detected in 1.2% (4/342) of patients. Of them with DNMT3A mutated, Pt 1. (M6, M4) harbored a S892S mutation was diagnosed leukemic infiltration of the gastrointestinal tract, and gave up after 38 days; Pt 2. (F/12, M3) harbored a V912A mutation and PML-RARA fusion gene got continuous complete remission for 60 months; Pt 3. (M1, M5) harbored a R885G mutation and two intronic mutations (c.2598-15C>T and c.2739+55A>C) was newly diagnosed myeloid sarcoma and was combined with testicular leukaemia and CNS leukaemia after 2 months. After 10 months, he undertook the BM Transplant but got relapsed in testicular after 39 days and then died after 8 months; Pt 4. (F/2, M3) harbored a Q886R mutation was found to be PML-RARA and FLT3-ITD positive, and dead of retionic acid syndrome after 22 days.

Conclusion: DNMT3A mutation can be found in 1.2% Chinese childhood AML. The mutation positions were different from the hotspots reported in adult AML. We supposed that DNMT3A mutations may have adverse prognostic impact at earlier ages in childhood AML.

P-0469 | Epigenetic Therapy Allows to Improve Survival Children with Acute Myeloid Leukemia

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Background/Objectives: Epigenetic changes play an important role in the development of acute myeloid leukaemia (AML). Valproic acid (VPA), all-trans retinoic acid (ATRA) and Decitabine could inhibits histone deacetylase and activates gene expression in AML.

Design/Methods: Sixteen children with newly-diagnosed AML were included into AML-2012 protocol. The average was 6.6±1.3 years. There were Standard one (6.3%), Intermediate 4 (25.5%), and High risk 11 (68.8%) groups. AML-2012 protocol included one course of the induction chemo for Standard and two for Intermediate and High risk groups. Then the patients got the intensification, consolidation and maintenance therapy. Chemotherapy included high doses of cytarabine and anthracycline antibiotic. We added VPA (25mg/kg), ATRA (45mg/m²) and Decitabine (20mg/m², from 16 to 20 days) to chemo. ATRA was given per os for 14 days each courses of chemo and each month maintenance therapy.

Results: The early response to the Induction therapy was estimated on day 15. The good response had 13 (81.3%), partial response – 1 (6.3%) and non-response 2 (12.5%) patients. After induction chemo with VPA, ATRA and Decitabine complete remission was achieved in 100% patients. Probability of 3-year disease free survival was 76.9±11.7% (median follow up 24.6±2.4 month), for Standard risk group – 100%, Intermediate – 50.0±25.0% and High risk one – 87.5±11.7%. Probability of 3-year overall survival was 88.9±10.5% (median 27.1±2.1 month).

Conclusion: Epigenetic therapy combined with chemo allowed to improve survival of patients with acute myeloid leukaemia.

P-0470 | Hematologic Abnormalities in Down Syndrome: Experience at King Chulalongkorn Memorial Hospital, Bangkok, Thailand

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Background/Objectives: Hematologic abnormalities are common in infants and children with Down syndrome (DS). Transient myeloproliferative disorder (TMD) is found exclusively in DS infants with an incidence of approximately 10%.

Design/Methods: Retrospective study.

Infants and children with DS, who were diagnosed with hematologic abnormalities between June 1997 and October 2015, were investigated.

Results: Twenty-eight patients (17 males and 11 females) were included.

TMD was diagnosed in eleven infants, the median age at diagnosis was 9 days (range, 1 to 30 days). Ten patients had resolved spontaneously without treatment within the four months, and one patient died due to hyperleukocytosis resulting in necrotizing enterocolitis. The 5-year overall survival (OS) was 90.90%.

Acute myeloblastic leukaemia (AML) was diagnosed in fifteen patients; the median age at diagnosis was 18 months (range, 1 to 47 months). Acute megakaryoblastic leukaemia (M7) was identified in ten patients, and acute erythroblastic leukaemia (M6) occurred in three patient. Six patients had a history of myelodysplastic syndrome (MDS). Fourteen patients with AML were treated with protocol for AML with DS which was less intensive chemotherapy consisted of cytarabine (100 mg/m²/d) and 6-thioguanine (100 mg/m²/d). The estimated 5-year event-free survival and OS was 73.33%.

Acute lymphoblastic leukaemia (ALL) was diagnosed in two patients (age 4 and 5 years). They were treated with conventional standard risk ALL protocol. Both of them achieved remission but one patient relapsed and died 30 months after remission. The other patient still survives without disease. There was only one DS patient who was diagnosed with MDS but lost to follow-up after first admission.

Conclusion: The most common hematologic abnormalities in DS is acute leukaemia, mainly AML. Most of MDS cases will progress to acute leukaemia in an average time of 3.4 months. Almost all of TMD cases will regress spontaneously without subsequent developing to acute leukaemia.

P-0471 | Treatment of Acute Myeloid Leukemia in Resource Limited Countries - The Nepal Model

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Background/Objectives: The treatment of children with different types of acute myeloid leukaemia is sophisticated and entails numerous complications and poor outcome with about 40% overall survival with chemotherapy-only protocols without bone marrow transplantation. We describe below the treatment of acute myeloid leukaemia in children other than AML-M3 using four courses of chemotherapy, modified to suit the resource and other constraints of a resource limited country like Nepal.

Design/Methods: Four patients ranging in ages from forty eight months to a hundred and forty four months of age diagnosed as different types of acute myeloid leukaemia, other than ML-M3, based on blood and bone marrow examinations were enrolled on the chemotherapy only (without bone marrow transplantation) protocols of treatment. Diagnostic methods included blood and bone marrow examination, lumbar punctures, routine tests and imaging studies. Bone marrow examination was performed at diagnosis, on day 28 of induction I and induction 2 chemotherapy to assess minimal residual disease morphologically. Four courses of chemotherapy were given. Induction I included Ara-C + Daunomycin + Etoposide on a 10+3+5 day combination. Induction II included Ara-C + Daunomycin + Etoposide on an 8+3+5 combination. Intensification I included high dose Ara-C and Etoposide for 5 days. Intensification II included the Cappizzi II (CLASP) with high dose Ara-C and native Asparaginase.

Results: All the four patients are alive and doing well, one seven years after completion of chemotherapy.

Conclusion: Certain AML patients with non-AML-M3 may be successfully treated with only four courses of chemotherapy without bone marrow transplantation.

P-0472 | Treatment Related Myelodysplastic Syndromes (t-MDS) in Children with Cancer: A Single Center Experience

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Background/Objectives: Treatment related myelodysplastic syndrome (t-MDS) represents a rare complication of cancer therapy in childhood. The major factors related to t-MDS are exposure to alkylating agents and radiotherapy. The incidence of t-MDS varies between 1-6% in different studies. Aim of our study was to estimate the incidence in our centre in the last 15 years.

Design/Methods: We searched databases of the Department of Pediatrics (hematological malignancies, solid tumors) at the AHEPA Hospital for patients registered from 2000 to 2015. For each patient we registered clinical and pathological characteristics (initial diagnosis, age, sex, treatment, latency period, age at the time of diagnosis of the t-MDS).

Results: Overall, 287 patients were recorded in the databases and we identified 3 (1.04%) with t-MDS. The primary cancer diagnoses were Langerhans disease (one patient) and acute lymphoblastic leukaemia (ALL; two patients). Mean age of patients was 12.1 years. Conventional cytogenetic analysis performed on bone marrow aspirates demonstrated pathological findings in 2/3 patients. The first patient developed t-MDS after chemotherapy with antimetabolites and cytarabine due to relapse of the primary disease (Langerhans disease) followed by progression to ALL. The second patient with ALL developed t-MDS during induction treatment with cytarabine and the third patient during consolidation treatment for ALL. Two patients had received systemic antifungal treatment for invasive pulmonary aspergillosis before the presentation of t-MDS. Two patients (66%) remain alive after a median follow up period of 3.5 years.

Conclusion: According to our findings t-MDS represents a rare but serious complication of cancer treatment in children. Our results are in concordance with international data from multicenter studies.

P-0473 | High Mitochondrial Respiratory Chain Complex V is Associated with Inferior Survival in Acute Myeloid Leukemia: A Study of 57 Paediatric Patients

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Background/Objectives: Dysregulation of mitochondrial metabolism and biogenesis have been studied extensively in acute myeloid leukaemia (AML); however, relevance of mitochondrial function on outcomes is unknown. This study was aimed to assess clinical significance of mitochondrial respiratory chain activities in paediatric AML.

Design/Methods: This prospective study included paediatric AML patients enrolled from July 2013-May 2014. Activities of mitochondrial complexes (I-V) were determined in cell lysates of bone marrow (BM) samples by ELISA (Abcam) and normalized to total protein concentration (Bicinchoninic assay). Comparison of complex activities between controls [BM from patients with solid tumors and peripheral blood (PB) from normal subjects] and AML patients was done using Mann-Whitney test. Pearson's chi-test or Fischer's exact test were used for correlation of complex activity with clinical parameters. Overall-Survival (OS) and Event-Free-Survival (EFS) were compared using log-rank test by categorizing complex activities into high or low based on their median value.

Results: Fifty-seven AML patients were enrolled, median age 9 (range: 0.3-18 years). Complex V activity was significantly higher in AML BM lysates than in the BM of subjects with solid tumors (Median 17×10^2 vs 8.3×10^2 nmolesmg⁻¹min⁻¹, $p=0.0273$) and peripheral blood in healthy subjects (Median 17×10^2 vs 5.3×10^2 nmolesmg⁻¹min⁻¹, $p=0.0005$). Mean complex V activity was significantly lower in patients with chloroma (13×10^2 vs 51×10^2 nmolesmg⁻¹min⁻¹, $p=0.05$) and AML-ETO translocation (17×10^2 vs 45×10^2 nmolesmg⁻¹min⁻¹, $p=0.05$). Higher blast percentage in bone marrow (>70%) correlated with higher complex V activity ($p=0.035$).

Patients with high complex V activity had significantly inferior EFS (38.8% vs 61.2%, $p=0.027$) and OS (35.8% vs 64.2%, $p=0.04$).

Conclusion: Lower levels of complex-V activity in paediatric AML are associated with AML-ETO translocation, and high levels of the same significantly predict inferior EFS and OS. Thus, inhibiting the mitochondrial respiratory chain complex activity could be a potential therapeutic target for the treatment of AML.

P-0474 | Childhood Acute Promyelocytic Leukemia (APML): Early Mortality is A Major Hindrance to An Otherwise Excellent Survival: A 12-Years' Study

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Background/Objectives: APML is considered to have a favorable outcome. Early mortality is however a concern and is often not highlighted.

Design/Methods: A retrospective study of children (<13 years) with APML treated over a 12 years' period (2004-2015) at a single center is presented. Chemotherapy was ATRA/anthracycline/cytarabine based (Modified PETHEMA). Induction was followed by 3-courses of consolidation and maintenance for 2-years. Patients were classified based on WBC count as standard (<10x10⁹/L) or high-risk ($\geq 10 \times 10^9$ /L).

Results: The cohort included 41 patients. The median age was 8 years (range: 1-13). Four patients did not opt for treatment. Cytogenetic or molecular confirmation was available in 20 (49%). In the remaining, diagnosis was based on morphology/cyto-chemistry. Nineteen (46.3%) patients were high-risk. The mean dose of ATRA was 26.4 ± 2.7 mg/m²/day. ATRA syndrome was observed in 10/34 (29.4%) and was non-fatal. Coagulopathy (PTI<75%) and severe thrombocytopenia (<20x10⁹/L) was observed in 67% and 54%, respectively. Sixteen (39%) patients died; the majority - 15 (94%) died within 15 days of diagnosis. The cause of death included, intracranial bleed (82%) and septicemia (18%). There was merely one mortality beyond induction from febrile neutropenia following the first cycle of consolidation. The risk category did not predict mortality ($p=0.52$). There was no correlation of <15 day mortality with platelet count ($p=0.61$) or coagulopathy ($p=0.12$). No patient died or abandoned treatment following 2 months of treatment. The median follow-up of patients who continued treatment beyond 2 months was 22 months (range: 1.5-141). No patient relapsed. The 10 year OS/EFS of the cohort (n=41), and of patients who survived ≥ 15 days from diagnosis (n=26) was $58.4 \pm 8\%$ and $95.2 \pm 4.6\%$, respectively ($p=0.01$).

Conclusion: The EFS of all children with APML, and of those who survived ≥ 15 days from diagnosis was $58.4 \pm 8\%$ and $95.2 \pm 4.6\%$, respectively. Early (<15 days from diagnosis) mortality is a major impediment to survival in children with APML.

P-0475 | Prophylactic Antimicrobials, Survival and Toxicity in Patients with Acute Myeloid Leukemia. 12 years Experience in SOLCA, Quito

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Background/Objectives: We analyzed survival and toxicity during a period of 12 years and the effects of implementing prophylactic antimicrobials.

Design/Methods: We reviewed the medical records and POND online database, from January 2003 to December 2014.

Results: 54 patients were diagnosed. Thirty were males. We include 8 patients (15.3%) with secondary AML previously exposed to etoposide. AML-M2 was the predominant subtype (21), followed by M1 (18), M4 (10), M5 (3), M0 (1) and M6 (1). The average age was 9.5 years at diagnosis. Seven patients (13.7%) had hyperleukocytosis. Nine had CNS involvement (17.3%) and 8 (15.3%) had chloromas. We identified translocations in 19 patients: 10 with t(8;21), 2 inv 16, 2 t(9;11), 2 11q2,3, and 3 other cytogenetic features.

Fourty-two patients (77.8%) were treated with the BFM 87/93 protocol, 5 (9.3%) received AHOPCA LMA 2007 Protocol, 4 (7.4%) other protocols and 3 did not get any therapy due to poor condition and died. Twenty-two patients relapsed (43%).

Including patients with secondary AML, overall survival was 27% (35% if we exclude abandonment). There were 33 deaths (61.1%), 5 during induction. Fifteen with refractory disease, 14 with sepsis, 2 with hemorrhage, 1 cardiogenic shock and 1 post-BMO transplant.

There were 267 episodes of toxicity. All patients received trimetoprim sulfamethoxazol three times a week. Comparing 36 patients (66.7%) who did not receive additional prophylaxis (Group 1) versus 18 (33.3%) with prophylactic voriconazole and ciprofloxacin (Group 2), we observed Grade I toxicities in 5 vs. 2, Grade II 13 vs. 4, Grade III 79 vs. 35, Grade IV 77 vs. 38 and Grade V 11 vs. 3. The overall survival was 27% for group 1 and 42% for group 2.

Conclusion: AML remains an important cause of death among paediatric cancer patients. With antimicrobial prophylaxis we evidenced less toxicity and better outcome.

P-0476 | Clinical Study of Children with Acute Promyelocytic Leukemia Treated with Arsenic Trioxide: A Multicenter Study

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Background/Objectives: To evaluate the efficacy of Children with acute promyelocytic leukaemia (APL) treated with arsenic trioxide (ATO) in multicenter.

Design/Methods: From Jan. 2004 to Jun. 2014, 25 newly diagnosed APL patients were included in this study with 16 male and 9 female, while 20 from Shanghai Children's Hospital

and 5 from Children's Hospital of Fudan University. The regime of 25 patients included induction treatment, consolidation chemotherapy and maintenance therapy. The induction treatment regime was ATO combined with all-trans retinoic acid (ATRA). 1 or 2 courses of consolidation chemotherapy were given including daunorubicin, idarubicin and Ara-C. The maintenance therapy consisted ATRA followed by ATO. 25 patients were also separated into low risk group, intermediate risk group and high risk group according to different risk level, retrospectively. All statistical analyses were carried out using SPSS software version 19.0.

Results: 24 of 25 patients achieved HCR for APL with a median time of 34 days (range, 26-63 days). 1 patient failed to achieve HCR because of early death. The median date to achieve molecular complete remission was 56 days (range, 30-207 days). The 5-year event-free survival (EFS) was (85.3±8.0%). The 5-year overall survival (OS) was (96.0±3.9%). 2 patients were divided into low risk group, 13 into intermediate risk group and 10 into high risk group. The 5-year EFS of low plus intermediate group and high risk group patients were (93.3±6.4)% and (72.9±16.5)% (P=0.34). ATO related side effects were mild, including abnormal liver tests and electrocardiogram, but were invertible after supportive therapy. No chronic arsenic toxicity or second malignancies were found during the follow-up period.

Conclusion: The regime mainly included ATO was a promising and better treatment for childhood APL. No ATO related chronic arsenic toxicity or second malignancies were found during the long period. It was necessary to make risk stratification in APL patients.

P-0477 | Study of Clinical Outcome and Prognosis Related Factor in Children with Acute Myeloid Leukemia

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Background/Objectives: To analyse the clinical outcome and the prognostic factor of children with acute myeloid leukaemia (AML).

Design/Methods: 61 newly diagnosed AML patients diagnosed from 2000 to 2013 were included in this study. The clinical characteristics, the event-free survival (EFS), the overall survival (OS) and the prognostic analysis were evaluated.

Results: 61 AML patients with 38 boys and 23 girls were involved in the study. They had a median follow-up duration of 36 months (range, 1.1-182.2 months) and Kaplan-Meier estimates of 5-year event-free survival (EFS) and overall survival (OS) were 56.5%±7.1% and 69.6%±6.4%. According to single factor analysis, patients with extramedullary infiltration and CD56+ antigen expression when diagnosed earned worse outcome (P=0.03, 0.04). 46 of 61 AML patients achieved complete remission (CR) under 1 course with a 66.1%±8.0% 5-year EFS, while 10 of 61 AML patients achieved CR at least 2 courses with a 30.6%±11.2% 5-year EFS (P=0.03). Multivariate analysis demonstrated a significant favorable relationship among extramedullary infiltration, CD56+ antigen expression, recurrence in one year, failure to achieve CR under 1 course and 5-year EFS. The extramedullary infiltration and failure to achieve CR under 1 course were the main risk factors to recurrence.

Conclusion: AML patients with extramedullary infiltration and CD56+ antigen expression when diagnosed earned worse outcome. The number of courses to achieve CR was the risk factor of prognosis and relapse. To decrease relapse rate was one of the crucial procedure to improve prognosis.

NEUROBLASTOMA

P-0478 | Prevalence and Clinical Correlations of Somatostatin Receptor-2 (SSTR2) Expression in High-Risk Neuroblastoma

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Background/Objectives: As only a third of children with relapsed neuroblastoma respond to ¹³¹I-Metaiodobenzylguanidine (MIBG) therapy, other radiolabelled targeted agents e.g. ¹⁷⁷Lu-DOTATATE are being investigated. DOTA-TATE targets somatostatin receptors (SSTRs) in particular SSTR2, which is expressed on neuroblastoma cells. This study aimed to describe the prevalence of SSTR2 expression in High risk (HR) neuroblastoma tumors and correlate SSTR2 expression with clinical features, Norepinephrine Transporter (NET) expression and MIBG avidity.

Design/Methods: 54 neuroblastoma patients diagnosed and treated at a single institution 1999-2015 were included. SSTR2 and NET immunohistochemistry scores were calculated using digital image analysis on slides from tumour biopsy samples. The score (0-300) was established as a function of staining intensity and distribution. Clinical data was retrospectively reviewed from patient charts. Wilcoxon rank-sum tests were performed to assess correlation of SSTR2 expression with clinical and biological features.

Results: Of our 54 patients, 22 had HR neuroblastoma (MYCN-amplified n=5) and 32 non-high risk (NHR). 11 patients had MIBG non-avid disease. Median SSTR2 score was 138 [1-255] for the entire group (39% had score ≥ 200) and NET score was 134 [15-252].

19/54 patients (12 HR, 7 NHR) had relapse, progressive or refractory disease. 8/19 (5 HR, 3 NHR) had SSTR2 score ≥ 200; all were MIBG avid, none were MYCN amplified, and none had NET score above 200 (median 121 (62-169)).

SSTR2 expression was positively correlated with MIBG avidity (median 147 vs 93) (p=0.016). There was no significant correlation between SSTR2 and other clinical features, or NET scores.

Conclusion: This study found that SSTR2 expression is statistically significantly associated with MIBG avidity and is not significantly correlated with NET expression. Patients with high SSTR2 scores included HR and relapsed patients. A larger study could confirm if a select neuroblastoma patient population with high SSTR2 scores who failed MIBG therapy could benefit from ¹⁷⁷Lu-DOTATATE targeted radiolabelled therapy.

P-0479 | The Role of MXI1 in Neuroblastoma Pathogenesis and Chemoresitivity

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Background/Objectives: Neuroblastoma is the most common extracranial malignancy of childhood. The Myc family regulates cell growth and is implicated in the etiology of many cancers. MYCN amplified neuroblastoma is associated with a poor prognosis. Mxi1, a member of the MAD family, inhibits N-Myc activity. In neuroblastoma, N-Myc overcomes the inhibitory effects of Mxi1, leading to uncontrolled proliferation. Understanding the role of Mxi1 in neuroblastoma will lend insight into its function. The objective of this project is to test the impact of Mxi1 on modulating N-Myc effects on neuroblastoma cell proliferation and chemoresistance.

Design/Methods: We utilized neuroblastoma cell lines with inducible expression of Mxi1. Cell proliferation and survival were quantified using BrdU and MTT assays, respectively. Apoptosis was measured by propidium iodide staining. *mxi1*-specific knockout mice were created by inserting LoxP sites in exon 1 and crossing with Cre-expressing mice to knockout Mxi1 (but not Mxi0).

Results: Overexpression of Mxi1 inhibits neuroblastoma cell viability. Further analysis reveals that this effect is due to a decrease in cell proliferation as well as an increase in apoptosis. Compared with uninduced control cells, Mxi1 expression results in less chemoresistance to doxorubicin and etoposide. To investigate its importance *in vivo*, we created *mxi1*-specific knockout mice. These mice display poor growth and exhibit excessive vessel wall growth and abnormal lymphoproliferation.

Conclusion: Mxi1 expression in neuroblastoma cells leads to inhibition of N-Myc-mediated cell proliferation and an increase in apoptosis. Mxi1 expression also enhances chemoresistance. *In vivo*, *mxi1* knockout leads to abnormal vascular growth and lymphoproliferation. A better understanding of the interactions between Mxi1 and N-Myc and their impact on neuroblastoma physiology may aid in developing more effective targeted therapies to improve outcomes in neuroblastoma. Furthermore, our *in vivo* *mxi1* knockout model will prove useful in understanding the role of Mxi1 in neuroblastoma tumors.

P-0480 | Activation of the P53 Pathway by MDM2 Inhibition using the Small Molecule DS3032b as a Therapeutic Option for Neuroblastoma

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Background/Objectives: Neuroblastoma is the most common extracranial childhood tumour and represents a clinical challenge in paediatric oncology, since survival of patients with high-risk neuroblastoma, which represent the majority of patients, is less than 50%. Inactivating mutations in the *TP53* tumour suppressor gene are rare, but overexpression of its major negative regulator MDM2 resulting in functional p53 inactivation is commonly detected in neuroblastoma. Pharmacological inhibition of MDM2 may therefore have relevant clinical impact.

Design/Methods: Neuroblastoma cell lines with different *TP53* genetic background were employed to determine the response on viability, proliferation, senescence, migration, cell cycle arrest and apoptosis to the small molecule DS3032b. A murine subcutaneous neuroblastoma xenograft model was used to assess the effect of DS3032b on tumour growth.

Results: Here, we show that targeted inhibition of MDM2 using DS3032b leads to a selective activation of the p53 pathway in neuroblastoma cells with wild-type *TP53*. DS3032b showed antiproliferative and cytotoxic activity by inducing G1 cell cycle arrest and apoptosis independent of *MYCN* amplification status. In contrast, no effect of DS3032b was detected in neuroblastoma cells harboring *TP53* mutations or expressing dominant negative p53. Oral treatment with DS3032b resulted in tumour growth inhibition and prolonged survival in a murine subcutaneous neuroblastoma xenograft model.

Conclusion: The observed effects *in vitro* and *in vivo* suggest that inhibition of the MDM2-p53 interaction by DS3032b is a promising therapeutic option for patients with neuroblastoma independent of *MYCN* amplification status.

P-0481 | Induction of a Metabolic Switch in Neuroblastoma and Medulloblastoma Cells Upon Targeting MYC

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Background/Objectives: Neuroblastoma is one of the most aggressive solid tumors of early childhood. Amplification of the *MYCN* oncogene has been found in 30% of neuroblastoma patients and is associated with rapid tumour progression and poor prognosis. As metabolic adaptations are crucial for cancer cell survival, identifying metabolic discrepancies of aggressive tumors may be central in order to develop new treatment strategies. We have demonstrated that a small chemical molecule, 10058-F4, previously identified as a c-MYC inhibitor also targets the MYCN/MAX complex resulting in apoptosis and neuronal differentiation in *MYCN*-amplified neuroblastoma cells. Importantly, we found that inhibition of MYCN results in changes in neuroblastoma cell metabolism including mitochondrial dysfunction leading to accumulation of intracellular lipid droplets (Zirath 2013; Muller 2014).

Design/Methods: Analysis of lipid droplet formation, differentiation markers and metabolic flux measurements using Seahorse analyzer in medulloblastoma and neuroblastoma cells following treatment with compounds targeting MYC.

Results: We have analyzed the effects of several different MYC inhibitors including 10074-G5 and the BET-domain inhibitor JQ1 on neuroblastoma cells. Our data show that treatment with both compounds resulted in lipid droplet accumulation. Next we extended our study to a panel cancer cell lines derived from different tumour types, including medulloblastoma, glioblastoma, melanoma, hepatocarcinoma, cervical and prostate cancer to analyze how general this phenotype is. We found a cell type-dependent response, some cells showing accumulation of neutral lipids while others not. Importantly, some of the treatments gave rise to morphological changes resembling cellular differentiation into neural or glial lineages. We are now

performing functional assays using Seahorse Flux Analyzer to study the metabolic changes as well as analyzing expression of neural and glial differentiation markers in response to treatment in neuroblastoma and medulloblastoma cells.

Conclusion: Targeting of MYC may be an attractive approach for development of future tailored therapies for medulloblastoma and neuroblastoma.

P-0482 | Metronomic Chemotherapy with Vinblastine, Cyclophosphamide, Methotrexate and Celecoxib in Progressive or Relapsed Childhood Cancers

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Background/Objectives: Metronomic chemotherapy (MC) presents the opportunity of reducing side effects of chemotherapy in heavily pre-treated patients, prolonging survival with acceptable tumour control and improving the quality of life. A regimen with vinblastine, cyclophosphamide, methotrexate and celecoxib was reported with objective responses by Andre et al. This study was planned to assess the outcome in children with relapsed/refractory tumors with same regimen.

Design/Methods: 10 children whom have no other chemotherapy option due to cumulative drug doses were given the MC regimen of weekly vinblastine 3 mg/m², daily oral cyclophosphamide 30 mg/m² in first three weeks, methotrexate 10 mg/m² twice weekly next three weeks, and celecoxib 100 mg to 400 mg twice daily for 7 weeks. The outcome was evaluated retrospectively.

Results: The median age was 8.5 years (3.3-18y). Tumors were neuroblastoma in four and osteosarcoma, Ewing sarcoma, PNET, inflammatory myofibroblastic tumour, retinoblastoma and yolk sac tumour each in one patient. Patients received MC until disease progression for median 3months (1-12 months). One patient had complete response and 4 more patients had stable diseases at median 2.2 months and still on MC. Five patients had progressive disease at median 3.8 months. At last follow-up, 5 patients (50%) are alive. No severe toxicity was observed.

Conclusion: The low-dose and continuous chemotherapy of MC strategy shows encouraging results with increased compliance, less side effects, prolonged survival and improved quality of life. The 4-drug metronomic regimen with vinblastine, cyclophosphamide, methotrexate and celecoxib is a well-tolerated schema. With the objective responses and one complete response, this regimen presents a reliable treatment option for patients who have limited treatment choice. Clinical trials with larger groups will help understanding the antitumor effect and impact on outcome or quality of life of MC in patients.

P-0483 | Dicentric Chromosome (DC) Assay as a Biodosimetry Complementary Tool for Individualized Physical Dosimetry Assessment in Sequential Therapeutic mIBG for High Risk Neuroblastoma. A Feasibility Study

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Background/Objectives: ¹³¹I-metaiodobenzylguanidine (¹³¹I-mIBG) is an emerging targeted radiopharmaceutical for patients with refractory or relapsed neuroblastoma. Recent studies indicate better response if a target dose of 4 Gy is achieved, so sequential infusions are performed in order to reach that dose. Our aim was to use the DC assay as a biodosimetry complementary tool for Whole-Body-dose (WBD) assessment to better calculate the second dose of mIBG necessary to reach 4 Gy in a personalized approach.

Design/Methods: Cytogenetic procedures were performed to carry out the DC-assay, chromosomal aberrations considered were dicentric chromosomes. Blood samples from patients were obtained before (d0) and 7 days after ¹³¹I-mIBG administration (d7), were in vitro irradiated to set-up a dose-effect curve (cultured 48 hours, fixed, stained with Fluorescence Plus Giemsa). Frequency of dicentrics was obtained from 100 first-division metaphases analysis. WBD estimation was carried out taking into account the frequency of dicentric and the Chromosomal Aberration Calculation Software (Deperas 2007) using the dose-effect calibration curve from Montoro 2005. Standard WBD was performed based on external measurements of dose rate, according to the standard MIRD schema.

Results: The frequency of dicentrics for d0 and d7 were 0.03±0.017 and 0.44±0.066, respectively. So, WBD were 0.47 (0.12-1.01) for d0 and 2.71 (2.25-3.21) Gy for d7.

Standard WBD after fitting the dose rate measurements to an exponential of three phases was 1.44±0.15 Gy for d7.

Conclusion: WBD estimations from *in vitro* irradiations is useful for getting an individualized dose-effect curve from which standard WBD of the patient can be adjusted.

We do not expect the same value obtained from both methods, because biodosimetry is studied in blood, but there is a good concordance.

Further studies with larger populations should be performed to evaluate the correlation between both methods and to elucidate whether biodosimetry can be considered a complementary tool for WBD assessment.

P-0484 | Polymorphism in MTHFR 677 C>T and 1298 A>C is Associated with Increased Risk of Retinoblastoma in Indian Children

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Background/Objectives: Retinoblastoma (RB) is the most common primary intraocular malignancy in children. The incidence of RB in Indian children is 1 in every 20,000 live births but its exact causative factors are not known. Methylentetrahydrofolate reductase (MTHFR) is a key regulatory enzyme in folate and homocysteine metabolism. Polymorphisms in the gene encoding MTHFR have been found to be associated with some forms of cancers by affecting DNA synthesis, repair and methylation. The present study was planned with an aim to analyse polymorphism in two essential MTHFR SNPs 677 C>T and 1298 A>C in Indian children affected with RB.

Design/Methods: 65 RB cases (36.9±19.3 months) and 65 controls (38.6±17.3 months) were enrolled after obtaining ethical clearance and informed consent. Two essential SNPs of MTHFR gene i.e., 677 C>T and 1298 A>C were studied by PCR-Restriction Fragment Length Polymorphism (RFLP) technique using site specific restriction enzyme HinfI and MboII for MTHFR SNPs 677 C>T and 1298 A>C respectively.

Results: T allele frequency distribution for the MTHFR SNP C677T was seen to be 0.38% in cases and 0.04% in controls (p<0.05), while MTHFR SNP A1298C, C allele frequency in cases was 0.34% and 0.05% in controls (p<0.05). None of the cases showed the mutant genotype TT and CC in SNP 677 and 1298 respectively.

Conclusion: The present results showed a significant association between MTHFR C677T and A1298C polymorphism and an increased risk of RB in Indian children. Therefore, inadequate nutrient intake including folic acid deficiency during childhood may affect epigenetic regulation involving methylation via MTHFR gene which may have adverse clinical outcomes and increases risk for genetic diseases including childhood cancer RB. The present study can be further confirmed by increasing the sample size.

P-0485 | Heterogeneity of Neuroblastomas: Consequences Towards Clinical and Biological Diagnosis and Therapeutics in Vietnam

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Background/Objectives: Neuroblastoma (NB) is a solid tumour representing one of the most prevalent cancer diagnosed each year in Vietnamese patients. NB comprises a diverse spectrum of phenotypes based on clinical and biological features. The consequence of cancer heterogeneity affects the clinical outcomes ranging from -low, -intermediate and -high risk. Current treatment had not yet been effective due to the lack of sufficient biomedicine diagnosis and clinical cares. Therefore, the overall survival and response to therapy are poor.

Design/Methods: Using laser microdissection, PCR-based, whole-exome sequencing, SNP arrays and cell culture analysis we aim at addressing some of those needs. A total of 102 NB patients in Children Hospital II were enrolled in this study. Clinical imaging and histology were assessed by specific clinicians. The MYCN status, loss of 1p36, 11q or gain of 17q were measured using PCR-based. Whole-exome sequencing was used to decipher variants in 39 high-risk NB and compare the these variants with Sanger sequencing of HapMap individuals and with SNP arrays. The bioinformatics were performed using the in-house pipelines of Galaxy and GenABEL library in R.

Results: The landscape of the somatic mutations in the NB cancer genome was documented the appearance of mutations that relatively low frequency (12 to 1.3%) in ALK, ATRX, ARID1A/1B as reported previously. The significant mutations of ALK and ATRX correlated with low survival and recurrence of NB. 145 SNPs in the LIN28B gene and 43 SNPs in the NEFL gene were high-risk NB association. Among these markers, seven are located upstream of the gene close to promoters associated sequence.

Conclusion: Overall, this is the first study established the high-throughput sequencing and gene-based research in Vietnam. This study has validated a role of translational biomedicine coupled with clinical representations towards a better precised treatment of NB.

P-0486 | Haematopoietic Progenitor Cell Collections using the Spectra Optia® MNC Protocol (V.11) on Patients < 12.5kgs

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Background/Objectives: Challenges of apheresis in small children (<12.5 kg) include small total blood volume (TBV), access issues, tolerable anticoagulant doses, and safe collection volume limits.

Limitations include:

1. Total Blood Volume
2. Inlet Flow Rate/ AC: Inlet:AC ratio was increased above the 15:1 maximum recommendation to facilitate a minimum IFR of 10ml/min and the risk of clotting in the circuit compensated by the addition of Heparin (10iu/ml) to the AC.
3. Collection parameters: Processing of 2 TBVs with collection of product volume not exceeding 13% of TBV was achieved by using the collection phase control on the advance control options, selecting inlet volume as a trigger for collection. On 4 collections, Optia defaulted to collect 0 chambers when patient data was inputted.

Design/Methods: Procedural data was collected from the Optia Apheresis reporting system for 11 collections from patients <12.5Kg. Laboratory analyses of pre-apheresis peripheral blood and harvested apheresis products were also examined. Spectra Optia® MNC performance was measured by CD34+ collection efficiency, expressing the total number of CD34+ cells collected as a proportion of the total number of CD34+ processed during apheresis.

Results:

Patient	Day	Wgt	Diagnosis	Results			
				Pre CD34 10 ⁶ L	CD34Yield10 ⁶ kg	Target CD34 dose 10 ⁶ kg	No TBV processed
1	D1	6.9	Neuroblastoma	200	9.1	3	2
2	D1	10.7	Neuroblastoma	83	6.2	6	2
3	D1	11	Atypical Teratoid Rhabdoid Tumour	330	18.9	3	2
4	D1	11.5	Medullo-blastoma	41	1.8	9	2
	D2			51	3.1		
	D3			87	4.1		
5	D1	10.6	Atypical Teratoid Rhabdoid Tumour	27	1.7	3	2
	D2			24	1.4		
6	D1	10.6	Neuroblastoma	43	2.1	3	2
	D2			81	3.4		
7	D1	10	Neuroblastoma	8	0.54	3	2

Conclusion: Eleven collections were completed during the period examined. 7/11 products collected have been successfully infused with engraftment times within target ranges in all cases.

From these data we conclude that with manipulation and operator intervention, Spectra Optia can be used effectively for HPC collection in this patient cohort.

P-0488 | MEG3, HCN3 and LINC01105 Influence Proliferation and Apoptosis of Neuroblastoma Cells Via HIF-1 alpha and P53 Pathway

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Background/Objectives: The purpose of our study is to investigate the differentially expressed lncRNAs in neuroblastoma, and to further study the role of lncRNAs in neuroblastoma.

Design/Methods: The tumour tissues and para-tumour tissues were collected and stored in the past two years (2011.12-2013.12). In this study, lncRNA microarray (Human LncRNA Microarray V3.0) was used to investigate the differentially expressed lncRNAs in 12 samples (6 tumour tissues, 6 para-tumour tissues) Some differentially expressed lncRNAs were chosen as target genes for next research.

Results: There were 4802 lncRNAs and 5130 mRNAs differentially expressed between the tumour tissues and para-tumour tissues (tumour VS para-tumour, 3098 lncRNAs and 2526 mRNAs up-regulated, while 1704 lncRNAs and 2604 mRNAs down-regulated). The expression levels of *HCN3* and *linc01105* were higher ($P < 0.05$ and $P < 0.01$, respectively), whereas that of *MEG3* was lower ($P < 0.01$) in neuroblastoma than in para-tumour tissue. There were negative correlation between the expression of HIF-1 α protein and cell proliferation, while positive correlation between expression of Noxa/ Bid and cell apoptosis. The proliferation of BE(2)C of linc01105 KD was promoted, but that of MEG3 OE group was inhibited and that of HCN3 KD had no change. The cell apoptosis in three intervention groups were all promoted. The Pearson correlation coefficient were -0.48, -0.58 and -0.55, respectively.

Conclusion: Our experiments provide a list of differentially expressed lncRNAs and mRNAs in neuroblastoma that could be useful for further study. The lncRNAs HCN3, linc01105, and MEG3 are likely important in the pathogenesis of neuroblastoma and act via a mechanism involving HIF-1 alpha, Noxa and Bid associated with p53 pathway. The expression of MEG3, HCN3 and linc01105 all had medium negative correlation with INSS stage of neuroblastoma.

P-0489 | Initial Bone Marrow Involvement Diagnostics in Neuroblastoma Patients. Comparison of Flow Cytometry and RQ-PCR Prognostic Impact

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Background/Objectives: Bone marrow (BM) is frequent metastatic harbor in neuroblastoma patients. Precise detection of BM involvement is crucial for correct staging and prognosis definition.

Aim is the comparison of BM disease detection results obtained by parallel application of flow cytometry (FC) and RQ-PCR, furthermore investigation of correspondent prognostic impact.

Design/Methods: Initial BM involvement detection in 42 neuroblastoma patients was performed in parallel analysis of 108 BM samples by FC and RQ-PCR. Presence of BM lesion by FC was stated if cells with tumour-associated immunophenotype (CD81+CD56+CD9+GD2+CD45-) were detected. Positivity by RQ-PCR was defined as detectable expression of *PHOX2B* or *TH* genes. Event-free survival (EFS) rates were calculated with median of follow up time 4.1 years.

Results: Analytical sensitivity of RQ-PCR achieved 1E-6, while for FC ranged from 1E-3 to 1E-5. 18 BM samples were positive and 63 were negative by both techniques. 17 samples were positive by FC and negative for RQ-PCR and 10 – vice versa. Thus, qualitative concordance of two methods achieved 75.0%.

Among 42 patients enrolled in the study 31(73.8%) had BM disease detected by both FC and RQ-PCR at least in one sample. 8 patients (19.1%) were positive by FC only, 3(7.1%) – only by RQ-PCR. Positivity of BM by FC led to dramatic decreasing of EFS: 0.30(0.10) vs. 0.84(0.09), $p < 0.001$, while deterioration of EFS in *PHOX2B/TH* expression was not significant: 0.40(0.13) vs. 0.69(0.09), $p = 0.061$. Within groups of patients divided by RQ-PCR positivity, presence of BM disease by FC retained prognostic significance ($p = 0.027$ in RQ-PCR-positive and $p = 0.022$ in RQ-PCR-negative cases).

Conclusion: BM infiltration by neuroblastoma cells detected by FC demonstrated powerful adverse prognostic impact. Positivity of BM for *PHOX2B/TH* expression was less significant. Nevertheless, due to high reproducibility and standardization of RQ-PCR and possible analytical complexity of FC parallel application of both techniques can be indicated.

P-0490 | Outcome of Patients with High-Risk Neuroblastoma and Positive MIBG-Scintigraphy at the End of the Treatment

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Background/Objectives: Neuroblastoma (NB), developed from sympathetic nervous system, is one of the more frequent cancers in childhood. Scintigraphy MIBG is very sensible and specific for its detection. In High Risk Neuroblastoma (HR-NB), metastatic tumour of patients older than 12 months or patients with amplification of N-Myc oncogene in the tumour, 2-year survival prognosis has recently increased around 60% with addition of immunotherapy in their treatment since 2000's. Before immunotherapy, positivity of MIBG scintigraphy at the end of the treatment was associated with refractory or relapsed tumors and really poor prognosis. Surprisingly, some HR-NB patients with positive MIBG at the end of the treatment are still alive with a relatively long follow-up in our cohort of patients in CHU Ste-Justine. The aim of this study is to describe these patients with long survival without relapse and to compare them with other HR-NB patients who relapsed when MIBG was positive at the end of the treatment.

Design/Methods: From 2000 to 2012, 54 HR-NB patients have been treated in CHU Ste Justine with a median age at diagnosis of 3.1 years (0.6-19.8 years).

Results: Among HR-NB patients, 5 of 12 patients (42%), who had positive MIBG scintigraphy at the end of the treatment, hadn't relapsed with a 2-years minimal follow-up. Majority of these patients (4/5) had still positive MIBG at the last MIBG scintigraphy. Age at diagnosis seems to be significantly younger in our non-relapsed group of patients (1.8 years vs 2.9 years). Other characteristics between groups are not statistically significant.

Conclusion: This study is the first one which demonstrates that MIBG positive scintigraphy is not always associated with relapse for these HR-NB patients, and not always exposes them to second line treatments, because of spontaneous remission with time.

P-0491 | Osteosarcoma Metastatic at Diagnosis with Age of Presentation out of the Ordinary Treated with Mifamurtide. A Case Report from Mexico

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Background/Objectives: Osteosarcoma is a malignant bone tumour. The age of presentation ranges is 10 to 22 years. With an average of 11.4 years and the average time from onset of symptoms is 12.8 weeks.

The current treatment for osteosarcoma achieves 60-70% of disease-free survival for patients without metastases and 20% in metastatic patients.

25% have metastases at diagnosis : 20% lung, 5% to other bones.

Objective: Clinical Case metastatic osteosarcoma at diagnosis with Presentation age out of the ordinary with proper response to surgical treatment and Chemotherapy and use of mifamurtide.

Design/Methods: We report the case of 5 years old male, with femur bone tumour and chest CT scan: identified 5 right pulmonary nodules, and 7 left nodules metastases so initiating treatment with chemotherapy with Doxorubicin, Cisplatin, Supracondylar amputation is performed. Histopathological report was osteoblastic osteosarcoma with 30% necrosis, and we continue with chemotherapy ifosfamide, Metothrexate HD, extension studies chest CT scan performed with only one metastatic lesion, which starts with handling with mifamurtide, treatment scheme ends. Pet-CT was reported without tumoral activity.

Results: Currently patient surveillance since January 2015 without tumoral activity.

The use of mifamurtide in this case was metastatic and we see that we can use this drug for metastatic patients, but even more studies are required.

Conclusion: Even though it is only used in osteosarcoma no metastatic, it can also be used in metastatic solid tumors. We present the case of a child with osteosarcoma and pulmonar metastasis that was treated with multiagent chemotherapy and mifamurtide, with a good response. Mifamurtide had a manageable safety profile. So we consider that this drug can be used in other solid tumors with pulmonary metastatic disease. More experience is needed.

P-0492 | Minimally Invasive Surgery in Children with Thoracoabdominal Neuroblastoma

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Background/Objectives: Improvement of surgical treatment of children with neuroblastoma thoracoabdominal localization.

Design/Methods: Radical surgery treatment was performed in 198 patients (01.2012 - 01.2016). MIS was performed in 54(27.3%). Patients were treated according to NB2004 protocol. Image-defined risk factors (IDRF) and size of the tumour were used to select patients for MIS. After initial work-up patients without IDRF and with a tumour less than 8 cm in the largest dimension were considered as eligible for MIS.

Results: Median age was 20 months (range 1-96). There were 26 patients younger 1 year old(48%). M:F ratio was 1:1.16. Distribution of stages according to INSS was as follows: stage 1 - 29(54%) patients, stage 2 - 11(20%), stage 3 - 0, stage 4 - 10(18.5%), stage 4S - 4(7.5%).Laparoscopic tumorectomy was performed in 40 (74%) patients, thoracoscopic resection - in 14(26%).The size of the tumour ranged from 1 to 7 cm. The mean duration of surgery was 119 minutes. Intraoperative complications: 2(3.7%) injury of major vessels required conversion to laparotomy, 1(1.8%) trauma of duodenum.We have met with technical difficulties during 2 operations (3.7%) which required conversion to laparotomy. Postoperative complications: 4(7.4%) injury of sympathetic ganglia after thoracoscopy complicated by Horner syndrome, 1(1.8%) sepsis, 1(1.8%) intestinal obstruction required open re-surgery. Early postoperative period in all patients after endosurgical operations was much faster and easier than in patients after open surgery: early shut-down of mechanical ventilation, less pain syndrome, early activation and better cosmetic effect. We have observed 1(1.8%) local relapse which required open re-surgery. Median follow-up time was 16 months.

Conclusion: MIS in children with thoracoabdominal neuroblastoma is an effective technique which enables to carry out radical surgery in the absence of contraindications and IDRF and provides minimally invasiveness and good cosmetic effect without worsening oncological prognosis.

P-0493 | Long-Term Follow-Up among Survivors of Neuroblastoma with Opsoclonus-Myoclonus Syndrome: A Report from the Instituto Nacional De Pediatría, Mexico City, Mexico

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Background/Objectives: Approximately 50% of patients with opsoclonus-myoclonus syndrome (OMS) have a hidden-neuroblastoma, where this paraneoplastic syndrome occurs in 2-3%. These patients often have neuroblastomas with favorable biological features and better clinical outcome. OMS is a chronic neurological condition and is associated with significant long-term neurological morbidity secondary to substantial consequences on the neurological development and behavior, cognitive deficits, motor deficits and language disorders.

Design/Methods: Retrospective, clinical and descriptive study, made from January 1990 to December 2012, in children younger 18 years old diagnosed with neuroblastoma.

Results: Six (3 girls and 3 boys) of 48 patients with neuroblastoma had OMS, with a median age at diagnosis of 23.1 months (11-47 months). Median time of onset of symptoms was 4.3 months (1-8 months). Location of the primary tumour was adrenal gland in 5 patients and one in the chest. Five of the 6 patients had positive metaiodobenzylguanidine. There were 4 patients with INSS-1 and 2 stages (low-risk) and 2 patients with INSS-3 stage (one intermediate and one high-risk respectively). Five patients had surgery of the primary tumour at diagnosis (4 were complete resection and one partial resection). Low-risk patients were treated with surgery alone. Patients at intermediate and high-risk were treated according to international protocols.

There were no relapses or progression of the disease. The OMS was treated with gamma globulin, prednisone and methotrexate, with an average duration of 33 months (19-48 months) which depended upon the clinical response. At long-term follow-up there were significant cognitive and motor sequelae, mainly disabling ataxia, delayed language development, dysarthria and delay in learning. At the moment, all patients are alive and without neuroblastoma, 50% persisted with ataxia.

Conclusion: Most of these patients are cured of neuroblastoma by having tumors with favorable biological features, but require a multidisciplinary follow-up including a proper motor and cognitive rehabilitation.

P-0494 | Imaging Flow-Cytometer Based Detection of ALK and MDM2 Amplification in Neuroblastoma Cell Lines

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Background/Objectives: Neuroblastoma is the most common extracranial childhood cancer with current survival rate of <40% for high-risk disease. This dismal survivorship can be partly attributed to failure in curing neuroblastoma hallmarked by *ALK* and *MYCN* gene amplifications which associate with poor clinical outcomes. Despite multimodal therapy neuroblastoma remains one of the main challenges in paediatric oncology. Targeted therapies against the oncogenes *ALK* and *MDM2* are undergoing clinical development; a non-invasive method to risk stratify patients for these targeted treatments is needed. Circulating tumour cells (CTCs) in peripheral blood have been shown to reflect tumour biology and thus may abrogate the current need for invasive biopsies. Our aim was to detect and quantify *ALK* and *MDM2* amplification in neuroblastoma cell lines using fluorescence *in-situ* hybridisation-in suspension (FISH-IS) on ImageStreamX imaging flow cytometer, followed by comparison with traditional slide-based FISH.

Design/Methods: Slide-based interphase FISH was undertaken on ten neuroblastoma cell lines of unknown *ALK* status and six previously characterised for *MDM2* amplification. Six cell lines of varying *ALK* and *MDM2* status then underwent FISH-IS with ImageStreamX analysis to detect *ALK* and *MDM2* amplification. Western blotting assessed *ALK* and *MDM2* protein expression.

Results: ImageStreamX confirmed previously known amplification status of both *ALK* and *MDM2* in all six cell lines. The detected amplification of both genes; mean FISH signal area was significantly greater in amplified than non-amplified cell lines (unpaired t-test $p < 0.05$). We were also able to correlate this with higher protein expression of *ALK* and *MDM2* in amplified cell lines using western blots.

Conclusion: ImageStreamX successfully determined *ALK* and *MDM2* amplification status in tested cell lines. Our results were consistent and comparable to traditional slide-based FISH. ImageStreamX based FISH-IS represents the next generation of FISH analyses with great promise for the non-invasive stratification of neuroblastoma patients for *ALK* and *MDM2*-targeted therapies.

P-0495 | Pembrolizumab in Paediatric Patients with Advanced Melanoma or A PD-L1-Positive (PD-L1+) Advanced, Relapsed, or Refractory Solid Tumour or Lymphoma: Phase 1/2 Keynote-051 Study

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Background/Objectives: The anti-PD-1 antibody pembrolizumab has demonstrated promising antitumor activity with manageable toxicity in adults with advanced solid tumors. The phase 1/2 KEYNOTE-051 study (NCT02332668) will determine the recommended phase 2 dose (RP2D) and activity of pembrolizumab in paediatric tumors. Here, we present safety, PK, and preliminary efficacy from the phase 1 dose-finding portion.

Design/Methods: Eligibility criteria included age 6 months to <18 years, advanced melanoma or a PD-L1+ advanced/relapsed/refractory solid tumour or lymphoma that is incurable and has failed prior therapy or for which standard therapy is unavailable/inappropriate, measurable disease per RECIST v1.1 (MIBG-positive evaluable disease for neuroblastoma), and performance score ≥ 50 (Lansky Play [≤ 16 years] or Karnofsky Scales [> 16 years]). PK analyses and modified 3+3 toxicity probability interval design with a 25% target dose-limiting toxicity (DLT; evaluated for first 3 weeks) rate were used to determine the RP2D; starting dose was 2 mg/kg Q3W (equivalent to adult dose). AEs were graded using NCI CTCAE v4.0. Primary efficacy end point was ORR per investigator-assessed RECIST v1.1.

Results: Twelve patients were enrolled (n=2 melanoma, n=4 neuroblastoma, n=2 soft tissue neoplasm, n=4 other solid tumors); median age was 13 years (range, 3-16). Eleven (92%) patients experienced treatment-related AEs (TRAEs), most commonly fatigue (25%); one serious TRAE (grade 2 hypertension) occurred. No grade 3-5 TRAEs or DLTs were reported at the 2 mg/kg dose level. PK profile at the 2 mg/kg dose was consistent with adults; no additional doses were evaluated. As of January 22, 2016 data cutoff, 8 (67%) patients discontinued treatment, all due to progressive disease. One patient achieved partial response; 4 had best response of stable disease.

Conclusion: Based on phase 1 results, the RP2D of pembrolizumab in the paediatric population is 2 mg/kg Q3W. Phase 2 will further evaluate safety and efficacy of this dose in paediatric patients.

P-0496 | Spontaneous Differentiation (Maturation) of Neuroblastoma

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Currently, 5 patients were alive with no evidence of progression and disease recurrence (mean follow-up 89.3 months). During the first year after treatment accumulation of MIBG gradually disappeared completely. Mean age of this group was 4.5 (1.5-6 months). In 2 patients - Stage 2A, at 1 patients - Stage 3 and 2 patients - 4S stage). Patients with stage 2A, 3 (n = 3) were removed > 90% of the tumour mass. Patients with stage 4S produced in both cases complete resection of the primary tumour. In all cases, biologically treated tumors with a good prognosis group with a favorable option by Y. Shimada. Nmyc-amplification and chromosome 1p36 and 11q23 aberrations were not found.

Conclusion: In some cases in patients under the age of 12 (sometimes 18) months with no molecular biological risk factors (amplification of the gene N-myc, aberrations chromosomes 1 and 11), there may be spontaneous regression of the tumour.

To determine the tactics of treatment of patients with neuroblastoma at the first stage is important complex diagnostics, including the molecular genetic studies to determine amplification of N-myc gene and chromosomal aberrations.

P-0497 | MYCN Knockdown Mediated Differentiation in Neuroblastoma is Dependent on ERK1/2 Signaling

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Purpose: The aim of this study was to elucidate the mechanisms involved in the neuronal differentiation associated with knockdown of MYCN in MYCN amplified neuroblastoma cells.

Design/Methods: MYCN inhibition was studied using MYCN amplified neuroblastoma cell lines Kelly and SK-N-BE(2)-C with inducible shRNA expression targeting MYCN. AP-1 activity was measured with a AP-1 specific luciferase reporter. Activation of Rac1 and Cdc42 was assessed using GST-pulldown. Activation of JNK and ERK1/2 was investigated by Western Blot with phospho-specific antibodies. Neuronal differentiation was detected by light microscopy.**Results:** shRNA mediated MYCN inhibition in the MYCN amplified neuroblastoma cell lines Kelly and SK-N-BE(2)-C induced neuronal differentiation. MYCN depletion also increased AP-1 mediated transcription. The increased AP-1 activity was not accompanied by a concomitant activation of the known AP-1 inducers Cdc42, Rac1 and JNK, but was associated with increased phosphorylation of ERK1/2. Furthermore, we showed that treatment with the MEK1/2 inhibitor U0126 attenuated the induction of AP-1 mediated transcription associated with MYCN inhibition. Finally, we show that treatment with U0126 also inhibited morphological differentiation in SK-N-BE(2)-C cells after MYCN knockdown.**Conclusion:** Our findings show that the neuronal differentiation observed after MYCN knockdown is associated with activation of AP-1 mediated transcription and is dependent on signaling through ERK1/2. These results provide new insight into the role of MYCN in neuroblastoma differentiation.

P-0498 | Prognostic Significance of P53 mRNA Expression in Neuroblastoma

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With ROC-analysis we assessed the optimal criterions for distribution of patients according to p53 expression (OC:>1.18 a.u., P=0.04, AUC:0.69 for high and OC:<0.09 a.u., P=0.006, AUC:0.84 for low MDM2 expression groups). We have analyzed 3-year event-free survival (EFS) of patients with neuroblastoma and established 100% EFS survival for patients with low

MDM2 and high p53 expressions, while in other groups significant decrease in survival was observed (P<0.05). EFS rates of patients with low p53 / high MDM2 and high p53 / low MDM2 expressions were similar (27.7% and 33.3%) and for p53/MDM2 overexpressed tumors it was only 18.2% (P<0.05).

Conclusion: Regulation of p53-mediated pathway is complex and multicomponent system. Alteration of p53 EL is independent from clinical features marker of neuroblastoma. Analysis of p53/MDM2 co-expression provides the possibility for better neuroblastoma outcome prediction.

P-0499 | Semaphorin 3A Suppresses Tumour Invasion in Human Neuroblastoma

Y. Ishizuka¹, Y. Watanabe¹, E. Maeoka¹, T. Hirano¹, S. Yoshizawa¹, H. Kawashima¹, H. Kaneda¹, T. Furuya¹, K. Sugito¹, T. Koshinaga¹, K. Fujiwara²¹Nihon University School of Medicine, Paediatric Surgery, Tokyo, Japan; ²Nihon University School of Medicine, General Medicine, Tokyo, Japan**Background/Objectives:** Semaphorin 3A (SEMA3A) was identified as a guidance factor of the nervous system cells. Current studies have shown that SEMA3A acts as a potent suppressor of tumour progression in various cancer models. Even though it has been known that lower expression level of Neuropilin 1 (NRP1), a receptor for SEMA3A, associates with higher disease stage in neuroblastoma (NBL), the roles of its ligand SEMA3A in the development of NBL are still unclear. In this study, we investigated the role of SEMA3A in NBL.**Design/Methods:** Human-derived NBL cell line SK-N-AS (AS) was used for the study. To figure out the function of SEMA3A, cell proliferation rate, motility and invasiveness were analyzed after knocking down of SEMA3A by siRNA or applying purified SEMA3A to the cells. Expression levels of Integrin beta 1 and FAK-PI3K pathway related proteins were analyzed by Western-blotting.**Results:** The motility and invasiveness of AS were significantly enhanced by knocking down of SEMA3A. On the other hand, 50nM administration of SEMA3A significantly suppressed the invasiveness of the cells. It was clearly shown that the expression level of Integrin beta 1, which is known to affect cell invasiveness, was increased, and FAK-PI3K pathway was activated in SEMA3A knocked down cells.**Conclusion:** SEMA3A inhibits migration and invasion of NBL cells at least in part by suppressing the expression of Integrin beta 1 and FAK-PI3K pathway. Our current data indicated that SEMA3A may act as a potent tumour suppressor in NBL. Since this is the first report demonstrating that SEMA3A inactivate Integrin beta 1 and its downstream pathway in tumour cells, we are now conducting further analysis to find the exact mechanism of SEMA3A affecting the activity of Integrin beta 1.

P-0500 | Dosimetric Comparison of Three-Dimensional Conformal Radiotherapy and Intensity Modulated Radiotherapy for Paediatric Neuroblastoma

M. Jiang¹¹Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine, Radiotherapy, Shanghai, China**Background/Objectives:** To evaluate the dosimetric difference between intensity modulated radiotherapy (IMRT) and threedimensional conformal radiotherapy (3DCRT) for paediatric neuroblastoma.**Design/Methods:** Images of 10 patients with paediatric neuroblastoma in our department were selected. Both 3DCRT and IMRT plans were respectively designed for each patient, and the prescribed dose was 21.6Gy/12 Fx. The dose of normal tissues of kidneys and liver, target volume dose, homogeneity index (HI), and conformity index (CI) were compared.**Results:** Dose volume histogram indicated that no significant differences were found in the dose coverage of 95% target volume, HI, approximate maximum dose D 2%, and approximate minimum dose D 98%, and that the CI of IMRT was obviously better than that of 3DCRT. The V 8 and V 15 of liver, and V 15 and V 18 of the left kidney, and the V 15 and V 18 of the right kidney of 3DCRT plan were respectively 40.3%±19.1%, 25.7%±16.7%, 37.4%±20.4%, 21.6%±12.2%, 29.4%±16.4%, and 20.6%±14%, while those of IMRT plan were respectively 45.5%±17.5%, 16.9%±13.3%, 15.3%±5.2%, 5.7%±3.6%, 13.3%±7.4%, and 5.9%±3.9%. No significant differences were found in the dose of liver between IMRT and 3DCRT. The dose comparison of kidneys showed IMRT had a better protective effect on kidneys.**Conclusion:** Compared with 3DCRT, IMRT for paediatric neuroblastoma has a better CI, and a better protective effect on kidneys. However, IMRT should still be used carefully in paediatric patients for the larger low dose volumes in the radiation volume.

P-0501 | Recent Treatment Analysis of 42 Children with Central Nervous System and Intracranial Metastases in High-Risk Neuroblastoma

M. Jin¹, D. Zhang¹, W. Zhao¹, X. Wang¹, Q. Zhao¹, X. Li¹, C. Huang¹, T. Hao¹, Z. Yue¹, X. Ma¹¹Beijing Childrens' Hospital-Capital Medical University, Haematology&Oncology, Beijing, China**Background/Objectives:** To summarize clinical features of high risk neuroblastoma(NB) in 42 children, and analyze the relationship between age, primary site, metastases and the efficacy of recent treatment. Further definition of clinical features may provide clues to the predisposing factors and treatment with high-dose chemotherapy regimens to improve their survival rates.**Design/Methods:** A retrospective analysis of 42 children with initial or recurrent central nervous system and/or intracranial metastases in high risk neuroblastoma who were diagnosed at Beijing Children's Hospital. According to neuroblastoma protocol in Beijing Children' Hospital (BCH-N-2007 protocol, based on Hong Kong NB N7 protocol). All children were followed up to June 31, 2015.

Results: The majority clinical initial symptoms with fever and/or extremities pain were in 25 cases (60%). 33 cases with LDH >500U/L (78.5%). 18 cases with NSE>370ng/L (43%). 36 cases at diagnosis and 8 cases at recurrence or relapse. In 36 cases at diagnosis, 3 cases of central nervous system metastases (1.9% of all high risk NB), 33 cases of intracranial metastases (17% of all high risk NB). 28 patients had isolated bones of the skull, 21 patients had isolated dura. Sixteen patients metastasis concomitantly in bones of the skull and dura. The CNS recurrence or relapse is in the majority progression. Using Kaplan—Meier analysis showed the expected 5-year overall survival rate was 21.3%.

Conclusion: NB is progressive disease. Children with CNS or intracranial metastasis have poor prognosis, especial CNS. The remission rate of recurrence or relapse is very low. The intensive chemotherapy through bold brain barrier, compounded with MIBG and immunotherapy may further improve survival.

P-0502 | Opsoclonus Myoclonus Syndrome in Children with Neuroblastoma: Experience of Interdisciplinary Cooperation in Russia

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Background/Objectives: Opsoclonus myoclonus syndrome (OMS) is a rare paraneoplastic syndrome associated with neuroblastoma (NB) in 50-80% cases. The aim of the study was to analyze characteristics of neuroblastoma associated with OMS treated in the multicenter study in Russia.

Design/Methods: 285 patients with sympathetic nervous system tumors were included for the period 01.2012-07.2015 (43 months). 19 (6.7%) patients had tumour associated with OMS. The diagnosis has been established on the basis of international criteria of OMS. The diagnosis of NB has been confirmed by histological examination in all cases. Patients were stratified and treated according to the German NB2004 protocol.

Results: Male: female ratio was - 0.35:1. The median age at the diagnosis of OMS and NB was 24.7 months (range 14.9-54.0). Paravertebral location was noted in 15/19 (78.9%) cases. Most tumors were small (median volume - 6.5 ml (range 0.4-80.9 ml)). In 11/19 (58.0%) patients the tumour was visualized only by CT/MRI. Increased neuron specific enolase was observed in 1/19 (5.3%) case. Scintigraphy with metaiodobenzylguanidine (MIBG) was positive in only 9/17 (53.0%) cases. Segmental aberrations were observed in 1 patient (11q deletion). All but 1 patient were stratified to the observation group. Comparing with non-OMS cases NB associated with OMS showed female preponderance, older age at tumour diagnosis (24.7 versus 11.2 months, $p=0.02$), non-adrenal primary tumour ($p=0.0008$), more differentiated histology ($p=0.0001$), lack of MYCN amplification ($p=0.057$) and 1p deletion ($p=0.04$), favorable stage ($p=0.003$) and risk group distribution ($p=0.003$). 3-year EFS was 82.6% in OMS group and 61.6% in non-OMS group ($p=0.22$), 3-year OS - 100.0% and 72.7% ($p=0.2$).

Conclusion: NB associated with OMS showed more favorable biologic characteristics. CT and/or MRI are the most informative diagnostic methods to detect tumors in patients with OMS given the small size, location and low metabolic activity of NB.

P-0503 | Treatment of High-Risk Neuroblastoma: Experience of Russian Federal Centers

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Background/Objectives: The prognosis of patients with high-risk neuroblastoma remains poor. The results of treatment of this group of patients in Russia are not fully studied. The aim of the study was to analyze the results of therapy of high-risk neuroblastoma in three federal centers in Russia.

Design/Methods: 270 patients with NB were treated for the period 01.2012-06.2015 (42 months). Patients were stratified and treated according to the German NB2004 protocol. 94 (34.8%) patients were stratified to the high-risk group. High-dose preparative regimens included carboplatin/etoposide/melphalan (CEM) (till June 2013) and treosulfan/melphalan (TreoMel) (since July 2013). Since July 2014 patients with clear MIBG-positive residual

primary tumour and/or metastases prior to hematopoietic stem cell transplantation (HSCT) received ¹³¹I-MIBG-therapy.

Results: Male: female ratio was - 1.18:1. The median age at the diagnosis was 32.0 months (range 1.3-128.4). MYCN amplification was observed in 43 (45.7%) cases. 82 (87.2%) patients had stage 4 NB. Induction therapy was completed in 90 (95.7%) patients. Median number of chemotherapy cycles prior to transplantation was 6 (range 6-10). 78/90 (86.7%) received high-dose chemotherapy: 28 - CEM, 50 - TreoMel. Contraindications for HSCT included tumour progression (n=7), organ toxicity (n=3), surgical complications (n=2). Transplant-related mortality was 3/78 (3.8%), all in CEM group. 14/82 (17.0%) of stage 4 patients with MIBG uptake after the induction received ¹³¹I-MIBG-therapy. Median follow-up time for alive patients were 22.1 months (range 5.3-49.7). 3-year EFS was 34.4±6.3% and 3-year OS - 46.6±7.5%. Stage significantly predicted EFS (stage 1-3, 4S - 81.4% versus stage 4 - 25.4%, $p=0.007$) in the high-risk NB patients.

Conclusion: Our results are consistent with other research groups. Intensive therapy allows achieving satisfactory results of therapy in high-risk NB patients with stages 1-3 and 4S. The introduction of novel therapies are urgently required to improve prognosis in stage 4 NB.

P-0504 | Childhood Ganglioneuromas

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Background/Objectives: Ganglioneuroma (GN) is the benign tumour of the neuroblastic cells and can be diagnosed de novo in healthy subjects. However, GN may slowly grow and become symptomatic. Few occurrences of late malignant changes have been reported. The aim of this study is to evaluate the outcome of our GN patients.

Design/Methods: Patients, under 19 years old with GN between January 1990 and 2016 were retrospectively evaluated.

Results: Eighteen GN (13 girls, 5 boys) with a median age of 6 years (2-12 years) were evaluated. Neuroblastoma patients comprise 6.8% of all patients and GN patients comprise 8% of tumors with neuroblastic origin in our series. There were 14 stage I, one stage II and three stage III patients. Primary localization was in the posterior mediastinum in seven patients, five at the adrenal gland and six in other sites, with one patient having 2 separate masses; one in the presacral and the other at the ovarian regions. Surgery was the only treatment approach for all in stage I and II patients. One had opsomyoclonus syndrome. Two had severe scoliosis. All are in remission for a median of 3,5 years (2 months-24 yrs). All stage III patients, had inoperable abdominal/pelvic tumors; one was also diagnosed concurrently with osteosarcoma that was treated successfully; the abdominal mass was only biopsied and is followed-up for 2 years. In the other two patients, pathology consultations revealed ganglioneuroblastoma intermixed; with no response to chemotherapy, further biopsies and retrospective consultations were consistent with GN and treatment was stopped. Both are alive with stable disease for 2,25 yrs and 21 yrs, respectively.

Conclusion: The histological diagnosis of GN has always been controversial. In our series, all patients with GN are alive with no recurrence or progression. Survival was not influenced by the extent of surgery, thus aggressive surgery should not be recommended.

P-0505 | Children with Neuroendocrine Tumors Presenting with Opsoclonus Myoclonus Syndrome

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Background/Objectives: Opsoclonus_myoclonus syndrome (OMS) is a rare disorder characterized by chaotic eye movements, ataxia, myoclonus and behavioral disturbances. It may be a sign of an infectious, metabolic or malignant disorder. Here we report two children presenting with OMS and diagnosed with ganglioneuroma and neuroblastoma respectively.

Design/Methods: Case report.

Results: Patient 1: A 3 year-old boy presented with one week history of frequent fall and abnormal eye movements. He had ataxia, tremor and nystagmus on physical examination. His cranial MRI, EEG, HSV PCR, urine heavy metal testing, thyroid function studies, neuron specific enolase(NSE) level and abdominal ultrasound (USG) were within normal limits. He was given pulse steroid for possible postinfectious cerebellitis/ataxia with no significant improvement. His repeat abdominal USG showed 12x11x21 mm right adrenal mass. His NSE level and urinary catecholamine levels stayed within normal limits. The mass was totally resected. Pathology showed ganglioneuroma. He was treated with monthly IVIG and steroid. He showed significant improvement neurologically during 8 months of follow-up.

Patient 2: A 5 year-old boy presented with ataxia, difficulty walking and abnormal eye movements. Spinal MR showed left posterior mediastinal mass at the level of T9-T10 vertebrates. Tru-cut biopsy showed neuroblastoma. He had no distant metastasis and underwent total resection of the mass. He was treated with IVIG and steroids with some improvement for paraneoplastic OMS. He was further treated with cyclophamide/steroids and further with mycophenolate mofetil with no response. He was switched back to monthly IVIG with improvement in his neurologic condition, he is under follow-up for 3 years after diagnosis.

Conclusion: OMS is a rare disease which may present as a paraneoplastic syndrome in children with neuroendocrine tumors. Close monitoring with repeated imaging is warranted when history and initial evaluation fails to identify the underlying etiology. Steroids, IVIG, cyclophosphamide should be considered in the treatment of OMS.

P-0506 | An Impact of Etoposide Treatment on Survival for High-Risk Neuroblastoma Patients

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Background/Objectives: We have treated thirty-seven patients with newly diagnosed high-risk neuroblastoma between 2002 to 2014 with or without etoposide (ETP). The purpose of this report is to analyze the additive effect of ETP in the first line treatment on the outcome of high-risk neuroblastoma.

Design/Methods: This is a retrospective analysis of patients' medical records. Thirty patients (0y8m-6y3m, median 2y10m) completed Japanese standard protocol, which includes induction chemotherapy with five cycles of vincristine, cyclophosphamide/irifosfamide, cisplatin/carboplatin, pirarubicin, with/without ETP, resection of the primary tumour, followed by high dose chemotherapy (HDC) with autologous PBST and local irradiation. HDC regimens were TT+LPAM/BU+LPAM (TB-group, an ETP-free HDC group) (n=26) or MEC (n=4). Among the fourteen patients whom ETP was given in the first line therapy, ten belong to the TB-group (ETP-treated TB-group).

Results: Mean observational period of all patients was 4.3 years. The 3-year OS and RFS for all 30 patients were 86+/-6% and 58+/-10% respectively. The 3-year RFS for all ETP-treated patients (in induction and/or HDC) (n=14) were 52+/-14%, for all ETP-untreated patients (n=16) were 62+/-12% (p=0.91). Among the fourteen patients with *MYCN*-amplified tumour, the 3-year RFS for ETP-treated patients (n=8) were 71+/-17%, for ETP-untreated patients (n=6) were 83+/-15% (p=0.73). Next, we analyze the additive effect of ETP among TB-group. The 3-year RFS of all TB-group (n=26) were 55+/-10%. The 3-year RFS of ETP-treated TB-group (n=10) were 39+/-17%, and ETP-untreated TB-group (n=16) were 63+/-12% (p=0.65). Nine of all the sixteen ETP-untreated patients survived without relapse. Five of the nine ETP-untreated survivors had *MYCN*-amplified tumour.

Conclusion: Although total amount of ETP and treatment schedule were various, we could not find any additive effect of ETP in first-line therapy for high risk neuroblastoma so far. ETP might not be essential for some patients.

P-0507 | Ketogenic Diet is A Potential Adjuvant Therapy for Neuroblastoma

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Background/Objectives: Neuroblastoma (NB) is characterized by a marked decrease of aerobic energy metabolism. Targeting of tumour metabolism by ketogenic diet (KD) has been demonstrated to be an effective adjuvant therapy, especially in brain tumours. Recent preclinical data indicate that targeting the metabolism of NB by KD (fat:carbohydrate/protein ratio 2.5:1), especially in combination with calorie restriction, is able to reduce tumour growth and support metronomic cyclophosphamide (MCP) therapy of NB xenografts. As calorie restriction might not be feasible as adjuvant therapy in most patients the aim was to optimize the KD to avoid the need of calorie restriction.

Design/Methods: Xenografts were established in CD-1 nu/nu mice with SH-SY5Y and SKNB(2) cells. Mice were randomized into control (normal and low protein content) and three KD groups (4:1) with varying composition of triglycerides in combination with MCP (10 and 40 mg/kg/day). The effect of the interventions on tumour growth, body weight, plasma parameters (glucose, ketone bodies, amino acids) and tumour vascularisation were evaluated.

Results: The effect of MCP treatment on SH-SY5Y and SKNB(2) xenografts was significantly enhanced by adjuvant intervention with KDs. Triglyceride composition of the KD was an important factor that influenced growth of the xenografts and survival. KDs induced a significant decrease in blood glucose and an extensive increase in blood ketone levels. Blood vessel density and intratumoural hemorrhage were also significantly decreased in KD treated animals. Albeit a reduction of essential amino acid levels in plasma and tumour tissue of KD treated animals was observed, the low protein content of the KDs was not responsible for the growth inhibiting effect.

Conclusion: Targeting the mitochondrial energy metabolism by KD with a special composition of triglycerides could open a new front in supporting standard therapy regimens for NB.

P-0508 | Inhibition of N-Myc Expression Sensitizes Human Neuroblastoma Imr-32 Cell Expressing Caspase-8 to Trail

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Neuroblastoma cells exhibit amplification of *N-myc* and lack of caspase-8 expression, which may be strongly correlated with resistance to chemotherapies. Tumour necrosis factor-related apoptosis-inducing ligand (TRAIL), either alone or in combination with other anti-cancer agents, is a promising new strategy of cancer treatment. In this study, we examined the effect of combination treatment with cisplatin and TRAIL on TRAIL-resistant IMR-32 neuroblastoma cells. Despite the increase of death receptor (DR) 5 (DR5, TRAIL-R2) expression by pretreatment with cisplatin, TRAIL treatment did not induce cell death in IMR32 cells. Even by pretreating interferon- γ to increase the expression of caspase-8 in IMR-32 cells, TRAIL sensitivity did not enhance in IMR-32 cells that treated with cisplatin and TRAIL. Furthermore, we established stable cell line down-regulating *N-myc* expression by introduction of shRNA targeting *N-myc* in IMR-32 cells. The combination treatment with cisplatin and TRAIL in these cells

expressing caspase-8 by interferon- γ significantly induced TRAIL-induced apoptosis, which abrogated by pretreatment with DR5:Fc chimera indicating that the expression of *N-myc* and caspase-8 involves in TRAIL susceptibility to TRAIL-resistant IMR-32 cells. These results suggest that the combination therapy with cisplatin and TRAIL is a promising strategy when it controls the expression of *N-myc* and caspase-8 in neuroblastoma cells, which may provide the useful information to develop therapeutic strategies against neuroblastoma.

P-0509 | Treatment and Outcome of Neuroblastoma with Intraspinal Extension: A Systematic Review

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Background/Objectives: Neuroblastoma (NBL) with intraspinal extension can lead to acute and long-term toxicity, caused both by spinal cord compression and/or by treatment. Despite multiple reports in the literature concerning treatment and outcome of this specific patient group, these data have not been evaluated systematically.

Design/Methods: A systematic literature search of the Medline/PubMed and Embase databases was performed to identify studies that reported on childhood NBL with intraspinal extension, aimed to define the long-term health problems (HP) and optimal treatment strategy. Pre-defined study characteristics and -population, symptoms at diagnosis, treatment, outcome, prevalence of long-term HP and quality of each study, were scored by two reviewers.

Results: Out of 685 studies identified in the literature search, 75 were selected for full text screening and 25 were included in the systematic review. NBL is complicated by intraspinal extension in 14.6%, of which 63.2% gives rise to neurological symptoms. The optimal treatment strategy for these patients could not be determined. The overall long-term HP burden is high, with a median of 50% neurological motor deficit, 25% bladder dysfunction, 16% bowel dysfunction and 30% spinal deformity. All studies had methodological limitations.

Conclusion: Long-term HP are a frequent consequence of disease and/or treatment in survivors of NBL with intraspinal extension. No conclusion could be drawn to what extent disease and/or treatment contributed to long-term HP. More well designed studies are needed to determine the optimal treatment strategy for these patients. Until then, we can only advise to follow SIOPEN protocol recommendations to limit neurosurgery to patients with rapid neurological deterioration only; to maintain a high index of suspicion for neurological symptoms as presenting symptoms of NBL with intraspinal extension; and to be aware of the frequency and severity of long-term HP in survivors and to develop targeted follow-up programs for this group.

P-0510 | Phase II Study of Arsenic Trioxide in Neuroblastoma and Other Paediatric Solid Tumors

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Background/Objectives: Arsenic trioxide (AT) has been successfully used in the treatment of acute promyelocytic leukaemia. In preclinical studies, AT induced cell death in a variety of solid tumors including neuroblastoma. A Memorial Sloan Kettering Cancer Center phase I study of AT treatment in paediatric solid tumors showed negligible toxicity. The recommended phase II dosage was 0.25 mg/kg/day intravenously (IV) over five days.

In the present study (NCT00024258), we investigated the efficacy of AT against relapsed or refractory neuroblastoma and other poor-risk paediatric solid tumors.

Design/Methods: Each cycle consisted of: AT 0.25 mg/kg/day IV \times five days, two days off, then AT 0.25 mg/kg/day IV \times five days. Patients could get a maximum of six cycles every 14 days. Disease status was assessed using International Neuroblastoma Response or RECIST criteria; after every second/third cycle and then, if the disease had responded, every two-three months through one year after completion of treatment. Toxicities were assessed by NCI Common Toxicity Criteria version 2.0.

Results: At enrollment, the 22 patients were 4-30 (median 10) years old. Diagnoses were stage 4 neuroblastoma (n=18), and one each with a parotid lymphoepithelial carcinoma, pontine astrocytoma, metastatic Ewing sarcoma, and desmoplastic small round cell tumour. Patients received a total of 56 (median 2; range 1-6) cycles. Nineteen were evaluable for response: one neuroblastoma patient had a partial response, two neuroblastoma patients had stable disease for three and six months respectively, and 17 developed progressive disease. Inevaluable patients included two who were withdrawn due to grade 3 toxicities: transient prolonged QT interval and myalgia, and one who had disease-related cardiopulmonary arrest. Eight patients experienced grade 1-2 toxicities including headache, fluid retention, hyperglycemia, and elevated hepatic enzymes.

Conclusion: As a single agent, AT did not show significant anti-tumour activity. Associated adverse events were manageable and transient.

P-0511 | The Expression and Significance of Epidermal Growth Factor Receptor in Neuroblastoma Cell Lines and Tumour Tissues

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Background/Objectives: Neuroblastoma is the most common abdominal malignant tumour in childhood. Immune Toxin (IT), which targets the tumour cell surface receptor, is a new supplementary therapeutic treatment to the traditional approach. The purpose of this study is

to detect the expressions of epidermal growth factor receptor (EGFR) in neuroblastoma cell lines and tissues, and to validate if IT can be used in refractory neuroblastoma.

Design/Methods: The EGFR expression levels of five neuroblastoma cell lines were measured using cell-based ELISA assay and western blot analysis. The measured expression in human neuroblastoma tissue samples was detected by immunohistochemistry staining. The analysis used tumour samples and clinical data obtained from 25 children admitted between August 2008 and April 2014 at the Department of Surgery, Children's Hospital of Fudan University, China.

Results: The expression of EGFR was higher in KP-N-NS cell line and BE(2)-C cell line. The positive rate of EGFR expression in neuroblastoma tissue was 81.0% (17/21), and 50% (2/4) in gangliocytoma, without statistical significance ($P=0.234 > 0.05$). The positive rate of EGFR expression in favorable type and unfavorable type was 62.5% (5/8) and 92.3% (12/13) respectively, also showing no significant statistical difference ($P=0.253 > 0.05$). Comparing the scores of ten pre- and post-chemotherapy samples, the EGFR expression of these two had no significant statistical difference ($P=0.3865 > 0.05$). [XM1].

Conclusion: The study confirmed that there are consistent and widespread expressions of EGFR protein in cell lines and neuroblastoma tissues regardless of chemotherapy. Thus, the treatment of neuroblastoma cells should be founded upon targeting this EGFR protein.

P-0512 | High Risk Neuroblastoma: Impact of Molecular Markers on Surgical Resectability and Survival

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Background/Objectives: Neuroblastoma, a malignancy of the developing sympathetic nervous system, is the most common extra-cranial solid tumour in children. There are a number of molecular markers which predict overall survival but there is a lack of information if they correlate with surgical resectability and overall survival.

The aim of this study is to correlate known neuroblastoma molecular markers with post induction chemotherapy and histological response, operative findings at time of surgical resection and review how these factors contribute to overall outcome.

Design/Methods: Case notes for all High Risk Neuroblastoma patients treated in the Royal Belfast Hospital for Sick Children (RBHSC) between August 2003 and February 2015 were collated. All patients were treated on the current High Risk trial for Neuroblastoma13 patients were identified. Information gathered included: molecular tumour markers, extent of local disease, histological response post-induction treatment and volume of residual primary disease on cross-sectional imaging post-surgical resection.

Results: Six patients were MycN amplified with 1p deletion and 17q gain. Six patients MycN non-amplified: two 11q deletion and 17q gain, two 1p deletion, 11q deletion and 17q gain and two with no other cytogenetics markers. One patient had no cytogenetics available.

Post induction chemotherapy, five had 90-99% reduction in primary disease and eight had a partial response. Post-surgical resection, five had minimal or no residual disease on cross-sectional imaging, this included two patients with Myc N amplification, 1p deletion 17q gain. Eight patients had histological evidence of viable disease post resection, three did not (two could not be surgically resected). Six patients remain alive (follow up range four months to thirteen years).

Conclusion: Based on this small single centre study, cytogenetics did not appear to predict rates of complete surgical resectability and subsequent mortality for patients being treated for high risk neuroblastoma.

P-0513 | Radiation Exposure to Family Caregivers and Health Care Providers of Paediatric Neuroblastoma Patients Receiving 131I-MIBG Therapy in Canada

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Background/Objectives: This retrospective study determined the measured radiation exposure to family Caregiver (FCG) and Health Care Providers (HCP) who cared for patients receiving ¹³¹I-MIBG therapy during hospital admissions during year one of operation.

Design/Methods: Design of our new ¹³¹I-MIBG therapy suite was guided by Canadian Nuclear Safety Commission (CNSC) regulations for occupational exposure to the general public (non-NEW). HCP completed mandatory class instruction and online education modules on caring for ¹³¹I-MIBG patients. FCG were provided with radiation safety education from a Radiation Safety Officer (RSO) and Neuroblastoma team. ALARA principles were a key component to the education programs. ¹³¹I-MIBG therapy was administered to 12 children (13 treatments) (average age 8, range 3-14 years) for relapsed and refractory neuroblastoma. Direct read dosimeters were used to measure radiation exposure and guide HCP and FCG care practices, from radioisotope administration until discharge.

Results: The administered activity ranged from 8.51 to 32.23 GBq (average 18.13 GBq). The average FCG exposure for 13 treatments was 0.309 mSv (range 0.028 to 0.947 mSv per FCG). The average HCP exposure was 0.038 mSv with a range from 0 to 0.165 per treatment. Length of stay was between 4 and 10 days (mean 8 days). Average length of stay is longer than comparable ¹³¹I-MIBG programs outside Canada.

Conclusion: Length of stay was dependent on CNSC requirements, pre-determined discharge levels, distance and travel requirements and family housing conditions. Exposure to HCP and FCG was well below CNSC regulatory limits and considerably less than that reported from other comparable institutions. The design of our facility enhanced shielding and unique urine drainage system likely contributed to the very low exposure for caregivers. Careful consideration of HCP assignments contributed to minimum exposure of staff. A robust education program led to increased HCP comfort in providing care to ¹³¹I-MIBG patients.

P-0514 | Phase II Single Arm Institutional Study to Assess Dinutuximab Combined with Granulocyte-Macrophage Colony Stimulating Factor (GM-CSF) and IL-2 in Patients with High-Risk Neuroblastoma

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Background/Objectives: first trial of Dinutuximab and GM-CSF/IL2 with the aim to demonstrate objective responses (OR) for newly diagnosed patients with primary refractory neuroblastoma (NB) limited to the osteomedullary (MIBG and/or PET/CT with < 5 spots) compartment (group 1); and reproduce reported results for patients with no evidence of disease at study entry (group 2).

Design/Methods: Dinutuximab was administered every 28 days at 17.5 mg/m²/day × 4 days for all 5 courses. GM-CSF at 250 micrograms/m²/day for 14 days (courses 1,3,5); IL-2 at 3 MIU/m²/day days 0-3; 4.5 MIU/m²/day days 7-10 (courses 2,4). All patients received 6 cycles of Isotretinoin given at 160 mg/m²/day divided into two equal doses for 14 days followed by 14 day rest. To evaluate response MIBG and/or PET/CT scans and analysis of minimal residual disease by quantitative RT-PCR methodology targeting GD2 synthase, Phox2b and Cyclin D1 mRNA, was performed every 2 cycles.

Results: 12 (6 in each group) stage 4 NB older than 18 months of age at diagnosis were enrolled from December 2014 until December 2015. Three patients did not complete therapy, one because of progression after cycle 4 and two because of toxicity (myelitis and macrophage activation syndrome, MAS). Four group 1 patients achieved complete remission (CR) -one after 2 cycles, one after 4 cycles and 2 after 6 cycles- and remained in CR, median 11.8 months from protocol entry. Two group 2 patients have relapsed <6m after completing therapy. Overall, 2 patients have died, one of disease and one of MAS with no evidence of NB. Overall survival is 80% CI95% = (59%, 100%) and event-free survival 44% CI95% = (22%, 89%), median 11.3 months from protocol entry.

Conclusion: Significant objective responses were obtained with dinutuximab and GM-CSF/IL2 for patients with refractory osteomedullary disease.

P-0515 | Does Salvage Chemotherapy Regimen Intensity Embark on Clearance of Bone Marrow Neuroblastoma?

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Background/Objectives: Neuroblastoma is the most common extracranial solid tumour in children. It accounts for 15% of the deaths from cancer in the paediatric age group. Approximately half of the newly diagnosed children are at "high risk" of treatment failure. This study aim was to evaluate the impact of salvage chemotherapy ICE (Ifosfamide, Carboplatin, and Etoposide) versus TC (Topotecan/Cyclophosphamide) when administered to neuroblastoma high risk patients having residual bone marrow disease after primary tumour control on first line treatment regimen.

Design/Methods: The present retrospective study included 2 matched groups of eligible stage 4 neuroblastoma patients with persistent bone marrow disease. Each group consisted of 36 patients. Group (1) patients received ICE whereas less intensive TC was administered to Group (2). Data analysis included epidemiological variables, pathology subtype, NMYC gene status, primary tumour response and their correlation with bone marrow disease clearance on each regimen.

Results: Higher tendency of complete bone marrow clearance was reported in patients received ICE compared to TC; 33.3% versus 22.2%, respectively. However, the difference was not statistically significant ($p=0.293$).

Conclusion: TC regimen appears to be non-inferior to ICE as salvage treatment in attempt to clear bone marrow neuroblastoma residual, with the privilege of being less toxic and can be given on outpatient basis. Yet, further randomized trials of larger study sample size and with survival impact analysis are warranted.

P-0516 | Optimization of Differentiation Induction through Combinational Treatment with miR-124-3p and ATRA in Relapsed Neuroblastoma In Vitro

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Background/Objectives: Treatment of high-risk neuroblastoma routinely involves multimodal chemotherapy followed by maintenance treatment with retinoic acid (ATRA) to drive cell differentiation. Despite this, over 50% of high-risk patients experience a relapse. We hypothesized that resistance to initiation treatment reduced sensitivity to ATRA in neuroblastoma and this decreased differentiation capacity could be restored by the differentiation inducing miR-124-3p *in vitro*.

Design/Methods: LC-MS was carried out on cisplatin resistant neuroblastoma cell lines developed in our lab and their parental counterparts. Bioinformatics analysis of altered proteins identified key pathways associated with resistance development. The ATRA sensitive/insensitive, Kelly/SK-N-AS cell lines and their drug resistant lines were treated with ATRA and miR-124-3p individually and in combination and phenotypic changes were determined over 96h. Expression of altered proteins was verified by western blot and qPCR.

Results: Ingenuity Pathway Analysis identified a network of altered proteins in Kelly/SK-N-AS resistant cells from "Nervous System Development and Function pathway" ($p=3.28 \times 10^{-4}$), represented by CRABP1 (16.5 fold), GAP43 (12.0), TUBB (12.8), TUBB2B (12.0), TUBB4B (157) and VIM (114.7). Reduced response to ATRA was observed in drug resistant cells.

The SK-N-AS parental and resistant cell lines were not differentiated by ATRA alone or in combination with miR-124-3p. However, Kelly and KellyCis83 cells responded to individual treatment with KellyCis83 exhibiting decreased axon outgrowth. This decrease in the Kelly-Cis83 was restored by co-treatment with miR-124-3p. Transfection of miR-124-3p reduced cell viability in cells at 96h by 50% ($p < 0.005$) and was found to target genes of the actomyosin complex, including MYH9, ROCK1, MYL12B, ACTN4 and VIM.

Conclusion: Our data suggests that drug resistance development can reduce cells differentiation capacity. However, sensitivity to ATRA is restored through co-treatment with miR-124-3p. Transfection of cells with miR-124-3p alone reduced cell viability and proliferation, targeting cytoskeletal genes in cells insensitive to ATRA. Therefore, miR-124-3p has potential as a miRNA based therapeutic in relapsed neuroblastoma.

P-0517 | Neuroblastoma of the Iris: Is it Metastatic or a Second Primary Tumour?

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Background/Objectives: To present a rare case of neuroblastoma with iris involvement.

Design/Methods: A 5-months-old-boy was referred with a diagnosis of iris neuroblastoma. When he was 1-months-old, the parents noticed a white lesion on his right eye. The lesion was thought as leukocoria and the patient was referred to an ocular oncologist. His ocular examination revealed a $4 \times 3 \times 2$ mm, nonmelanocytic lesion of the right iris. With a presumption of nonmelanocytic tumour of the iris, the lesion was totally excised. The pathologic examination was reported to be well differentiated neuroblastoma. Abdominal ultrasonography and MRI revealed a heterogenous left adrenal mass of about 40×44 mm and pathologic diagnosis was consistent with stroma poor, differentiated neuroblastoma, negative for myc amplification and loss of 11q23 but positive for gain of 17q25 and loss of 1p36 with hypodiploidy. No any other metastatic lesion was defined on the thorax CT and abdominal MRI. Bone marrow aspiration-biopsy were free of disease. MIBG scintigraphy was negative even for the primary tumour. He was discussed at the local tumour board and regarded to have stage IV, intermediate risk disease. National neuroblastoma treatment protocol (Vincristin, carboplatin and etoposide) was started and the adrenal mass was totally excised after 4 courses of chemotherapy. Post-operatively he was received 2 more chemotherapy courses. He is still on maintenance treatment and free of disease.

Results: Only three cases of neuroblastoma presented with iris involvement has been reported in literature. The both cases were reported in 1980's and do not have detailed pathologic and clinical information.

Conclusion: Our case is unique as the iris lesion has been proved to be neuroblastoma pathologically. Also it is controversial if the iris lesion is metastatic or a second primary tumour. The case is important in that it demonstrates the unusual presentation of a primary abdominal neuroblastoma.

P-0518 | BLM, AHCY and A Novel PKMYT1 Gene Mutations Identified in Children with Neuroblastoma

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Background/Objectives: Neuroblastoma, a neoplasia derived from ganglionic precursors of the sympathetic nervous system, is the most common extra cranial solid tumour of childhood. Previous reports have demonstrated, in MYCN-amplified neuroblastoma tumour samples and in MYCN-overexpressing cells, that elevated expression of AHCY, PKMYT1, and BLM are correlated with poor survival. Considering the potential implication of these genes on the clinical management of neuroblastoma patients, we hypothesize that the identification of genetic variations may have significant impact during development of the recurrent or progressive neuroblastoma.

Design/Methods: In this study, using DNA sequencing (targeted resequencing methodology), we performed mutational analysis of 3 genes (PKMYT1, AHCY and BLM) in tumour samples of 11 MYCN- amplified and 10 MYCN-non amplified neuroblastoma.

Results: Clinical and genetic results were correlated with either MYCN amplified or non-amplified status. BLM germline variants were found in two patients. One heterozygous missense mutation in BLM gene (p.T298M) was detected in an infant girl diagnosed with MYCN-non amplified stage 3 neuroblastoma who experienced multiple recurrences. Another heterozygous missense BLM mutation (p.A1043D) was found in a boy diagnosed with MYCN non-amplified and intermediate-risk neuroblastoma. In addition, one new missense mutation in PKMYT1 (p.S453F) was found in an infant girl with MYCN-amplified high risk neuroblastoma. We also found a rare missense mutation in AHCY gene (p.G123R) in a child with MYCN-amplified and high risk neuroblastoma. All of the genes variants reported in this study were not previously described in neuroblastoma.

Conclusion: Therefore, our findings suggested that mutations in BLM, AHCY and PKMYT1 genes, found in children with either MYCN-amplified or MYCN-non amplified neuroblastomas, may be associated with aggressive forms of disease.

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P-0519 | Can High Risk Group be Categorized as "High Risk" and "Ultra-High Risk" in Neuroblastoma?(on behalf of Turkish Society of Paediatric Oncology Group)

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Background/Objectives: Neuroblastoma is the most common extracranial solid tumour of childhood. Neuroblastic tumors exhibit extreme heterogeneity, which results in different therapy outcomes. Neuroblastoma is mainly categorized into three risk groups as low, intermediate and high. Molecular evaluation has come into prominence for determination of the risk categories. Recently, identification of new genes that may affect the therapy outcome, raised the possibility of the presence of sub-risk groups. With this study, we aimed to assess the expression of some genes that may play role in identification of "ultra-high risk" group of patients.

Design/Methods: We analyzed, 25 and 29, low- and high- risk group of patients, respectively, who were chosen according to molecular and clinical data of routine Turkish Society of Paediatric Oncology (TPOG) 2009-protocol. Expression of ALK, ATRX, HIF1a, HIF2a (EPAS), H2AFX and ETV5 genes were evaluated among these patients by using real-time PCR method.

Results: No significant relation was found between these genes and status of MYCN amplification, 1p loss, 11q deletion and 17q gain, except ALK, which is found to be highly expressed in patients with 17q gain ($p=0.018$). All genes found to be highly expressed in high-risk group compared to low-risk group, except ETV5. When "ultra-high-risk" and high-risk groups were compared, ALK found to be highly expressed in "ultra-high- risk" group ($p=0.027$) significantly, while ATRX found to be highly expressed in high-risk group ($p=0.01$).

Conclusion: Our results show that, ALK and ATRX may be the candidate genes that can be used to distinguish the "ultra-high risk" subgroup among high risk group of patients.

P-0520 | Assessment of the Clinical Importance of Molecular Basis of Neuroblastoma: A Proteomic Approach (on behalf of Turkish Paediatric Oncology Group)

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Background/Objectives: Identification of proteomic differences and biomarker for neuroblastoma, is still a demand for the therapy and prognosis of the disease due to its heterogenic molecular and clinical nature. The aim of this study was to compare the protein profiles of peripheral blood mononuclear cells (PBMCs) of different risk groups in neuroblastoma, in order to identify new possible molecular pathways or candidate biomarkers. Constituting sample pools eliminates personal differences and increase the possibility of identification of new biomarkers among different groups. Therefore, we compared the sample pools of different risk groups of neuroblastoma, in order to identify a possible candidate biomarker.

Design/Methods: In this study, PBMCs of $n=10$, $n=19$, $n=12$ and $n=11$ patients for control, high risk, intermediate risk and low risk groups, respectively, were pooled. Total protein isolations from groups were performed and the proteomic differences among these groups were identified by using MALDI-TOF/TOF mass spectrometry and MASCOT search engine.

Results: When control group and risk groups were compared, expression differences at 53 protein spots were identified. 9 out of 53 proteins, were identified at significance region in MASCOT search. Most of the proteins in the significance area belong to structural proteins such as fibrinogen and actin. Only protein change that was found to be significant and can be meaningful among risk groups was Manganese-superoxide dismutase(SOD2) protein. SOD2 protein showed a proportional expression difference among risk groups. This difference was significant at high-risk group, where SOD2 expression was 2.20 times higher compared to control group ($p < 0.05$).

Conclusion: Our results showed that Manganese-superoxide dismutase (SOD2) expression was proportionally expressed in different risk groups. SOD2 protein is unknown, although the exact impact on the development of neuroblastoma is not clear and studies are limited. Therefore, examining SOD2 protein expression in a variety of patients by immunohistochemically techniques, may be helpful to understand its role in neuroblastoma.

P-0521 | Clinically Importance of Prognostic Genetic Markers in Neuroblastoma (on behalf of Turkish Paediatric Oncology Group)

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Background/Objectives: Neuroblastoma is the most common extracranial solid tumour derived from neural crest. Approximately 50% patients are diagnosed at advanced stage and poor prognosis. The aim of this study was to evaluate the role some of the embryonic stem cell differentiation and apoptosis related genes and methylation status and relation with MYCN and risk groups in neuroblastoma.

Design/Methods: CASP8, PHOX2B, RASSF1A, HOXA9, LIMX1A, DCR2, THBS1, SOX2 and OCT4 gene expressions and methylation changes were studied in known MYCN amplification status in high risk($n=16$) and low risk($n=24$) neuroblastoma patients' tumors samples. Gene expressions and methylation status were analyzed by Real-Time PCR(qPCR) and quantitative multiplex-MSP, respectively.

Results: SOX2 and OCT4 gene expressions were increased while CASP8 expressions were decreased in high risk when compared with low risk($p < 0.05$). In MYCN positive samples SOX2, OCT4, LIMX1A genes showed increased expressions and HOXA9, THBS1, CASP8 genes showed decreased expressions in comparison with MYCN negative samples. SOX2, OCT4 and LIMX1A gene expressions were increased while CASP8 and THBS1 gene

expressions were decreased when the MYCN positive and high risk groups evaluated together. SOX2 and OCT4 gene expressions were increased and un-methylated in high risk group when compared to low risk group ($p < 0.05$). DCR2 and PHOX2B genes were determined as a methylated in low risk group, and un-methylated in high risk group. PHOX2B gene also showed higher expressions level at age of <18 months. According to Shimada, genes of PHOX2B and DCR2 were determined as un-methylated while SOX2 as methylated in good histologic group. Moreover, DCR2, THBS1, CASP8 and LIM1A gene expressions were significantly increased in good histologic group ($p < 0.05$).

Conclusion: Determination of OCT4 and SOX2 gene expressions and methylation status in MYCN amplified high risk group, also CASP8, LIM1A and THBS1 gene expressions and DCR2 and PHOX2B methylation status might be evaluated as a clinical prognostic marker in neuroblastoma.

P-0522 | Comparison of Cisplatin with Lipoplatin in Terms of Ototoxicity

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Background/Objectives: Cisplatin is an anti-neoplastic agent that has been used in treatments of both childhood and adult's cancers. It has many side-effects such as ototoxicity, nephrotoxicity, neurotoxicity. Lipoplatin is a liposomal cisplatin, consist of lipid and cisplatin. The aim of this study was to compare the ototoxic effects of lipoplatin versus cisplatin in the House-Ear-Institute-Organ of Corti-I (HEI-OC1) cells at the anti-tumoral doses.

Design/Methods: KELLY (NMYC-positive), SH-SY5Y (NMYC-negative) neuroblastoma and HEI-OC1 cells were cultured. LD50 doses of cisplatin and lipoplatin determined in KELLY and SH-SY5Y cells with WST-1 and then these doses were applied in HEI-OC1 cells. Apoptosis was determined by Flow-Cytometric Annexin-V/PI and Cell cycle tests.

Results: In the SH-SY5Y cells, LD50 doses of lipoplatin 750uM-1000uM cell viability was 57%-58%, the lowest dose of cisplatin is 50% of deaths from 10um achieved, dose increases with decreased cell viability. LD50 doses of lipoplatin 750mM-1000uM cell viability was 53%-51% and the 20um dose of cisplatin is 53% in KELLY cells. In the HEI-OC1 cells, 1000um lipoplatin led to 66% cell viability and from the doses of 50um of cisplatin decreased the cell viability below 50%(44%). Moreover, LD50 doses of cisplatin caused 62.3%-77.3% and lipoplatin 38.85-45.6% apoptotic cell death in KELLY cells. In SH-SY5Y, LD50 doses of cisplatin caused 75.8%-86.9% and lipoplatin also induced 25.3%-56.3% apoptosis. Cell cycle findings also determined the similar results with apoptosis. HEI-OC1 cells were kindly provided by Prof Kalinec and lipoplatin was provided by Gen-Pharmaceuticals.

Conclusion: In this study, the anti-tumoral and apoptotic effect of lipoplatin determined in neuroblastoma cells in a higher dose than cisplatin and at later time periods. Our study results suggest that lipoplatin has less ototoxic effect due to less apoptosis in cochlear cells compared to cisplatin. Further *in-vivo* comparative studies might be done for understanding the mechanism of ototoxic effects of lipoplatin versus cisplatin.

P-0523 | Effect of Mesenchymal Stem Cells and Tumour Infiltrating Lymphocytes on Cancer Stem Cells in Neuroblastoma (on behalf of Turkish Paediatric Oncology Group)

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Background/Objectives: Cancer stem cells(CSC) are small subset of cancer cells that are thought to play a central role in tumour initiation, progression and recurrence. Increased levels of CSCs is associated with poor prognosis. Recent studies showed that, CSCs and neuroblastoma cells differ in expression of some genes in Notch pathway. The aim of this study was to investigate the interaction between neuroblastoma cancer-initiating cells and the elements of the tumour microenvironment such as tumour infiltrating lymphocytes and mesenchymal stem cells(MSC).

Design/Methods: Single-cell suspensions of fresh neuroblastoma tissues were generated and cultured. CD133+ stem cells and CD54+/CD90+ mesenchymal stem cells were separated by magnetic isolation. Tumour infiltrating lymphocytes were isolated by AIMV migration method and expanded with GCSF and IL-2. Isolated cells, tumour infiltrating lymphocytes and cisplatin were seeded in multi-well plates in different combinations. The viability of cells were measured at 24 and 48 hours. Mann-Whitney-U test was used for statistical analysis and $p < 0.05$ was considered statistically significant.

Results: 20 neuroblastoma samples from 10 male and 10 female patients with mean age of 39 months were evaluated. It was observed that tumour infiltrating lymphocytes and mesenchymal stem cells protect the neuroblastoma cells from the effect of cisplatin. Tumour infiltrating lymphocytes has no effect on neuroblastoma stem cells, however mesenchymal stem cells was found to protect the neuroblastoma stem cells from the effect of cisplatin.

Conclusion: In this study, interactions between neuroblastoma CSCs and tumour microenvironment cells were investigated *ex vivo* for the first time. Our results showed that microenvironment favors the tumour via protection of neuroblastoma CSCs by mesenchymal stem cells from cytotoxic effects of cisplatin and protection of both neuroblastoma cells and neuroblastoma CSCs by tumour infiltrating lymphocytes. This interaction offers useful information to consider microenvironment in CSC-targeted therapies in neuroblastoma.

Note: This research was supported under the TPOG 2015 supporting project

P-0524 | Evaluation of Circulating Tumour Cell Load in Neuroblastoma (on behalf of Turkish Paediatric Oncology Group)

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Background/Objectives: Evaluating circulating tumour cell load has been determined in many cancers as a prognostic parameter for metastasis. Expensive methods such as FACS sorting flow cytometer based method or microfluidic dielectrophoretic method have been defined before but not used in neuroblastoma up to date. The aim of this study is to determine circulating tumour cell load in neuroblastoma by antibody labeled bead based method and to compare the load of circulating cells with clinical parameters.

Design/Methods: Total 63 neuroblastoma cases were included in this study from different risk groups. The blood samples collected during diagnosis were used. Mononuclear cells were extracted from blood and incubated with the anti-GD2 antibody attached beads. The number of neuroblastoma cells and the ratio of total cells were determined by cell counting device and flow cytometer.

Results: 30 of the cases were male, while 33 were female. The mean age was 31.7 months (1-168), 18 cases were low risk, while 14 cases were intermediate and 31 cases were in high risk. The mean GD2 positive cell ratio was 2.083% (0.18%-8.33%). GD2 positive cell ratio in peripheral blood was found statistically related with risk classification in Kruskal Wallis test ($p = 0.03$). This difference was related to high risk group. Circulating tumour cell loads were similar in low and intermediate risk groups. Circulating tumour cell load was not correlated with age, mycN, 1p LOH, 11q del, 17q gain, DNA ploidy histology, metastasis status alone.

Conclusion: Circulating tumors were found associated with high risk patients in neuroblastoma. Anti-GD2 antibody based bead separation method is a cheap and easy method to evaluate circulating tumour cells since neuroblastomas are known to express GD2 in 100%. The prognostic role of circulating tumour cells with survival should be evaluated after long term follow up.

P-0525 | Neonatal Cancer in Peru: 18 Years of Experience in the Rebagliati Hospital

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Background/Objectives: Cancer is detected in utero and neonatal diagnosis demands a multidisciplinary approach, that despite the immaturity of their organs and thanks the contribution of breastfeeding, patients tolerate cancer treatment.

Describe the epidemiology of neonatal cancer detection and multidisciplinary management, the important of breastfeeding during treatment and overall survival.

Design/Methods: Epidemiologic Descriptive Retrospective Longitudinal Study of thirtythree cases of neonatal cancer and survival analysis, period from January 1999 to March 2016, age from zero to 28 days of life; of one population of 2305 cases of childhood cancer in eighteen years and 108,353 livebirth in Rebagliati Hospital.

Results: Thirtythree patients, 36.36% diagnostic at birth by fetal ultrasound and 63.63% in the first month of life. Male 72.72% and female 27.27%.

Solid tumours 93.93%, all with increased tumour markers. Histology; germinal tumour 24.24%, followed by neuroblastoma 18.18%, hepatoblastoma 18.18%, retinoblastoma 15.15% sarcoma 9.09% and others 15.15% (leukaemia, brain tumours and wilms tumour). Location most common abdomen 30.3%, gonadal 24.24%, and ocular 15.15%. Metastasis in 27.2%. One cases RB1 mutation (+) and one case of polyhydramnios and wilms tumour. Treatment: 72.2% of cases received surgery and chemotherapy to 50% of the dose and 91.6% of them earned remission; 15.15% received only chemotherapy, 95 only surgery and 3% (one case) did not receive treatment.

The 93.95% of cases received breastfeeding, died only 12.9% of these by febril neutropenia and sepsis. In remission 69-69% (twenty three cases) and ten deaths (30.3%) by sepsis six, one relapse neuroblastoma, one default of treatment (botroid sarcoma), one kidney failure and one by disease progression (rhabdomyosarcoma metastatic). Overall survival 64.06 +- 2.6.

Conclusion: Fetal ultrasound and ocular screening at birth contribute to early diagnosis of childhood cancer.

Infant present a variety of oncological diseases predominating solid tumours; abdomen the most frequent location.

The breastfed infants tolerate post chemotherapy febrile neutropenia increasing their survival.

P-0526 | Tandem Peripheral Blood Stem Cell Transplantation as Treatment of Neuroblastoma in Children

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Background/Objectives: Currently investigate the feasibility of using tandem high-dose chemotherapy in the treatment of many malignant solid tumours. Nevertheless effectiveness convincing results haven't been obtained.

Design/Methods: From 2012 to 2015 year in the Department of Pediatric Oncology at the National Cancer Institute have been carried out 20 tandem transplantations (TT) in children with high-risk of neuroblastoma. Patient's age was 1 - 14 years. 14 pts. with primary neuroblastoma got TT after chemotherapy on HR-NBL-1/ESIOF protocol, 6 pts. as a consolidation of relapse second-line therapy. The first part of tandem transplantation was BuMel in all patients. Seventeen patients had topotecan-based regimens as the second part of tandem transplantation and three patients had CEM regimen. A time interval between parts of tandem was 1 - 3 months. For autologous transplantation have been used only peripheral stem cells. All patients received 13-cis retinoic acid after of conventional treatment.

Results: All patients successfully completed high-dose chemotherapy. There were neutropenia and thrombocytopenia 4th rate, oral mucositis with different degrees of severity in all patients. WBC count recovered more than 500/ μ L after first cycle on +10-15 day, PLT count recovered

on +13-28 day after PBSC. In 2 patient was observed neurotoxicity like short clonic and tonic seizures after second high-dose cycle. WBC count recovered more than 500/ μ L after second cycle on +9-14 day, PLT count recovered on +10-22 day. Currently, 10 of 120 patients are in CR, 3 patients had early relapse and continue treatment, 7 died of PD. The follow-up period after accomplishment of TT is 2 - 65 months.

Conclusion: Application of tandem transplantations in children with high-risk neuroblastoma resulted to three-year disease-free survival rate of about 46.8% and the overall three-year survival rate to 63.2%. With no possibility of mIBG therapy and antibody therapy, the use of tandem transplantation provides an opportunity to improve outcomes.

P-0527 | Perioperative Management of Hypertensive Neuroblastoma: A Study from the Italian Group of Paediatric Surgical Oncology (GICOP)

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Background/Objectives: Neuroblastoma is the most represented paediatric solid tumour. Hypertension is rarely reported with a lack of guideline on the perioperative management in literature. There is no evidence on the pathologic mechanism of hypertension in Neuroblastoma while in some cases it can be observed in patient without increased catecholamine.

Design/Methods: A retrospective survey was conducted by the Italian Group of Pediatric Surgical Oncology from 2006 and 2014. Patient with hypertensive symptoms were founded from the Italian Registry of neuroblastoma. All children that underwent surgical resection were included, and patient demographics, tumour histology, image defined risk factors, diagnostic urinary and blood analysis were studied in order to identify possible hypertensive risk factors. Perioperative medical treatment was analysed in order to identify a common national protocol.

Results: 1126 children were reported in the Italian Registry of Neuroblastoma from 2006 to 2014. 21 patients with hypertension (1.8%) were included in the study.

Anesthetic management was uniform in almost centers without hypertensive complications during the procedures. 28% (6/21) of patients needs an antihypertensive treatment for blood pressure control at a median follow-up of 36 months (range 4-96 months) despite the excision of the tumour. The involvement of the renal pedicle is the only risk factor ($p = 0.01$) for the persistence of symptoms hypertensive.

Conclusion: For the first time the involvement of the renal pedicle is described as a risk factor for the persistence of symptomatology hypertensive and all its possible cardiovascular consequences in addition to being a risk factor for surgical complications (nephrectomy, hemorrhage).

P-0528 | Reduction in Left Ventricular Myocardial Function in Long-Term Paediatric Neuroblastoma Survivors

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Background/Objectives: There are little data on the incidence of chemotherapy-induced myocardial dysfunction in long-term survivors of high-risk (HR) neuroblastoma. Our aim was to investigate the incidence of myocardial dysfunction in patients with high-risk (HR) neuroblastoma.

Design/Methods: We performed a retrospective case-control study between 2003 and 2012 of HR NBL patients treated according to the SIOPEN HR-NBL clinical trial at Our Lady's Children's Hospital, Dublin. Inclusion criteria were patients enrolled on the trial with an echocardiogram prior to commencement of chemotherapy and a subsequent echocardiogram on follow-up. Comparative echocardiograms were obtained on age-matched healthy controls.

Results: 36 patients met inclusion criteria. 53% were male ($n=18$). All patients received rapid COJEC induction, 83% received Busulfan/melphalan ($n=30$) and 61% topotecan ($n=22$). 21/40 over half received doxorubicin ($n=21$). Most recent echocardiography follow-up was an average of 22 months from initial study. There was no difference in fractional shortening (FS) pre- and post-treatment (36% and 34%) ($p=0.13$). Last measured FS in survivors and non-survivors (33% and 35%, respectively) was not significantly different ($p=0.18$). FS in older survivors (aged 8-15) reached significance when compared to controls ($p=0.0037$). There was also a significant difference between cases and age-matched controls when divided into quartiles by time since diagnosis ($p=0.079$, $p=0.01$, $p=0.07$, $p=0.04$, respectively). There was no dilation in left heart internal diameter at end diastole at any age between cases and controls.

Conclusion: Reduction in left ventricular fractional shortening is seen in older patients treated for HR neuroblastoma and this finding holds true when corrected for time since diagnosis. The mechanism of ventricular dysfunction is not due to progressive dilated cardiomyopathy, as

indicated by preserved left ventricular internal diameters in diastole between cases and controls. Further study is warranted.

P-0529 | Surgery with Extensive Resection Improves Survival in Patients with Stage IV Neuroblastoma

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Background/Objectives: Neuroblastoma (NBL) is the most common extracranial solid tumour in children. Despite a good overall prognosis, the outcome of children with stage IV NBL, even with multimodal intensive therapy, is still poor. The role of extended surgical resection remains controversial. Aim of this study was to analyze the impact surgical resection of overall and event free survival in stage IV NBL patients in a single center longitudinal study.

Design/Methods: We analyzed patient charts of 40 stage IV NBL patients treated in our institution between 01/1990 and 05/2012. Included were all clinicopathological findings of stage IV NBL patients exclusively. Extend of surgery was assessed from the operation records and was classified as subtotal (tumour biopsy, partial 50-90% resection) or radical (near complete >90% resection, complete resection). Overall (OS)- and event-free (EFS) survival was assessed using the Kaplan Meier analysis and log-rank test. A multivariate Cox regression analysis was used to demonstrate independency.

Results: 29/40 patients were operated radically (>90% resection), whereas 11 patients received subtotal resection or biopsy only. OS and EFS was significant higher in patients with radical surgery when compared to controls ($p=0.0003$ for OS, $p=0.004$ for EFS; log-rank test). A multivariate Cox regression analysis revealed radical surgery as significant and independent parameter for OS and EFS.

Conclusion: Our data indicate that radical (over 90% resection) surgery improves OS and EFS in stage IV NBL patients.

P-0530 | Neuroblastoma in Patients Under 18 Months, Single Institution Experience in Argentina

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Background/Objectives: The purpose of the review was to evaluate the outcome of patients under 18 months diagnosed with neuroblastoma.

Design/Methods: Between April 2006 and December 2013, 45 consecutive patients followed in Hospital de Pediatría Garrahan, were retrospectively reviewed.

Results: Median age of 9.5 months (1-18 months). Localization: adrenal gland (34%) paravertebral (29%), 2 or more sites involved (21%), cervical (9%), and mediastinal (7%). Histopathological diagnosis: poorly differentiated neuroblastomas ($n=31$), in differentiation ($n=3$), intermixed ganglioneuroblastoma ($n=1$), neuroblastoma uncharacterized ($n=9$), not biopsied ($n=1$). N-myc amplification was detected in 5 out of 38 patients (7 not studied), deletion of 1p (del1p) in 4 patients (12 without evaluating), and 11q aberration in one patient (only 8 patients studied). Two patients were excluded from the following analyses due to loss to follow up. According to INRG pretreatment classification schema, twenty-one L1 patients, were treated with chemotherapy ($n=1$), surgery ($n=15$), chemotherapy+surgery ($n=4$) and observation only ($n=1$). In eleven L2 patients, therapy consisted of chemotherapy ($n=3$), surgery ($n=4$) and combined surgery+chemotherapy ($n=4$) (1 N-myc amplified and 1 del1p). Nine stage M patients, (1 amplification of N-myc, one aberration of 11q, 3 amplification of N-myc with del1p) received treatment for intermediate-risk ($n=5$) and high-risk groups ($n=4$). Two patients classified as MS stage, received therapy strategy for intermediate and low-risk groups (observation). With a median follow-up of 53 (range: 6-109 months), at 24 months the EFS of all patients was 83% (SE 6%) and OS of 88% (SE 5%). Significant difference was found in OS and EFS between patients with stages L1, L2 and Ms vs stage M ($p=0.01$ and $p=0.01$ respectively). EFS for each stage: L1 85% (SE 7%), L2 100%, MS 100%, vs M 55% (SE 16%). OS: L1 90% (SE 6%), L2 100%, MS 100%, vs M 66% (SE 15%).

Conclusion: OS and EFS results are similar to those reported in international studies. However, better identification of biological prognostic factors will warrant accurate staging and consequently an appropriate treatment.

P-0531 | Dose Surgery Help If Biological Obscured Profile in Intermediate-Risk Neuroblastoma

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Background/Objectives: The survival rate among patients with intermediate-risk neuroblastoma who received reduced-dose chemotherapy is excellent. We performed a retrospective review of patients treated for intermediate-risk neuroblastoma to estimate event-free survival (EFS) and overall survival (OS) and to evaluate the impact of response to chemotherapy and degree of resection on the outcome of these patients.

Design/Methods: Medical records of patients with intermediate-risk neuroblastoma, who were treated at National Cancer Institute in Egypt from 2008 to 2012, were reviewed. First line chemotherapy was OJEC or OPEC or Vp16/CARBO & CADO. The patients were evaluated after 4 cycles for possibility of surgical excision and if not possible; they continued on the same

chemotherapy till being operable if there was response. Both OS & EFS were computed and analyzed in relation to different prognostic variables.

Results: Thirty two patients were candidate. We reported a complete response (CR) or a very good partial response (VGPR) to induction chemotherapy, with or without surgery in 34.3% of patients that has increased to 65.6% after 8 cycles. The 3-year OS and EFS were 89% and 77% respectively. There was significant difference in 3-years OS and EFS between patients who underwent $\geq 90\%$ versus $< 90\%$ resection of primary tumour (100% and 57% versus 93.3% and 32.4% respectively; $p=0.02$). The 3-years OS rate among those who achieved CR or VGPR post induction therapy was slightly higher than those achieved PR only (90.9% and 87.1% respectively; $p=0.5$).

Conclusion: Degree of surgical resection had a significant impact on survival especially those who still had bulky disease after induction therapy and were treated in institutes lacking biology tailored therapy.

P-0532 | Molecular Mechanism of Transcription Factor Gli in EMT Induced by TGF-Beta1 in SK-N-SH Cells

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Background/Objectives: Study on the molecular mechanism of transcription factor Gli in epithelial-mesenchymal transition (EMT) induced by TGF-beta1 in SK-N-SH cells.

Design/Methods: Elucidate the mechanism of Smad signaling pathway in EMT induced by TGF-beta1 through over expression and interference of Smad2/3 in SK-N-SH cells. Detected the expression of transcription factor Gli in SK-N-SH cells and the expression changes of cell proliferation, cell apoptosis, EMT key molecules induced by TGF-beta1 after SK-N-SH cells treated with GANT61 and siRNA.

Results: (1) The expression of Smad2 and Smad3 were not increased in EMT induced by TGF-beta1 in SK-N-SH cells. The EMT phenotype didn't been promoted by transfected with Smad2 and Smad3. Interference the expression of Smad2 and Smad3 did not affect the EMT induced by TGF- β 1 in SK-N-SH cells.

(2) SK-N-SH cells existed the positive expression of transcription factor Gli. GANT61 which was targeting transcription factor Gli/2 can inhibit the expression of Gli, and reduce the cell proliferation and promote the apoptosis of SK-N-SH cells.

(3) The expression of transcription factor Gli in EMT induced by TGF-beta1 increased significantly, while over expression or interference of Smad2/3 did not affect the increasing expression.

(4) Interfering with the expression of Gli1/Gli2 can inhibit the EMT induced by TGF-beta1 in SK-N-SH cells.

Conclusion: The EMT induced by TGF-beta1 in SK-N-SH cells does not depend on the Smad signaling pathway. Transcription factor Gli participates in the EMT induced by TGF-beta1 in SK-N-SH cells through non Smad dependent signaling pathways.

P-0533 | Staging and Assessing Functional Tumour Response in Children with Neuroblastoma with 18-Fluoro De-Oxy Glucose Positron Emission Tomography Computerized Tomography (FDG PET/CT)

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Background/Objectives: The aim was to assess the role of PET/CT in initial staging, restaging and determining the tumour response to chemotherapy in neuroblastoma.

Design/Methods: Children with neuroblastoma were subjected to conventional imaging and FDG PET/CT. A baseline study and a repeat PET/CT (after two courses of chemotherapy with gap of 8-9 weeks) were compared to determine early response to chemotherapy. The FDG uptake was classified as none, mild, moderate and intense. The response was measured as complete, partial, none or progressive disease.

Results: On conventional imaging, 14 primary lesions were seen in 12 cases. Of these 14 primary lesions, 10;3;1 were adrenal; pelvic/extra-adrenal abdominal and mediastinal in location. Of 10 primary adrenal lesions, 3;3;3;1 lesions showed none;mild/moderate; intense FDG uptake. Of 3 primary pelvic or extra adrenal abdominal lesions, 1;2 showed moderate; intense uptake. Mediastinal lesion showed moderate uptake. Three lesions in 2 cases of stage 4S neuroblastoma showed no uptake. PET/CT staging matched with conventional imaging staging in 6/12 cases. In 4/12 patients, FDG PET/CT demonstrated 5 new lesions not detected with conventional imaging modalities: 2 cervical lymph node lesions, 1 splenic lesion, 1 vertebral lesion, and diffuse radiotracer uptake in the bone marrow. Thus, PET/CT scan upstaged 4/12 (33.3%) patients. However, PET/CT missed malignant lesions in 1 patient (8.3%) when compared with conventional imaging.

Follow-up PET/CT scan was done in 11 patients with primary lesions. The 11 lesions on baseline PET/CT had shown no; mild/moderate; intense FDG uptake in 1; 2; 5 and 3 patients. The initial response after chemotherapy was complete; partial; none (not evaluable as negative uptake) and progressive in 3;6;1 and 1.

Conclusion: FDG PET/CT is instrumental in picking up active lesions for accurate staging and also following up the functional tumour response to chemotherapy despite differentiating fibrotic lesions from active residual lesions.

P-0534 | A Phase II Study of Bold Delayed Local Control Strategy in Children with High Risk Neuroblastoma: Japan Neuroblastoma Study Group (JN-H-11) Trial

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Background/Objectives: The survival rates of high risk neuroblastoma (HR-NB) patients are still unacceptable. The 5-year OS and EFS for 50 patients of the Japan Neuroblastoma Study Group (JNBGS) phase II clinical trial (JN-H-07) were 48.4 \pm 7.2% and 32.2 \pm 6.8% respectively. The increase of time intensity and dose intensity are both key strategy of the treatment for HR-NB. In Japan it had taken too much time to restart the chemotherapy after surgery. Sometimes we needed more than one-month because of surgical adverse effects. The increase of time intensity for the chemotherapy is important problem to solve. JNBGS has examined a clinical trial of time - intensive multimodal treatment with bold delayed local control strategy (DLC) prospectively.

Design/Methods: Between May 2011 and September 2015, seventy-five patients with newly diagnosed HR-NB patients were enrolled. DLC consisted of induction chemotherapy (IC), myeloablative chemotherapy (MAC), and local control treatment after MAC. IC consisted with cisplatin (100mg/m²), pirarubicin (40mg/m²), vincristine (1.5mg/m²), and cyclophosphamide (2,400mg/m²). After 5 courses of IC, all patients were immediately followed by MAC with carboplatin (1,600mg/m²), etoposide (800mg/m²), and melphalan (200mg/m²)(MEC) with autologous PBST. After these treatments, local tumour eradication with surgery and irradiation (21Gy) were performed.

Results: Total 75 patients were enrolled, 70 were evaluable: 46 male, 66 > 18 months-old, 61 stage4, 22 MYCN amplified. 41 patients were completed protocol treatment, while discontinued in 21 patients. No patients died during the protocol treatment nor within 30 days after completion of the protocol treatment. The Grade 4 adverse effects were seen in 24 cases. The surgeries were performed safely without affecting the overall schedule in these cases.

Conclusion: Local control treatment could be postponed until after MEC in a notable number of cases. Bold DLC strategy was feasible. In the currently ongoing high-risk NB study (JN-H-15), bold DLC is performed after BU/MEL treatment.

P-0535 | Significance of Molecular-Biological Prognostic Factors in High-Risk Neuroblastoma Patients

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Background/Objectives: In past few decades prognosis in low and intermediate risk neuroblastoma was significantly improved but in high-risk patients it remains dismal instead of multimodal treatment.

Aim is the investigation of molecular-genetic prognostic markers in high-risk neuroblastoma patients.

Design/Methods: According to NB2004 protocol, high-risk group encompasses patients with MYCN amplification (MNA) and stage 4 disease above 12 months of age. In 50 high-risk patients detection of genetic aberrations was performed by MLPA. Molecular-genetic detection of bone marrow (BM) involvement and minimal residual disease (MRD) was investigated by PHOX2B/TH genes expression in 34 cases. Event-free (EFS) and overall survival (OS) rates were calculated with median of follow-up time 2.16 years.

Results: In the analyzing cohort of high-risk patients EFS was 0.25(0.06), OS - 0.32(0.07). 22 of 50 patients had MNA. Neither of genetic abnormalities detected by MLPA (deletions of 1p,3p,4p,9p,11q,14q; gains of 2p(MYCN),4p,7q,12q,14q,17q and MNA) did not show prognostic significance in total and MYCN single copy high-risk patients. Presence of BM disease detected by PHOX2B/TH expression at the time of primary diagnostics did not reveal adverse prognostic impact. At the same time patients free from MRD during the induction treatment had superior survival rates: EFS 0.50(0.20) vs. 0.21(0.17), $p=0.022$, OS 0.67(0.19) vs. 0.21(0.17), $p=0.044$. Persistence of MRD until the completeness of the induction chemotherapy (6 courses N5/N6) was fatal (both EFS and OS 0.00 vs. 0.51(0.18) and 0.64(0.17), $p=0.013$ and $p=0.012$ respectively). Presence of MRD before hematopoietic stem cells apheresis (HSC) was marker of dismal prognosis despite of proved purity of HSC preparation and CD34+ selection (both EFS and OS 0.00 vs. 0.52(0.12) and 0.65(0.12), $p=0.026$ and $p=0.013$ respectively).

Conclusion: Presence and persistence of MRD detected by highly sensitive technique during and after the induction chemotherapy is powerful marker of adverse prognosis in high-risk neuroblastoma patients. HSC apheresis after the achieving of MRD-negativity is extremely important.

P-0536 | The Changes of Neutrophils and Lymphocytes after Chemotherapy in Children with High-Risk Neuroblastoma and Factors Related to Severe Infection

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Background/Objectives: Investigation of the changes of neutrophils and lymphocytes during chemotherapy courses in children with high-risk neuroblastoma, as well as severe infection rate, therefore to provide guidance to prevent infection in these children.

Design/Methods: Analyzed 34 cases of children with high-risk neuroblastoma, who were hospitalized in Xinhua hospital from July 2012 to September 2014, we recorded reactions after chemotherapy and the results of routine blood test on every 5 days during the whole chemotherapy period.

Results: The counts of neutrophils and lymphocytes dropped to minimize in the tenth day or so during chemotherapy, risen near the 15th day. Infections were negatively correlated with the number of neutrophils and lymphocytes in the tenth day. Persistent lymphopenia occurred after the fourth course of chemotherapy. Occurrence of grade IV bone marrow suppression after chemotherapy was 90%, and occurrence of grade III or IV infection rate was 15.5%. There were significant differences in infection rates between combination chemotherapy regimens used in high-risk neuroblastoma children.

Conclusion: Children with high-risk neuroblastoma had obviously high rate of bone marrow suppression and high incidence of severe infection after chemotherapy, especially after CTX + Adr + VCR regimens. More attentions should be paid to this group of children and preventive measures were worthy of taking into account.

P-0537 | A Study on Effects of the National-Wide Mass Screening for Neuroblastoma in 6-Month-Old Infants in Japan for Incidence of Ganglioneuroblastoma and Ganglioneuroma

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Background/Objectives: A nationwide mass screening for neuroblastoma (NBL) in 6-month-old infants (MS6M) in Japan was carried out for 18 years, and was discontinued in 2004. Among neuroblastic tumors, ganglioneuroblastoma, intermixed (GNBL-I) and ganglioneuroma (GN) are known to show excellent prognosis. Effects of MS6M for incidence of GNBL-I/GN are studied.

Design/Methods: Three hundred and ten cases were diagnosed as neuroblastic tumour at our hospital during 1970 to 2015. Chart review and histological reevaluation according to International Neuroblastoma Pathology Classification were carried out.

Results: Out of 310 cases, 148 cases were detected by MS6M, 8 cases were detected by routine examination for pulmonary tuberculosis using chest X-ray, which was carried out for school-age children until 1993 in Japan, and the remaining 145 cases showed some clinical symptom. On histological examination, 16 of 145 cases were diagnosed as GNBL-I, and 10 were GN. Eight were patients before starting MS6M (22-167 months old at diagnosis), 4 were during MS6M (22-77 months old at diagnosis), and 14 were after discontinuance of MS6M (28-148 months old at diagnosis). The proportion of GNBL-I/GN to all neuroblastic tumors with clinical symptom were 22.2%, 8.2%, and 20.3%, in the period before, during, and after MS6M, respectively.

Conclusion: Incidence of GNBL-I/GN decreased during MS6M, and re-increased after discontinuance of MS6M. During MS6M, a considerable number of MS6M detected neuroblastomas of infants were surgically resected. It is assumed that tumors which would develop as GNBL-I/GN in older age, might be included in these resected neuroblastomas in infantile period. The results of the present study implied spontaneous maturation of a subset of infantile neuroblastic tumors. Extensive national-wide investigations and data analysis are desirable to confirm probability of the present study.

P-0538 | Two Extreme Presentations of Perinatal Neuroblastoma – Case Series and Review of Literature

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Background/Objectives: Neuroblastoma is well known for dramatic clinical heterogeneity, which spans from spontaneous regression or differentiation in some patients, to relentless disease progression despite intensive multimodality therapy in others. Here we report two cases of perinatal neuroblastoma, which are on the two extremes of clinical spectrum.

Design/Methods: Case 1: Antenatally diagnosed at 37 weeks, delivered by normal vaginal delivery, MRI abdomen revealed a localized right supra renal mass, MIBG scan was negative. Biopsy of the lesion revealed favourable histology. Bone marrow biopsy revealed no blasts, N MYC amplification was negative. Periodic ultrasonogram every month revealed no progress in size of the lesion, child is thriving well, Nil intervention.

Case 2: Antenatally diagnosed at 37 weeks, delivered by normal vaginal delivery, had massive abdominal distention at birth, developed respiratory distress on day 2 of life, needing oxygen support. MRI abdomen revealed localized retroperitoneal mass, MIBG was negative. Biopsy of the lesion revealed neuroblastoma with poor stroma and undifferentiated histology, N MYC amplification was negative. Child received two cycles of Etoposide and Carboplatin; Poor response to chemotherapy. Radiation therapy was deferred after discussion with family and chemotherapy changed to cyclophosphamide, after which reduction of liver size and adrenal mass noted. Currently on cyclophosphamide third cycle.

Results: Neuroblastoma-most common neonatal malignancy, arising from the sympathetic nervous system.

Patients with stage IV S disease without life- or organ-threatening symptoms or adverse genetic features (N MYC amplification or segmental chromosomal abnormalities) can be safely observed for spontaneous regression. Aggressive treatment may not always be necessary.

Conclusion: Infants with antenatally diagnosed neuroblastoma with unfavorable features should undergo early surgical excision, whereas patients with favourable features could be observed awaiting spontaneous regression of the mass, reserving delayed surgery for tumors that increase in size or do not regress.

P-0539 | A Case of Rubinstein-Taybi Syndrome and Neuroblastoma with Heterozygous EX1 Deletion; Ex4-Ex16 Duplication Crebbp Mutation

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Background/Objectives: Rubinstein-Taybi syndrome (RTS) is rare autosomal dominant genetic disease, characterized by typical facial features, microcephaly, broad thumbs and first toes, intellectual disability, postnatal growth retardation, eye anomalies, congenital heart defects and mental retardation. Besides the classical features and medical problems, patients with RTS have an increased risk of developing malignancies. It can be explained by the lack of tumour suppressor activity of CREBBP. Here we describe a patient with RTS and neuroblastoma with new mutation.

Design/Methods: The male, seventeen months old patient, was admitted to our hospital with complaint of cough, fever, wheezing and recurrent lower respiratory tract infections. On physical examination, he has dysmorphic features with frontal bossing, micrognathia, high palate, flattened nasal bridge, neuromotor retardation and undescended testis on the right side. There wasn't any mass in the abdomen. RTS was confirmed with genetic testing showing genomic rearrangement, CREBBP mutation EX1 deletion, EX4-EX16 duplications. On the laboratory investigation, sedimentation was 5 mm/h, LDH 230U/L, NSE 33 ng/mL, VMA 7 mg/d. There wasn't any bone marrow involvements and rosette formation on bilateral bone marrow aspiration. Ultrasound and MRI of the abdomen revealed (after the mass was detected in lower thorax CT section) solid mass in the left adrenal with 33x21x24mm diameter. Small right to left shunted patent foramen ovale was detected by echocardiography. The mass was excised with surrectomy.

Results: The diagnosis of differentiated neuroblastoma was confirmed after histopathologically examination of the mass. Patient was classified as stage I, low risk neuroblastoma according to INSS and followed without any additional therapy after 61 months of operation.

Conclusion: This patient was presented due to emphasize the association RTS with neuroblastoma and informed newly identified mutation. RTS have an increased risk of developing malignancies, so after the diagnosis of RTS clinically or genetically, patient must be investigated and followed for malignancies.

P-0540 | Epithelial to Mesenchymal Transition and Minimal Residual Disease Monitoring in Neuroblastoma

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Background/Objectives: Not all neuroblastoma patients that relapse can be recognized by PCR-based monitoring of bone marrow (BM) and peripheral blood (PB). Because epithelial to mesenchymal transition (EMT) is shown to be involved in tumour progression and therapy resistance and it also has recently been demonstrated that neuroblastoma consists of neuroepithelial (NE) and mesenchymal (MES) cells, the aim of this study was to identify MRD-markers that can specifically detect MES-neuroblastoma cells and to study the dynamics of these markers during treatment.

Design/Methods: Microarray data were used to identify genes differentially expressed between NE and MES neuroblastoma cell lines. This was followed by extensive RQ-PCR testing in cell lines, control BM, PB, PBSCs and cell subsets. After selecting a specific panel of markers several serial PB, PBSC and BM-samples from high-risk neuroblastoma patients were tested. Detection of MES-RNA markers was compared with NE-RNA markers. For a cohort of patients PBSC samples were tested and survival analyses were performed.

Results: PRRX1, POSTN and FMO3 were selected as MES NB marker panel. MES-mRNA was not frequently detected in PB-samples. However, MES-mRNA was frequently detected in PBSC-samples and was associated with a poor event free survival. In 95 serial BM-samples from 13 patients in complete remission and 16 relapse patients MES=RNA markers showed different dynamics during treatment compared to NE-RNA markers. Furthermore, MES-mRNA was more frequently detected in BM samples from relapse patients (53%) than in BM from patients in CR (32%) (p=0.03).

Conclusion: We propose to use POSTN, PRRX1 and FMO3 as marker panel for the detection of MES neuroblastoma cells in PB, BM and PBSCs in neuroblastoma patients. MES markers show different dynamics during treatment and are more frequently positive in patients with adverse outcome. To study the clinical significance these markers should be used alongside the current MRD markers in large prospective studies.

P-0541 | RNA-Seq Discovers New lncRNA Regulators in High-Risk Neuroblastoma

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Background/Objectives: Neuroblastoma is a heterogeneous tumour that has poor survival and ineffective treatment for high-risk patients. Our objective is to identify long non-coding RNAs (lncRNAs) that play an important function in these patients using RNA-seq of matched cell-line pairs from individual patients.

Design/Methods: 5 high-risk cell line pairs were selected for RNA-seq from the COG repository using the Illumina HiSeq 2000 platform and a strand-specific library (SMS-KANR, NBL-WR, SK-N-BE(2), CHLA-20, CHLA-136). Bioinformatics were performed using the STAR-Cufflinks pipeline. Differentially expressed lncRNAs were knocked-down and were further functionally characterized using the AlamarBlue-, Caspase 3/7 Glo-, scratch- and transwell assay. Of the functionally characterized lncRNAs, three lncRNAs were chosen for RNA-seq on the NextSeq 550 platform to elucidate their genetic function.

Results: From the knock-down studies, one of the lncRNAs expressed at the 1p36 tumour suppressor locus showed a >2 fold increase in Caspase 3/7 activity and a reduction in viability. Another gene, expressed at the tumour suppressor locus 14q32 had a lower rate of migration in the transwell and the scratch assay. A third gene, showing negative correlation to MYCN expression, had impact on the viability and the expression of the TP62 gene. Interpretation of the RNA-seq results of the respective knock-down are finished during April 2016. The HUGO gene names of these lncRNAs are purposely not disclosed here.

Conclusion: These lncRNAs are important regulators in neuroblastoma tumorigenesis. One or more of these lncRNAs will be presented at the conference.

P-0542 | Profile of Neuroblastoma Patients Using the "Ultra High-Risk" Classification

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Background/Objectives: Background: Children with high-risk neuroblastoma constitute a heterogeneous group, but little attention has been paid to further subdivision of the high-risk group, and recent work in this group define a new subclassification as ultra high risk which achieved only 12% of event free survival to 5-year. These studies did not include hispanic patients and in Mexico 80% of neuroblastoma cases are diagnosed in advanced stages.

Objectives: To present the casuistry of immunohistochemical, molecular diagnosis and nuclear medicine diagnostic of ultra high-risk neuroblastoma in an oncologic paediatric hospital in Mexico.

Design/Methods: Methods: Evaluation with histopathological routine studies including immunohistochemical techniques and molecular studies searching for MYC-N amplification plus imagenology studies like CT scan and MRI and bone scan and evaluation of bone marrow involvement. A description of these findings is describe in this study.

Results: Neuroblastoma patients with new diagnosis were received and evaluated Seven paediatric patients: 5 male and 2 female, with an average age of 2.6 years were evaluated attending diagnostic assessment for the first time with retroperitoneal or mediastinal tumors in most cases. Two of the seven patients filled the requisites for the diagnostic of ultra-high risk neuroblastoma as follows: bone metastasis and amplification of MYC-N. These two patients died because of tumour activity and the other five are alive until now.

Conclusion: In our experience there are a suggestive evidence of the relationship of the expression of, Ki67 and MYCN amplification and nuclear medicine of diagnosis methods, with the degree of differentiation of neuroblastic tumors, being higher in less differentiated tumors. Although the data presented here are modest, they are suggestive of a patient population with characteristics of an alleged group of ultra high risk, it will require further studies with a bigger cohort of patients to assess their relevance in our population.

P-0543 | Catecholamines Profiles at Diagnosis: Increased Diagnostic Sensitivity and Correlation with Biological and Clinical Features in Neuroblastoma Patients

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Background/Objectives: Neuroblastoma accounts for 10% of the paediatric malignancies and is responsible for 15% of the paediatric cancer-related deaths. Vanillylmandelic acid (VMA) and homovanillic acid (HVA) are most commonly analyzed in urine of neuroblastoma patients. However, their diagnostic sensitivity is suboptimal (82%). Therefore, we performed in-depth analysis of the diagnostic sensitivity of a panel of urinary catecholamine metabolites.

Design/Methods: Retrospective study of a panel of 8 urinary catecholamine metabolites (VMA, HVA, 3-methoxytyramine, dopamine, epinephrine, metanephrine, norepinephrine and normetanephrine) from 301 neuroblastoma patients at diagnosis. Special attention was given to patients with MIBG non-avid tumors and patients without elevation of VMA/HVA.

Results: Elevated catecholamine metabolites, especially 3-methoxytyramine, correlated with 9 out of 12 neuroblastoma characteristics such as stage, age, MYCN amplification, loss of heterozygosity for 1p and bone-marrow invasion. The combination of the classical markers VMA and HVA had a diagnostic sensitivity of 84%. Normetanephrine was the most sensitive single diagnostic metabolite with an overall sensitivity of 89%. When all 8 metabolites were combined, a diagnostic sensitivity of 95% was achieved. Among the VMA and HVA negative patients, were also 29% with stage 4 disease, which usually had elevation of other catecholamine metabolites (93%). Diagnostic sensitivity for patients with MIBG-non-avid tumour was improved from 33% (VMA and/or HVA) to 89% by measuring the whole panel.

Conclusion: Our study demonstrates that analysis of a urinary catecholamine metabolites panel, comprising 8 metabolites, ensures the highest sensitivity to diagnose neuroblastoma patients.

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P-0544 | Catecholamine Metabolites, Clinical Outcome and A New Insight into Risk Stratification of Patients with Neuroblastoma

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Background/Objectives: Neuroblastoma patients receiving the same treatment can still have a markedly different clinical course, indicating the necessity for more accurate prognostic parameters. The intrinsic property of most neuroblastoma to excrete catecholamine metabolites is being used for diagnostic purposes, however, their prognostic value with respect to clinical outcome has hardly been investigated. Therefore, we performed an in-depth analysis of the prognostic value of a panel of urinary catecholamine metabolites.

Design/Methods: Retrospective study of 8 urinary catecholamine metabolites [vanillylmandelic acid (VMA), homovanillic acid (HVA), 3-methoxytyramine (3MT), dopamine, epinephrine, metanephrine, norepinephrine, and normetanephrine] from 301 neuroblastoma patients at diagnosis. For metabolites that correlated with event-free survival (EFS) and overall survival (OS), optimal cut-off were calculated based on Cox proportional hazard for further survival analysis.

Results: Multivariate analysis, using the new cut-offs, revealed that only HVA and 3MT were independent risk factors for event-free survival and overall survival. EFS and OS of stage 4 patients without elevated 3MT were significantly better compared to those with elevated 3MT (5-years EFS 54.7% versus 18.1%, 5-years OS 58.3% versus 25.0%, both $p < 0.001$). Similar subdivision was achieved with 3MT in other clinical subgroups. By implementing 3MT as an independent factor in risk stratification, a new group of ultra-high-risk patients with very poor prognosis was identified.

Conclusion: Measuring catecholamine metabolites, in particularly 3MT, can identify patients with poor outcomes. The observation that elevated levels of 3MT are associated with clinical outcome, even more specifically than the current risk factors (such as stage), suggests that 3MT might be used as an additional independent marker for further risk stratification assessments.

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P-0545 | Association of MYCN Status with Certain Prognosis Factors of Vietnamese Neuroblastoma from 2013-2015

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Background/Objectives: Neuroblastoma (NBL) is the most common extracranial cancer of early childhood. It accounts approximately 15% of all childhood cancer-related mortality. There are the some common prognostic factors, like age, stage... NBL genetic features have been used for risk stratification for more than 20 years, in which the amplification of the MYCN gene, observed in 20-25% of NBL, is the most widely used as the most powerful prognostic factor.

Design/Methods: We study, in a series of 13 patients (2013-2015), the association of MYCN status with age, stage, histopathology, VMA/HVA ratio, LDH level.

Results: Amplification of MYCN is found on 27/131 (21%) patients.

For the age of diagnosis, the over 18 months group have the largest number of MYCN amplification (14/27 patients), the next one is the 0-12 months (9/27 patients), the remaining is the 12-18 months (4/27 patients).

There are 84/131 patients, who staged following INGRSS. The MYCN amplification is found highest in L2 (11/18 cases) and M (5/18 cases) group. This number in other groups is both 1/18 cases in L1 and M5.

The favorable and unfavorable histology groups show the same frequency of MYCN amplification, (11/24 patients) and (13/24 patients), respectively. There are 12 unclassified cases

Only 1 patient, who have the VMA/HVA ratio above 1, is amplified MYCN. The remaining group (VMA/HVA ratio below 1) has 20/21 amplified MYCN patients.

About 118 patients, who are performed the LDH test, are divided in 3 groups ($\leq 1N$, $1N-3N$ and $\geq 3N$). The *MYCN* amplification in each group is 3/24, 4/24 and 17/24 patients.

Conclusion: The amplification of *MYCN* is strongly associated with worse prognosis factors, like age > 18 months, stage M, unfavourable histology, VMA/HVA ratio below 1 and high LDH level. The other prognosis factors could be easily accessed, however, the *MYCN* status determined by FISH is one of the most important tools for treatment stratification.

P-0546 | Clinical Analysis and Treatment Experience of Rupture of Children with Retroperitoneal Neuroblastoma

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Background/Objectives: Neuroblastoma is a childhood high incidence of malignant tumors, tumour rupture hemorrhage is a serious complication, rapid progress, the treatment is very difficult, with low success rate and high mortality rate. To summary the clinical features, diagnosis, and treatment of the children with neuroblastoma.

Design/Methods: To retrospect the clinical data of 9 cases of neuroblastoma combined with tumour ruptured in our hospital from January 2013 to November 2014. Delineate the clinical and laboratory features. Analysis of treatment plan and treatment effect.

Results: 9 cases showed for the hypotension, poor peripheral circulation, which 8 cases showed abdominal circumference increased quickly and abdominal pain; 1 cases of hemoptysis; 1 case of hematuria. All cases were diagnosed as tumour rupture and symptomatic treatment: 2 cases of survival after chemotherapy, 4 cases tumour rupture in chemotherapy, 3 cases of tumour rupture and low blood volume shock, death.

Conclusion: The tumour rupture of the children's neuroblastoma tumour is sudden, rapid and high mortality, and there is no clear indicator of tumour rupture.

P-0547 | Primary Identification of Genomic Markers of Drug Sensitivity for Individualized Therapy in Children with Neuroblastoma in III-IV Stage

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Background/Objectives: Acquired multi-drug resistance and followed tumour recurrence and metastasis are the main challenge for the treatment of neuroblastoma, and recent studies found that difference of genomic markers of drug sensitivity correlated the different response for chemotherapy. Our study is to identify the significance of genomic markers of drug sensitivity for individualized therapy in children with neuroblastoma.

Design/Methods: The surgical specimens and peripheral blood samples in 13 children with neuroblastoma were collected between Apr.2011 and Apr.2013. The genomic markers of anticancer drug sensitivity were examined, including gene expression or mutation of 12 chemotherapeutic agents and 1 targeted drug by methods of immunohistochemical (IHC) staining, enzyme linked immunosorbent assay (ELISA), fluorescence in situ hybridization (FISH), polymerase chain reaction (PCR) amplification and sequencing.

Results: The tumour tissue of the targets for chemotherapeutic agents such as topoisomeraseIIA (TOPOIIA), Tubulin β 3, excision repair cross-complementing 1 (ERRC1), topoisomerase (TOPOI), 06-methylguanine-DNA methyltransferase (MGMT), dihydrofolate reductase (DHFR), thymidylate synthase (TS) were examined. What's more, the peripheral blood of the targets for chemotherapeutic agents such as CYP2C9*3 genotypes and dihydrofolate reductase (DHFR C829T) genotypes were detected. It showed that tumour/blood samples had high sensitivity to fluorouracil (5-Fu), vincristine(VCR), cyclophosphamide (CTX) and methotrexate (MTX), while had low sensitivity to paclitaxel, temozolomide/carmustine/semustine, anthracycline/etoposide, topotecan/irinotecan and platinum. Additionally, tumour tissues or blood samples of the genomic markers for targeted drugs, such as vascular endothelial growth factor receptor-2 (VEGFR-2) and intercellular cell adhesion molecule-1 (ICAM-1) were examined. The results showed samples had high sensitivity to Bevacizumab (Avastin). On the basis of the above test results, therapeutic strategy for the patients who had unsatisfactory curative effect were promptly adjusted and improved. Then, we achieved favourable results, and created surgical opportunities for some patients.

Conclusion: This study firstly examined the genomic markers of drug sensitivity in children with neuroblastoma, which provide laboratory basis and clinical experiences for individualized treatment selection.

P-0548 | Factors Affecting Recovery of Neurological Deficits in Surgical Management of Intraspinal Ganglioneuroma: Report of 2 Paediatric Cases and Literature Review

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Background/Objectives: Ganglioneuroma is a rare benign neuroblastic tumour. Intraspinal ganglioneuroma, which invade into the spinal canal and cause neurological symptoms, has been reported. Here, we report 2 cases of intraspinal ganglioneuroma with surgical removal; a case with good neurological recovery, the other suffering severe neurological deficits. Possible correlation of pathological findings and ¹²³I-MIBG SPECT on a case, and appropriate timing of resection surgery for good neurological outcome is discussed referring past articles.

Design/Methods: Two paediatric cases of intraspinal ganglioneuroma is shown here; a case of 2-year-old girl and a case of 3-year-old boy.

Results: The girl was suffering from gait disturbance. The tumour had a large mass in posterior mediastinum, invading into spinal column between C6 to T5. Surgical decompression of the tumour was performed and gait disturbance ameliorated. Pathological findings revealed it ganglioneuroma. The lesion had strong uptake on ¹²³I-MIBG SPECT in the left thoracic cavity that is remained without pathological examination on the spot. Active pathological features like neuroblastoma were speculated with elevation of Vanillylmandelic acid and Homovanillic acid in urine test of the girl. In the second case, the boy complained motor weakness of the lower extremities that had appeared almost 1 year before. Surgical decompression of intraspinal ganglioneuroma from T11 to S1 was also performed, resulting with poor neurological outcome. That was considered due to the long duration of the neurological symptoms.

Conclusion: Early surgical excision is recommended for neurological symptoms of intraspinal ganglioneuroma. Predicting factors other than timing of surgical removal for the outcome of surgical decompression are still unknown; therefore more research needed to be done for it.

P-0549 | The Risk of Post-Surgical Kidneys Dysfunction in Children with Neuroblastoma (NBL) - the Role of Image Defined Risk Factors (IDRF) in Preoperative Evaluation

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Background/Objectives: The risk of kidneys function disturbance after surgery in children with localized and disseminated neuroblastoma was evaluated on the basis of presence of presurgical IDRF related to kidneys.

Design/Methods: From 2002- March, 2016, 100 patients with NBL stage 2-4 were treated in the Department of Pediatric Oncology and Haematology, Institute of Pediatrics in Krakow; 73 with tumors in abdomen had tumors removed in the Department of Pediatric Surgery. In all patients with abdomen tumour, imaging performed before surgery was analyzed for the presence of IDRF.

Results: In 23 children (31.5%), IDRF defined as renal pedicle infiltration and/or infiltration of one or both kidneys were present at presurgical imaging. In this group, kidneys in post-operative imaging as well as GFR were evaluated and compared with the GFR results in children with other tumour localization or abdominal tumors without IDRF related to kidneys.

In 5/23 (22%) children the postoperative kidneys dysfunction was found. Ischemic lesions were found on control post-operative imaging, described as partial (n=3) or total (n=2) kidneys dysfunction. In 1 child it was necessary to remove the kidney after chemotherapy because of uncontrolled hypertension with the loss of kidney function. In this group, if kidneys dysfunction was described in post-operative imaging, GFR was lower than in children without any pathologies at this time. Present IDRF related to kidneys may predict the increased risk of increased GFR after surgery.

Conclusion: Evaluation of IDRF before surgery may be helpful in predicting the risk of post-surgical kidneys dysfunction, which may occur in patients without obvious kidneys injury during surgery. It is especially important in high risk patient, in whom the kidney function has the crucial meaning for the course of further therapy.

P-0550 | Comparison of Diagnostic Accuracy of PET (CT) and Mibg on Patients with Neuroblastoma: A Systemic Review and Meta-Analysis

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Background/Objectives: To perform a systemic review and meta-analysis of the diagnostic accuracy of PET(CT) and MIBG in patients with newly diagnosed, metastasis and/or relapsed neuroblastoma (NB).

Design/Methods: An electronic search was performed on PubMed/Medline, EMBASE, the Cochrane Library, the Web of Knowledge and the CNKI database for reports prior to Feb 2016 that assessed at least one examination for the neuroblastoma. The diagnostic accuracy of MIBG and PET(CT) was calculate for NB, primary NB, and relapsed/metastasis NB based on their sensitivity, specificity, positive predictive value, negative predictive value, and area under the receiver operating characteristic curve (AUROC).

Results: Forty eligible studies matched the inclusion criteria and 1,134 patients with 939 NB lesions were included. The per-lesion AUSROC value of MIBG for the diagnosis of NB, primary NB and relapsed/metastasis NB were 0.8064 ± 0.0414 , 0.8612 ± 0.0376 and 0.7457 ± 0.0657 . The per-lesion AUSROC value of PET(CT) for the diagnosis of NB, primary NB and relapsed/metastasis NB were 0.9366 ± 0.0166 , 0.9173 ± 0.0347 and 0.9354 ± 0.0166 . The per-patient AUSROC value of MIBG for the diagnosis of NB, primary NB and relapsed/metastasis NB were 0.8771 ± 0.0230 , 0.8896 ± 0.0331 and 0.8717 ± 0.0381 . The per-patient AUSROC value of PET(CT) for the diagnosis of NB, primary NB and relapsed/metastasis NB were 0.6851 ± 0.2111 , 0.9718 ± 0.0443 and 0.5000 ± 0.3205 .

Conclusion: PET(CT) showed higher per-lesion accuracy than MIBG and should be the preferred modality for the diagnosis of patient with NB, primary NB and relapsed/metastasis NB.

P-0551 | Absolute Peripheral Monocyte Count at Diagnosis: Could it be a Marker for High Risk Neuroblastoma?

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Background/Objectives: Some studies reported that absolute monocyte count (AMC) at diagnosis is associated with worse prognosis in adult cancers. In this study, we aim to investigate the relation between AMC at diagnosis and prognostic factors of neuroblastoma.

Design/Methods: This study is retrospective analysis of neuroblastoma patients treated at Akdeniz University Hospital, Division of Pediatric Haematology and Oncology, between January 2002 – December 2015.

Results: We analyze the AMC values of 46 neuroblastoma patients at diagnosis. There were 21 girls and 25 boys with a median age of 21.5 months (range 1-105 months). The number of patients with stage I, III and IV were 5, 7 and 34, respectively. MYCN amplification status was available for only for 27 patients (58.6%). Fifteen patients (32.6%) had positive MYCN amplification. Mean AMC values are significantly higher in positive MYCN group compared to negative group ($769.33 \pm 91.84/\text{mm}^3$ versus $374.17 \pm 53.97/\text{mm}^3$, $P=0.001$). ROC analysis revealed that AMC is a good marker for MYCN amplification [AUC: 0.88 (95% CI 0.74 – 1.00)]. AMC cut-off value is found to be 420 for 93% sensitivity and 75% specificity to predict MYCN amplification. Mean AMC values are found to be $742.06 \pm 158.13/\text{mm}^3$ and $396.67 \pm 70.93/\text{mm}^3$ in stage IV and lower stage groups respectively ($P=0.027$). ROC analysis revealed that AMC is a moderate marker for stage IV disease [AUC: 0.71 (95% CI 0.54 – 0.88)]. AMC cut-off value is 305 for 85% sensitivity and 50% specificity to predict stage IV disease.

Conclusion: In paediatric cancers, the relation between AMC at diagnosis and prognostic factors has not been investigated exactly. In spite of the low patient number, AMC at diagnosis seems to be sensitive to show the MYCN amplification. We think that this result has to be verified with prospective studies involving high patient number.

P-0552 | Analysis of Related Factors in Nephrotoxicity Caused with Cisplatin in Advanced Neuroblastoma

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Background/Objectives: Nephrotoxicity caused by cisplatin (CDDP) is one of the therapy related problems in neuroblastoma. In the kidney CDDP is taken up into the renal proximal tubular cells mainly via SLC22A2 organic cation transporter 2 (OCT2) and secreted into lumen via other transporters including SLC47A1 multidrug and toxin extrusion 1 (MATE1) (Clin Exp Nephrol. 2012;16:843-51). In adult a few study was reported on the focus between single-nucleotide polymorphisms (SNPs) in OCT2/MATE1 and CDDP-induced renal toxicity.

Design/Methods: We analyzed 31 patient of advanced neuroblastoma in the relationship with nephrotoxicity caused with chemotherapy including CDDP and several clinical parameters. All patients were treated with multiple chemotherapy courses including CDDP. There were differences in method for administration of CDDP in each protocols (ie. drip infusion in one day and/or continuous drip infusion for 5 days). We evaluated serum creatinine and estimated glomerular filtration rate (GFR) before the initiation of chemotherapy and after the treatment up to cumulative dose of CDDP reached to 430 to 500 mg/m² in each patients. Ratio (after/before treatment) of creatinine and GFR was compared in several parameters such as patient's age, gender, disease stage, number of treated chemotherapy courses, administration methods in CDDP, and SNPs at 808G>T in OCT2 and rs2289669 G>A in MATE1.

Results: Ratio of creatinine and estimated GFR in after/before the chemotherapy in each patients were each (0.63 to 2.17, median 1.05) and (0.47 to 1.60, median 0.92). When we compared these scores using several variables, OCT2 SNPs at 808G>T was associated with less nephrotoxicity (low creatinine and high GFR ratio, $p<0.05$). SNPs in MATE1 and other variables did not show the significances.

Conclusion: Although number of patients in this study was still limited the variation in OCT2 may be useful predictor of nephrotoxicity caused with CDDP including chemotherapy even in paediatric populations.

P-0553 | A Technique for Excision of Abdominal Neuroblastoma

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Background/Objectives: The aim of this study was to discuss the technique for excision of neuroblastoma which encased abdominal vessels.

Design/Methods: From Jun. 2006 to Jun. 2015, a retrospective review was performed of 123 patients with abdominal neuroblastomas. Seventy-seven were males and 46 females. A mean age were 21 ± 17.5 months (1 month to 10 years). The primary site was adrenal (in 64) and retroperitoneal (in 59). The tumour of 45 cases encased major abdominal vessels. All of the 123 cases underwent surgery. Thirty-nine cases underwent surgery under the major blood vessel tunica adventitia. Four cases were palliative resections, and two cases were just biopsy intraoperative. Four cases repaired vessels.

Results: Macroscopically complete or near complete tumour clearance was 95% (117/123). No perioperative death. No bleeding and thrombogenesis after operation. There were 4 patients who needed vessel repaired, 2 aortas, 1 renal, and 1 inferior vena cava. One of them had kidney failure after repair aortas, and died 2 months later. The others were recovery well. There was a boy whose kidney was atrophy and calcification, even though resected tumour from renal artery without vessel repaired intraoperative. His kidney function was normal and finished chemotherapy. Chyloperitoneum 2 cases and adhesive ileus 2 cases. All of them were cured by intravenous nutrition.

Conclusion: It is relatively safe and feasible for the excision of neuroblastoma which encased abdominal vessels under the tunica adventitia. It improves the excision rate of the abdominal neuroblastoma obviously.

P-0554 | The Assessment of Renal Glomerular and Tubular Function in Children with Cancer after Nephrotoxic Chemotherapy: A Single Center Experience

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Background/Objectives: Survival rate for childhood cancer is increasing which has resulted in an increasing focus on long-term treatment-related morbidity and mortality.

Design/Methods: There are 59 childhood cancer survivors who had completed their treatment with cisplatin, carboplatin, ifosfamid and HD-MTX. We investigated glomerular and tubular dysfunction.

Results: The median age of patients was 10.5 years, median age at diagnosis was 6.5 years and median follow-up time was 2 years. Median GFR was $129\text{ml}/\text{min}/1.73\text{m}^2$ (range 48-414ml/min/1.73m²) and median TPR was 91.2% (range 42-98.9%). Fifteen survivors (28%) had GFR below $90\text{ml}/\text{min}/1.73\text{m}^2$ and 5 survivors had TPR below 85%. No survivors had end stage renal disease. Eleven patients had hypomagnesemia, and 16 patients had hypophosphatemia.

Pathologically elevated relative beta 2 microglobulin were noted in 12 survivors: similar distribution was found within solid tumour and lymphoma groups. Pathological microalbuminuria was found in 16% of survivors and pathologically elevated NAG exceeding age-related reference values were noted only in 2. Cumulative cisplatin dose was significantly lower in the group of younger age at treatment (median 350 mg/m² and 540 mg/m², respectively, $p=0.005$). Younger than 3 years at treatment group had decreased GFR, increased serum phosphorus concentration, increased urinary B2 M-creatinin ratio. Follow-up time longer than 3 years was associated with increased serum creatinin and increased urinary microalbumin excretion and decreased tubular phosphorus reabsorption. Survivors treated with platin analogues and combined chemotherapy had significantly lower TPR and increased FeNa than survivors treated with HD-MTX. Survivors who had febrile neutropenia courses during their treatment, had significantly lower GFR. Survivors treated with abdominal irradiation had significantly elevated urinary microalbumin, b-2M and FeNa excretion than others.

Conclusion: The significant impairment in glomerular filtration rate and overt renal tubular protein excretion in CCS diagnosed under 3years were meaningful for late nephrotoxicity. Our study results warrant periodic long-term follow-up of childhood cancer survivors regarding development of renal late complications.

P-0555 | The Application Value of 18F-FDG PET/CT Imaging in Clinical Staging for Childhood Neuroblastoma

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Background/Objectives: The aim of this study was to compare the accuracy of 18F-FDG PET/CT imaging with the performance of bone scan, cranial MRI, bone marrow puncture and biopsy in children neuroblastoma (NB).

Design/Methods: Seventy-two patients confirmed with NB by histopathological and imaging results who had undergone PET/CT, bone scan, cranial MRI, bone marrow puncture and biopsy for staging were retrospectively evaluated. Then we compared the maximum standardized uptake value (SUVmax) of tumour and metastasis. The accuracy, sensitivity, specificity, positive and negative predictive value of PET/CT image were calculated on a per-patient basis.

Results: All patient cases showed clear uptake of FDG. Sixty-four out of seventy-two (87.5%) positive metastasis detected by PET/CT were pathologically confirmed. Both PET/CT and bone scan revealed bone metastasis. Thirty (41.7%) patients were negative in bone marrow cytology, while PET/CT suggested positive, their stage was adjusted after PET/CT scanning. One patient had cranial metastasis only detected by MRI.

Conclusion: PET/CT can manifest the whole part of metastasis, especial latent region as lymph nodes, indicating that PET/CT has potential for the evaluation of metastasis. Bone scan can display the metastatic location more specific than PET/CT. About intraparenchymal metastasis, MRI screening is superior than PET/CT.

P-0556 | Expression and Clinical Significance of UBE2C in Neuroblastoma

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Background/Objectives: To detect the expression of UBE2C in neuroblastoma (NB) tissue and analyze the association with the clinical features of NB patients.

Design/Methods: Paraffin-embedded surgical tissue specimens from 51 NB patients treated in Xinhua Hospital from January 2012 to January 2015 were collected. The expression of UBE2C protein was detected by immunohistochemistry and the clinical characteristics of these patients were analyzed retrospectively. The survival curve was established with Kaplan-Meier analysis. Log-rank test, Chi-square test and Cox regression analysis were used to explore the correlation of UBE2C protein expression with clinicopathological features and prognosis of NB patients.

Results: The male-to-female ratio was 1.8:1. The median age at diagnosis was 36 months and median duration of follow-up was 25.6 months. The results showed that the UBE2C protein positive expression rate in stage III and IV group (90.0%) was significantly higher than that of the stage I, II and IVs group (47.6%) ($P<0.001$); the UBE2C positive expression rate in recurrence group (91.3%) was also higher than that of the non-recurrence group (57.1%) ($P=0.001$). The survival curve revealed that patients with UBE2C positive expression had poor prognosis (P

= 0.006). The two-year overall survival of patients with UBE2C expression was (48.6±8.2)% and that of patients without UBE2C expression was (92.9±6.9)%. Both univariate and multivariate Cox regression analysis revealed that expression of UBE2C protein was independent prognosis factor for NB ($P < 0.001$).

Conclusion: The expression of UBE2C was closely related with the stage and the relapse of NB patients. Positive expression of UBE2C implied the poor prognosis for NB. UBE2C may play an important role in the invasion, metastasis and relapse of NB. It might become a new biomarker and potential drug target to NB.

P-0557 | Fluorescence In Situ Hybridization Analysis of Mycn Amplification in Bone Marrow Metastatic Neuroblastoma

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Background/Objectives: The role of MYCN amplification for risk assessment in neuroblastoma (NB) is undisputed, therefore it is important to identify accurately the level of MYCN as early as possible. Patients with bone marrow metastatic NB need chemotherapy before surgery, but they can not identify the level of MYCN gene timely due to the limited tumour biopsies. The purpose of our study was to clarify the clinical value of interphase fluorescence in situ hybridization (FISH) in detecting MYCN amplification of bone marrow cells and evaluate the biological characteristics and prognostic impact of MYCN amplification in bone marrow metastatic NB.

Design/Methods: Interphase FISH analysis was performed to detect MYCN amplification in 81 newly diagnosed NB with bone marrow metastasis. Microscopic examinations of BM aspirates and biopsies were performed to determine the presence of neuroblastoma cells. Serum tumour markers such as LDH and NSE levels were detected at diagnosis of all patients.

Results: MYCN amplification were observed in 13(16.0%) of 81 patients. An significant association were observed between MYCN amplification with age and LDH levels ($P=0.038$, $P<0.001$). Patients older than 2 years exhibited the highest prevalence of MYCN amplification (53.8%) compared with any other groups. The clinical outcome were poorer in patients with MYCN amplification than those without amplification (3-year EFS 25.6±19.6% vs. 68.0±6.3%, $P=0.044$; 3-year OS 76.2±12.1% vs. 94.1±2.9%, $P=0.046$).

Conclusion: MYCN amplification was found to correlated with advanced stage and poor outcome in this study of bone marrow metastatic NB. Detecting the bone marrow cells by FISH can identify the levels of MYCN gene timely without surgical operation, so as to guide chemotherapy which is based on the risk stratification.

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P-0558 | Associations of Interleukin-6 Level and its RS1800795 Gene Single Nucleotide Polymorphisms with Neuroblastoma in Chinese Children

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Background/Objectives: To investigate the associations of interleukin-6 (IL-6) level and its rs1800795 gene single nucleotide polymorphisms (SNP) with Neuroblastoma (NB) in Chinese children.

Design/Methods: We used polymerase chain reaction and gene sequencing to analyze 130 Chinese NB patients and 50 controls, and evaluated the impact of IL-6 level and its rs1800795 SNP on disease risk and phenotype. Kaplan-Meier analysis was used to verify the association between IL-6 gene expression and patients' survival.

Results: No significant association was found with NB risk when allele and genotype frequencies of the rs1800795 polymorphism were compared between patients and controls ($P>0.05$); The GG genotype and G allele frequencies were higher in high-risk NB patients than that in moderate- and low-risk NB patients ($P=0.02$ and 0.03); In NB patients with GG genotype, periphery blood IL-6 level were much higher than that in moderate- and low-risk NB patients ($P=0.03$); NB patients of high-risk with homozygous for the G allele had a lower 3-year EFS and OS than those who are carrying one or more C alleles (EFS, 18%±3% versus 47%±5%, $P=0.02$; OS, 22%±3% versus 52%±7%, $P=0.03$).

Conclusion: The rs1800795 SNP is shown to correlated with production of IL-6, and represents a novel prognostic marker for both EFS and OS in high-risk NB patients.

NEW DRUGS/EXPERIMENTAL THERAPEUTICS

P-0559 | Polatumumab Vedotin (PV, ANTI-CD79B-VC-MMAE) Significantly Increased Apoptosis/ Reduced Cell Proliferation and Improved Survival Against Burkitt Lymphoma (BL) and Primary Mediastinal Large B- Cell Lymphoma (PMBL)

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Background/Objectives: B-NHL, including BL/PMBL express CD79b+ and have an excellent prognosis with chemo-immunotherapy (Cairo et al Blood. 2007, Goldman/Cairo et al. Leukaemia, 2013, Gerrard/Cairo et al. Blood. 2013). However, a subset of patients with relapsed/refractory mature B-NHL has chemoimmunotherapy resistant disease and a dismal prognosis ($\leq 20\%$ 5 years, EFS, Cairo et al. JCO, 2012). PV has been demonstrated to possess

significant preclinical activity against indolent CD79b+NHL (Polson et al. Can. Res. 2009). More recently PV has been well tolerated in adults with CD79b refractory NHL (Palanca-Wessels et al. Lancet Oncol, 2015) However; its preclinical activity against mature BL/PMBL is unknown.

To determine the in-vitro/ in-vivo efficacy of PV against CD79+ BL/PMBL.

Design/Methods: Rituximab sensitive (Raji)/rituximab resistant (Raji4RH) and Karpas1106P cells were incubated with PV and/or anti-CD79b, MMAE, huIgG1 (Genentech Inc.) at 10 μ /ml for 24 hrs. Apoptosis /cell proliferation was analyzed by flow-cytometry, n=3. Six to 8 week old NSG were divided into 5 groups: control, IgG, PV, anti-CD79B and MMAE. Mice were xenografted with Luc+Raji cells at 5 \times 10⁶ cells/mouse and treated twice a week for 6 weeks.

Results: PV compared to anti-CD79b or IgG1 alone significantly enhanced apoptosis in Raji, 47.2±1.3% vs 29.1±6.0% vs 28.2±4.3% ($p=0.0008$ and $p=0.00006$), Raji4RH, 29.8±9.1% vs 25.4±3.9% vs 18.0±8.2% (NS and $p=0.03$), Karpas1106P, 46.8±5.3% vs 33.8±3.5% vs 26.2±0.4% ($p=0.02$ and 0.006), respectively. PV also significantly reduced cell proliferation compared to CD79b or IgG1 alone. Raji, 56.1±5.1% vs 38.1±0.7% vs 14.8±0.4% ($p=0.001$ and $p=0.0008$), Raji4RH, 53.4±5.4% vs 23.4±5.51% vs. 11.3±0.8% ($p=0.004$ and 0.006), Karpas1106P, 46.4±0.3% vs 29.0±1.5% vs 15.9±0.6% ($p=0.005$ and 0.00007), respectively. Overall survival in mice receiving 5 mg/kg of PV was significantly increased when compared to anti-CD79B Ab ($p=0.001$).

Conclusion: Our preliminary data indicates that PV significantly enhances apoptosis/reduced cell proliferation in BL/PMBL. Furthermore, PV significantly increased survival in BL NSG xenografts.

P-0560 | Parental Perspectives and Recall of Involvement of their Child in Longitudinal, Observational Biological Studies

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Background: Parental consent for their child to participate in research in clinical trials and research at the time of a diagnosis of cancer is a contentious, but necessary for patient recruitment to novel treatments and open trials, and the timely collection of samples early in treatment and often before the first administration of chemotherapy. Questions are sometimes asked whether consent is truly informed and whether parents recall research aims and objectives in the longer term.

Methods: A literature review was conducted using medline, cinahl, embase and psych info to explore parental perspectives on engagement in observational, non-interventional research studies, including reasons for involvement, consent and recall. From a cohort of 60 patients recruited to a single centre study at our institution, qualitative data exploring these considerations was conducted using mixed methods.

Results: 42 articles were identified and included for data extraction.

Parents recognise the concept of 'non-essential research'. Their reasons for involvement in research include hope and altruism. Motivation for involvement in clinical trials especially interventional are different from involvement in biological and observational studies.

Conclusion: Parents of children diagnosed with cancer recognise the need for research for both the benefit of their own children and other families.

P-0561 | "Including" Patients in the North. Development of an Early Phase Trials Network in the North of Britain

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Background/Objectives: Bringing new treatments into practice for childhood cancer poses substantial challenges but is crucial for the 20% of children not currently cured and the large proportion of patients who suffer long term effects despite cure. Availability of new therapies in clinical trials has been limited. Early phase trials require substantial infrastructure and resources to run. As a result of these factors despite the need for new agents trials have historically been conducted in only a small proportion of possibly suitable patients and predominantly in only a few sites.

Design/Methods: The changes in EU regulations have lead to an increased number of new agents being available for investigation. To capitalise on this opportunity we need to make the trials that include these new agents available to as many children and young people as possible. In the Principal Treatment Centres (PTC) for Cancer in Glasgow and Newcastle upon Tyne we have long aspired to study new agents for children's cancer and make more new treatments available. Availability of new agent trials to offer patients has been one limiting step but another has been having patients with a suitable diagnosis eligible for a trial if it does become available.

Results: By joining with our colleagues in the other PTCs in the north of Britain to form the INCLuDe network we have increased the populations we can offer trials to from around 3 million each to a total of 10 million. This makes trials available to more patients and enables us to widen the portfolio of trials we can offer.

Conclusion: The co-operation and communication that this network has permitted has already resulted in increased recruitment to new treatment studies and a larger and wider portfolio of studies for this population. The network model is one that can and should be adapted for other geographical regions.

P-0562 | Prognostic Factors of Early Mortality in Children and Adolescents Participating in Dose-Finding Trials Within the ITCC European Consortium

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Background/Objectives: Dose-finding trials are crucial in the development of novel agents for children with recurrent/refractory solid tumours. Two clinical scores have been validated to optimise patient selection in adult oncology: the Royal Marsden Hospital (RMH) score - albumin, lactate dehydrogenase (LDH), number of metastatic sites-; and the MD Anderson Cancer Center (MDACC) score -RMH score plus performance status and gastrointestinal tumour type-. Children/adolescents participating in dose-finding trials across the Innovative Therapies for Children with Cancer (ITCC) consortium were assessed to determine prognostic factors of early mortality and the predictive value of the RMH and MDACC scores.

Design/Methods: Patients aged <18 years with solid tumours, enrolled between 2000-2014 in their first phase I trial, were assessed retrospectively. Risk-estimate analyses of mortality at 90 days from cycle1-day1 and the predictive capacity of the RMH and MDACC scores were conducted.

Results: Overall 257 patients from 8 centres (4 countries) were included. Median age: 11.0 years (range 1.0-17.9). Main diagnoses: medulloblastoma/supratentorial PNET (14.4%), neuroblastoma (12.8%), diffuse intrinsic pontine glioma (11.3%). The 90-day mortality was 28.0% (95%CI 22.5-33.5). Factors with an odds ratio significantly associated with increased 90-day mortality included: Lansky/Karnofsky $\leq 80\%$, no school/work attendance, requirement of strong opioids, total bilirubin >upper limit of normal and RMH score ≥ 1 . The sensitivity, specificity, positive and negative predictive values of clinical scores for 90-day mortality were, respectively, with RMH score 0 Vs ≥ 1 : 73.8%, 48.6%, 35.6% and 82.1%; and with MDACC score 0 Vs ≥ 1 : 74.4%, 36.7%, 29.6% and 80.0%.

Conclusion: Factors related to the performance status of the patient, such as Lansky/Karnofsky scales, school/work attendance and requirement of opioids seem good indicators of early mortality on trial. Although the RMH and MDACC scores have a prognostic impact in the overall survival of adults and children, they are not good predictors of early mortality in paediatric dose-finding trials.

P-0563 | Choosing the Right Genotyping Array: More than just Coverage

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Background/Objectives: Since the dawn of GWAS the number of genotyping arrays has exploded, which makes the choice of array challenging. We compared all currently available arrays on several array characteristics (coverage and imputation efficiency) and focused on several SNP categories such as pharmacogenetics, actionable genes and mtDNA. In order to help readers determine which array would work best in a given population, an example of a multi-ethnic population of childhood cancer survivors has been worked out. Besides GWAS, we are interested in the response to treatment (pharmacogenetics) and side-effects of treatment (actionable genes).

Design/Methods: SNP-manifest-files for all arrays were obtained from Illumina and Affymetrix. Calculations of coverage were based on the 1kG reference panel, which was divided in its separate ancestries. Imputations using HapMap samples were performed to 1kG. For pharmacogenetics 388 genes and for "actionable genes" 56 genes proposed by ACMG were considered. For mtDNA 71 mt-loci were evaluated.

Results: Twenty-three arrays were included in the comparison. The coverage increased with the size (number of variants) of the array. Imputation quality also increased with the size of the array, indicating that coverage is a good predictor of imputation quality. For both pharmacogenetics and actionable genes a similar trend was observed. However, for pharmacogenetics the DrugDev array from Illumina had over double the number of variants in these genes compared to other arrays of similar size ($P < 0.0001$). Similarly, for actionable genes the Axiom_UKB had 7 times more variants than expected ($P < 0.0001$). No trend was observed for mtDNA, however 3 of the arrays had no mtDNA content, while the global array had a much larger mtDNA content than average ($P = 0.001$).

Conclusion: In conclusion, choosing the right genotyping array will depend on the questions to be answered. However, comparing the different arrays using objective criteria can help make this decision more manageable.

P-0564 | RIST-RNB-2011: A Prospective Randomized Multicenter Trial of a Molecularly Targeted Multimodal Strategy for Patients with Relapsed and Refractory Neuroblastoma: An Update of the Ongoing Trial

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Background/Objectives: The prognosis for children with recurrent or refractory high-risk neuroblastoma (rNB) remains dismal. Novel therapeutic approaches are needed. RIST was designed based on in vitro data generated in stably transfected cell lines expressing constitutively activated receptor tyrosine kinases and in xenotransplant models. RIST is a metronomic, multimodal molecular based treatment protocol consisting of 8 repetitive courses of rapamycin/dasatinib (R/S) for 4 days followed by 5 days of irinotecan and temozolomide (I/T). In phase I, 1 R/S course is followed by 1 I/T course. In phase II, 2 courses of R/S are followed by 1 course of I/T. In a pilot trial consisting of 21 unselected patients with rNB RIST demonstrated very promising results with a long-term survival of 40%. Furthermore, RIST exhibited strong activity in high grade glioma, Ewing sarcoma and a treatment-refractory pineoblastoma.

Design/Methods: Trial design and purpose: RIST-rNB-2011 (EudraCT: 2011-004062-15) is a prospective randomized international multicenter treatment trial comparing in the control arm I/T alone with RIST in patients with rNB. Included are patients with high-risk rNB (stage IV and all MYCN pos. stages) or progressive disease during primary treatment.

Results: The trial was initiated August 2013 and is conducted in 46 international centers. With approximately 50% of required patients recruited we will provide an update of this ongoing investigator initiated trial including trial related aspects of documented AEs/SAEs, which are covered by the NCI CTCAE.

Conclusion: The RIST concept represents a promising and modern multimodal approach, for which evidence is generated in a prospective randomized trial in rNB.

P-0565 | Personalized Targeted Therapy in Refractory or Relapsed Cancer in Childhood (TRICEPS Study)

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Background/Objectives: Despite all recent advances in cancer's treatment, 18% of children will die from their cancer. New tools that enable better individual tumour characterization and classification are required to improve patient care and outcomes on children. Personalized targeted therapy has proven to be a promising strategy for first line treatment in adult cancer.

Design/Methods: A feasibility study is currently underway at the CHU Sainte-Justine, where 30 relapse or refractory cancer patients between 0 and 21 years, are being offered in-depth genomic and transcriptomic investigation to identify patient-specific alterations that may be targetable with alternative therapies. The main objective of this study is to assess the feasibility of obtaining high quality/quantity biospecimen, performing genomic sequencing and data analysis, identifying a drug based on the genomic data and offering this information to the medical team, the patient and the family within a 10-week time frame.

Results: Over a period of 16 months (April 2014-Sept 2015), 17 patients have been recruited in TRICEPS (solid tumors and hematologic malignancies). Nine patients have undergone extensive genomic investigation in a real-time manner within a median timeframe of 9.9 weeks. Patient screen failures occurred in 8 cases. For the remaining 9 patients, we identified clinically relevant genomic alterations that can be used to inform clinical management for all of them. Identified relapse-specific mutations allowed follow-up of minimal residual disease (MRD), influenced surgical interventions, guide treatment to immunotherapy or revealed alternative therapeutic options for future personalized targeted therapy.

Conclusion: The following step toward translating our results into novel personalized therapeutic approaches will then be the development of phase I/II clinical trials to evaluate the efficacy of these targeted therapies in terms of therapeutic response, survival, and overall quality of life. Our overarching goal is to be able to offer personalized targeted therapy options to all patients upon primary diagnosis of their cancer.

P-0566 | Preliminary Results of the Moroccan Metronomic Chemotherapy Protocol: Report from the Moroccan Society of Paediatric Haematology and Oncology

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Background/Objectives: Cure rates in paediatric cancer can reach 80% in high income countries. However, 80% children are living in low income countries where survival rates usually don't reach 35%.

In Morocco, we have previously reported cases of disease stabilization and/or second complete remission in children with recurrent or relapsed malignant disease (SIOB Africa Ghana 2005) under prolonged low dose of cyclophosphamide treatment. Regarding these findings, a study has been done by Moroccan paediatrician to use for the first time the concept of metronomic

chemotherapy (MC) for children with cancer. This project is supported by the Lalla Salma Foundation Prevention and Treatment of Cancer and the Cancer research Institute in Morocco.

The objective of the protocol is to evaluate the efficacy and safety of 3 drug MC regimen in paediatric patients.

Design/Methods: We initiated in 2014 a prospective multicentre metronomic phase II trial in Moroccan paediatric haematology/oncology units with a cyclophosphamide, etoposide, and valproic acid combination in children with either a relapsing/refractory tumors or a very advanced disease.

On a period of eighteen months (July 2014 - December 2015) 54 children were included in this trial.

Results: Thirty eight boys and 16 girls were included during this period. The median age was 10 years. The indication of the MC was relapse (26), progression (22), resistance (4) and 2 cases for very advanced disease. The patients included have as diagnosis neuroblastoma (13), Ewing (11), Osteosarcoma (7), Rhabdomyosarcoma (6), medulloblastoma (3). A total of 324 cycles of MC were given for 54 patients. Tolerance of treatment was good in 265 cycles of MC (82%). In 32 Cycles of MC, transfusion was needed (10%). Analgesic treatment was used in 81 cycles (25%).

Conclusion: The study is ongoing and 54 patients from 4 Moroccan paediatric oncology centers have been included. Tolerance of treatment and compliance are excellent.

P-0567 | Protective Effect of Diclofenac and Enoxaparin in L-Asparaginase Induced Acute Pancreatitis in Rats

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Background/Objectives: This study was designed to evaluate the protective effect of enoxaparin and diclofenac against L- asparaginase induced pancreatitis.

Design/Methods: Acute pancreatitis was induced in rats by intra-muscular injection of L-asparaginase (1,000 I.U/Kg) given daily for five days. Enoxaparin was given subcutaneous (100 I.U/Kg) daily for five days and diclofenac was given intraperitoneal (2 mg/Kg) daily for five days. Twenty four hours after injections, all parameters were analyzed with histopathological study of the pancreatic tissue.

Results: During acute pancreatitis, oxidative stress biomarkers were significantly changed as indicated by reduced tissue glutathione and increased malondialdehyde levels. This was accompanied with significant increase in immune cells infiltration as indicated by high level of myeloperoxidase and pro-inflammatory cytokine TNF-alpha. Triglyceride only showed increase level. Administration of enoxaparin or diclofenac or their combination restored biochemical parameters including serum alpha-amylase, reduced glutathione, malondialdehyde, pro-inflammatory cytokine TNF-alpha, myeloperoxidase and triglyceride. Histological injuries of pancreatic tissues as vacuolation and necrosis of epithelial lining pancreatic acini, inflammatory cells infiltration and focal pancreatic hemorrhage were also reduced.

Conclusion: Our study emphasizes the potential protective effect of enoxaparin and diclofenac against L-asparaginase induced pancreatitis.

P-0568 | iMATRIXcobi: A Phase I/II, Dose-Escalation Study of the Safety, Pharmacokinetics, and Preliminary Efficacy of Cobimetinib in Paediatric and Young Adult Patients with Refractory/Relapsed Tumours

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Background/Objectives: Cobimetinib is a selective inhibitor of MEK, a central component of the RAS/RAF/MEK/ERK pathway implicated in the pathogenesis of some paediatric tumours. The iMATRIXcobi study (NCT02639546) will evaluate safety, pharmacokinetics, and preliminary efficacy of cobimetinib in paediatric and young adult patients with refractory/relapsed solid tumours.

Design/Methods: Paediatric patients (aged ≥6–<18 years) with refractory/relapsed solid tumours will be enrolled. Eligible diagnoses include tumours with known/potential RAS/RAF/MEK/ERK pathway activation, including, but not limited to, glioma, embryonal rhabdomyosarcoma, neuroblastoma, malignant peripheral nerve sheath tumour, rhabdoid tumour, or neurofibromatosis- or RASopathy-associated tumours. The study has two stages; firstly, the dose-escalation stage: using a rolling six design, dose escalation in paediatric patients will commence at 0.6 mg/kg (approximately 80% of adult dose) to determine the recommended phase II dose and dose-limiting toxicities. With a tablet formulation, to allow dose finding that gives consistent exposure and correct dosing of drug in smaller patients, the daily dose will be calculated from a desired cumulative weekly dose. Dose finding with a liquid formulation, to allow enrolment of patients as young as 6 months, is planned to commence in late 2016. In the expansion stage, paediatric patients treated at the recommended phase II dose will be enrolled in tumour-type cohorts to obtain first signals of activity, and additional safety, tolerability, and pharmacokinetic data. Young adult (aged ≥18–<30 years) patients with paediatric tumour types will be eligible for treatment with the adult dose. An initial assessment will be performed after a minimum of 10 patients have been enrolled in a tumour-type cohort.

Results: NA.

Conclusion: Comparison of objective response rate to historical tumour-type outcomes in phase I studies will guide the decision whether to expand the cohort for additional response

assessment, allowing for a targeted evaluation of cobimetinib in diseases for which patients are most likely to derive clinical benefit.

P-0569 | The Rist Design: A Molecularly Targeted Multimodal Approach for Patients with Relapsed and Refractory Pineoblastoma

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Background/Objectives: The prognosis for children with recurrent or refractory pineoblastoma (rPB) remains dismal. Novel therapeutic approaches are urgently needed. RIST is a multimodal metronomic approach, which we developed originally for relapsed/refractory Neuroblastoma (rNB), combining molecular targeted drugs (rapamycin and dasatinib) with chemotherapy (irinotecan and temozolomide). Beyond rNB RIST demonstrated significant efficacy in relapsed and refractory Ewing sarcoma and high grade glioma.

Design/Methods: Based on in vitro data, results of a pilot trial for an ongoing prospective randomized trial for rNB (EudraCT 2011-004062-15; NCT01467986) and the biological vicinity of the RIST design. Treatment phase 1 consists of one course of molecular-based therapy with four days of rapamycin/dasatinib (R/S) alternating with five days of irinotecan and temozolomide (I/T) completing four chemotherapy courses. Treatment phase 2 consists of two courses of R/S followed by one course of I/T again with a total of four chemotherapy courses.

Results: After completion of treatment phase 1, MRI imaging presented a significant tumour reduction of almost 50% and at the end of phase 2 the tumour vanished completely. No major adverse effects were observed during treatment with RIST. For the remaining course of disease the primary site remained relapse free but after five months leptomeningeal metastases were confirmed and the patient developed progressive refractory disease.

Conclusion: The RIST treatment design demonstrated high efficacy on the primary rPB but was not active in leptomeningeal dissemination, possible due to poor drug permeability or expansion of a resistant subclone. Inasmuch due to the unexpected efficacy and low toxicity RIST is evaluated now in a pilot trial for rPB (2015-004304-27; NCT02596828). If reproducible, a confirmatory prospective trial is warranted.

P-0570 | Expression of Inhibitory Ligands and Receptors on Human Leukemia Cells and Expanded Gamma-Delta T Cells from Healthy Volunteers

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Background/Objectives: Therapeutic blockade of inhibitory immune checkpoint pathways can augment antitumor immune response in solid tumors. However, its benefits are still to be explored in hematologic malignancies. This study was performed to analyze the expression of inhibitory ligands on leukaemia cells and inhibitory receptors on gamma-delta T cells.

Design/Methods: The expression of PD-L1, B7-1, and B7-2 on leukaemia and lymphoma cell lines (CEM1, MOLT4, K562, HL-60, SU-DHL-6, and OCI-LY7) and leukemic blasts from 3 patients with AML were determined by the flow cytometry. Transcript of HVEM was quantified by real-time PCR. The expressions of inhibitory receptors, PD-1, NKG2A, ILT2, BTLA, and CTLA-4 on gamma-delta T cell from healthy donors were analyzed 2 weeks after culture with IL-2 and zoledronic acid.

Results: CEM1 and MOLT4 showed augmented expression of PD-L1 and B7-2, OCI-LY7 showed augmented expression of PD-L1 and B7-6, and K562, HL-60, and SU-DHL-6 showed augmented expression of PD-L1, B7-1, and B7-2. HVEM was highly expressed in MOLT4 and CEM1. Inhibitory ligands were variably expressed on the leukemic blasts from individual patients. Patient 1 showed augmented expression of PD-L1, B7-1, and B7-6, whereas patient 2 had no augmentations and patient 3 had high expression of B7-6. In vitro expanded gamma-delta T cells showed no significantly increased inhibitory receptors on their surface. Of 3 paired samples before and after incubation, two did not show alterations in expression of inhibitor receptors, whereas the other one showed decreased expression of PD-1 and increased expression of ILT2.

Conclusion: Immune checkpoint ligands were variably expressed on the leukemic blasts from each patient. Thus, therapeutic benefits of immune checkpoint inhibitors should be evaluated based on individual expression of ligands. Gamma-delta T cells from healthy donors showed stable expression of inhibitor receptors after in vitro expansion. This suggests that proliferated gamma-delta T cells can be used therapeutically without increasing immune regulation.

P-0571 | TNF- α Inhibitor Etanercept does not Alter the Severity of Methotrexate-Induced Gastrointestinal Mucositis in the Rat

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Background/Objectives: Gastrointestinal (GI) mucositis is a severe side effect of chemotherapy and radiotherapy. Pro-inflammatory cytokines are thought to play an important role in the pathophysiology of GI mucositis. We aimed to determine the effect of the TNF- α inhibitor Etanercept on the severity of mucositis in a previously established methotrexate (MTX)-induced GI mucositis rat model.

Design/Methods: Male Wistar rats received a single iv injection of MTX 60 mg/kg at day 0. Rats were treated with a daily injection of either Etanercept (TNF- α inhibitor) 5 mg/kg or NaCl 0.9% sc from day -3 till day 3 (each n=10). Control rats (n=6) received NaCl 0.9% iv and Etanercept sc. The severity of mucositis was determined by intake, bodyweight, plasma citrulline, and by an oral glucose absorption test. At day 4 and day 10 rats were terminated. Villus length, crypt length, intestinal MPO and plasma Etanercept levels were determined.

Results: The administration of MTX induced mucositis in all rats. Etanercept did not cause a change in the degree of mucositis. Bodyweight, intake and glucose levels were not altered by Etanercept, villus length was comparable, and there was no difference in MPO and citrulline level. Etanercept levels in plasma were significantly increased in the Etanercept rats ($p < 0.05$).

Conclusion: TNF- α inhibitor Etanercept did not alter the severity of mucositis in the rat, suggesting that only targeting the inflammatory pathway of TNF- α is not effective for decreasing the severity of GI mucositis induced by high dose MTX. Etanercept alone is not useful for the treatment of MTX-induced GI mucositis.

P-0572 | Effect of Oral Insulin on the Severity and Recovery of Methotrexate-Induced Gastrointestinal Mucositis in the Rat

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Background/Objectives: Gastrointestinal (GI) mucositis is a severe side effect of chemo- and radiotherapy. Oral insulin has been suggested as possible intestinal growth factor and possible intervention for GI mucositis. We aimed to determine the effect of oral insulin on the severity and recovery of mucositis in a methotrexate (MTX)-induced GI mucositis rat model.

Design/Methods: Male Wistar rats (n=24) received a single injection of 60 mg/kg MTX iv at day 0. From day -3 oral insulin was added to the drinking water. Group MTX received normal drinking water, group MTX+INS0.5 received 0.5 U/ml insulin and group MTX+INS1 received 1 U/ml insulin in drinking water. The severity of mucositis was determined by intake, bodyweight, illness and plasma citrulline. In the recovery phase the function of the gut was tested with an oral glucose tolerance test, and villus and crypt length of the small intestine were measured.

Results: MTX induced mucositis in all three groups and oral insulin did not cause a change in the severity of mucositis, with comparable bodyweight, food intake and water intake. Oral insulin did not alter the enterocyte mass, determined with plasma citrulline. The glucose level after bolus was higher in the MTX group compared to MTX+INS1 group ($p < 0.05$). Histology was not significant different between all groups.

Conclusion: In contrast to an earlier study, oral insulin does not alter the severity or the acceleration of recovery of mucositis. Therefore, we conclude that it is not useful to further study oral insulin as possible intervention to prevent or treat chemotherapy induced GI mucositis.

P-0573 | RIST, a Molecularly Targeted Multimodal Strategy for Patients with Relapsed and Refractory Neuroblastoma, Demonstrated Superior Activity in Neuroblastoma Cell Lines Positive for MYCN

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Background/Objectives: Neuroblastoma (NB) is after brain tumors the most common solid tumour in infancy accountable for about ten percent of paediatric-oncological mortality. Of these are genotypic high-risk NB with amplified MYCN among the most fatal and until to today correlate with poor prognosis. RIST is a multimodal metronomic approach combining molecular targeted drugs (rapamycin and dasatinib) with conventional chemotherapy (irinotecan and temozolomide) currently evaluated in a clinical trial (RIST-rNB 2011, EudRACT: 2011-004062-15).

Design/Methods: Five NB cell lines (2 with MYCN amplification and three without MYCN amplification) were used. Cell viability and EC50 were determined after treatment with the combination of SN-38 (active metabolite of irinotecan) and temozolomide alone or with pretreatment of a combination of rapamycin and dasatinib (RIST therapy).

Results: In MYCN amplified cell lines (Kelly, LAN-5) pretreatment with rapamycin and dasatinib (RIST therapy) leads to a significant reduction of the EC50 of SN-38 and temozolomide.

Conclusion: MYCN is a significant prognostic marker in high-risk NB. The RIST multimodal metronomic therapy demonstrated clinical activity in a pilot trial of relapsed and refractory NB independently of MYCN amplification and is therefore evaluated in a prospective trial. This multimodal approach with its synergistic activity of rapamycin and dasatinib on PI3K/AKT/mTOR and others alike could explain the effect on MYCN related pivotal pathways in NB. These preliminary data in cell lines put traditional prognostic markers like MYCN into perspective of the applied treatment.

P-0574 | The National Children's Cancer and Leukaemia Group Tissue Bank ~ Facilitating a Comprehensive Range of Paediatric Oncology Research

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Background/Objectives: Paediatric cancers are extremely rare, therefore collaboration is essential to pool together sufficient numbers of high quality samples with supportive clinical data, to undertake translational research. In 1998, the Children's Cancer and Leukaemia Group (CCLG) established a national tumour biobanking initiative, comprising of a network of 19 treatment centres throughout the UK and Ireland, to facilitate biological research in the UK and abroad, into all paediatric solid cancers. In 2011, a central sample storage repository was established in one location (Newcastle), to streamline access to samples.

Design/Methods: Although the Bank primarily supports biological research into the more common paediatric cancers e.g. neuroblastoma, lymphoma; over the past 3 years it has adapted to support a broader range of research activity. These include supporting CCLG-funded pilot studies every year investigating several extremely rare paediatric cancers; banking cerebrospinal fluid (CSF), circulating tumour DNA (ctDNA) and plasma samples for use in research, collaborating on projects aimed towards providing rapid genomic tumour analysis to influence patient treatment and care, and contributing samples to research on national and international clinical trial cohorts.

Results: The Bank has supported 7 pilot studies to date, investigating various types of cancers including rhabdoid tumours, hepatoblastoma, neuroblastoma, craniopharyngioma and Hodgkin lymphoma. The collection of CSF and ctDNA samples has supported 2 paediatric brain tumour studies. Next generation sequencing analysis of banked tumour is now underway. Currently, 8 national and international projects are accessing tumour samples from clinical trial cohorts supported by trial datasets.

Conclusion: This well-established network of biobanking centres is a highly valuable framework for supporting biological research into solid tumours, including genomic analyses that benefits patient treatment and care and is one of the most successful national biobanks for childhood cancer to date.

Acknowledgements: The CCLG tissue bank is funded by cancer research UK and CCLG

P-0575 | A Phase 1, Multi-Center, Open-Label, Dose De-Escalation Study of the Oncolytic Virus Talimogene Laherparepvec (T-VEC) in Paediatric Patients with Advanced Extracranial Solid Tumors

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Background/Objectives: Survival for children with high risk solid tumors (comprising those with metastases, relapse, or poor prognosis genomic features) is still low and there is an unmet need to develop new therapies for these patients. T-VEC, an intravesically-delivered oncolytic immunotherapy, is a herpes simplex virus-1 engineered to selectively replicate in solid tumors resulting in lytic cell death, antigen release, and production of GM-CSF to enhance systemic antitumor immune responses. Recently, T-VEC became the first US FDA- and EMA-approved oncolytic virus therapy. T-VEC has shown preclinical evidence of tumour growth inhibition in a number of paediatric cell lines and mouse xenograft models including neuroblastoma, soft tissue sarcoma, Ewing sarcoma, and osteosarcoma. We describe a phase 1 study assessing safety and efficacy of T-VEC in injectable paediatric extracranial solid tumors.

Design/Methods: The primary objective is to assess dose limiting toxicities. Key secondary objectives include objective response rate, duration of response, time to response, time to progression, progression-free survival by irRC-RECIST, and overall survival. Key eligibility criteria: histologically or cytologically confirmed non-central nervous system solid tumour recurrent after standard therapy or for which no standard therapy is available, injectable (non-visceral) lesions, and Karnofsky/Lansky performance status $\geq 70\%$. Treatment with T-VEC continues until complete response, disease progression, or intolerance for up to 2 years or when there are no longer injectable lesions. Approximately 18 to 36 patients will be enrolled and stratified by age and baseline HSV-status into 6 cohorts. Patients will be enrolled into each cohort by a standard 3+3 design and will be treated at the recommended adult dose regimen of T-VEC. A stratification factor matched dose de-escalation cohort will be available for intolerability at each dose cohort. The study will open at approximately 17 centers in the US, Switzerland, France, Spain, and Canada.

Results: Not applicable.

Conclusion: Not applicable.

P-0576 | Genomic Profiling in Nonmalignant Paediatric Haematology Patients

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Background/Objectives: To utilize comprehensive genomic profiling to characterize nonmalignant paediatric haematology conditions.

Design/Methods: Patients with nonmalignant hematologic conditions were consented to participate in a clinical trial piloting the use of comprehensive genomic profiling (CGP) at our institution. CGP was performed by Foundation Medicine (Cambridge MA) using profiles for hematologic malignancies and sarcomas. Genomic alterations, therapies available to the specific genomic alteration, and variants of unknown significance were reported for each sample. Results were reviewed by combined Medical and Pediatric molecular tumour board.

Results: Four patients were entered on the study, 1 with aplastic anemia, 1 with neurodegenerative Langerhans' Cell Histiocytosis (LCH), and 2 patients with Clove syndrome. The two patients with Clove syndrome did not have analysis completed secondary to specimen failure. The aplastic anemia sample showed the following genomic alterations: FGFR3 S249C; second specimen only BCOF S672*42. There are 2 FDA approved therapies targeting the FGFR3 S249C alteration: pazopanib and ponatinib. The sample from the patient with LCH showed

the genomic alteration: BRAF V600E. There are currently 4 FDA approved therapies targeting this genomic alteration: dabrafenib, regorafenib, trametinib and vemurafenib. These therapies can be considered if the patients fail to respond to standard treatment.

Conclusion: CGP may be of benefit by identifying targetable genetic alterations in certain paediatric nonmalignant hematologic conditions.

P-0577 | Impact of the Food and Drug Administration (FDA)-European Medicines Agency (EMA) Common Commentary (CC) on Paediatric Cancer Drug Development

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Background/Objectives: The United States (US) and the European Union (EU) have specific legislation which directs their respective regulatory agencies, the FDA and the EMA in the evaluation of drug development for children. Despite similar objectives, differences exist in requirements and timing of study plan submissions and decisions regarding regulatory actions. Cancer drug development is a global enterprise especially in children where there is increasing need for international clinical trial collaboration. FDA and EMA have a comprehensive confidentiality agreement which permits their scientific exchanges around specific drug development plans during monthly teleconferences. When warranted, a summary of discussion and integrated scientific opinions from both agencies, the CC, can be provided to sponsors as informal and non-binding advice and recommendations.

Design/Methods: We retrospectively reviewed the agendas for monthly calls from 10/2012 to 3/2016 to assess prevalence of oncology product discussion and the number of resulting Common Commentaries.

Results: Forty-six discussions of 26 distinct oncology products and a single master protocol platform under review by the EMA and FDA occurred. Areas of focus included toxicity concerns from adult or non-clinical studies and appropriate monitoring plans, emerging study results, feasibility, potential indications, trial design including eligible populations and appropriate study endpoints, and recommendations to assure that study plans in the US and EU were either collaborative or complementary and not duplicative. Discussion of 8 of these products led to the development of CCs, 7 of which were provided to sponsors. The CC informed subsequent paediatric development plans.

Conclusion: Coordinated international scientific review and discussion of initial paediatric development plans and clinical trials contribute to early and efficient evaluation of new drugs in children.

P-0578 | Therapeutic Experience of Sorafenib for Paediatric Patients with Refractory Solid Tumors Based on Collagen Gel Droplet-Embedded Culture-Drug Sensitivity Test (CD-DST)

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Background/Objectives: Collagen gel droplet-embedded culture-drug sensitivity test (CD-DST) is an *in vitro* chemosensitivity test. The efficacy of sorafenib, multi-kinases inhibitor controlling tumour growth and angiogenesis, is not clear in paediatric cancer patients.

Design/Methods: Between April 2014 and March 2015, CD-DST was performed in solid tumour patients that informed consent was provided. Two - five anticancer drugs including sorafenib were tested by CD-DST. The results of CD-DST for sorafenib were compared with the clinical effects of sorafenib monotherapy or sorafenib based combination therapy with other anticancer drug (bevacizumab 1, irinotecan 1) in 4 patients with refractory or relapsed tumors.

Results: CD-DST was applied to 10 patients, and 9 of those were eligible. CD-DSTs for each drug were as follows: sorafenib, 9 cases; topotecan, 7 cases; imatinib, 3 cases; dasatinib, 3 cases; sunitinib, 3 cases. Among tested samples, the growth inhibitory rate by 72 hours exposure of sorafenib were 0.76-49% at 1µg/mL and 0.04-35.0% at 5µg/mL. We performed sorafenib monotherapy for 1 patient with hepatoblastoma (HBL) and 1 patient with Wilms tumour and the sorafenib based combination therapy was performed for 2 patients with HBL. Sorafenib was administered 100-200mg/m²/dose twice daily. Treatment responses were complete remission 1, stable disease 1, and progressive disease 2, respectively. Severe adverse events (Common terminology criteria of adverse event grade 3-4) were observed in two patients. One received combination therapy suffered AST/ALT elevation, cytopenia, febrile neutropenia, diarrhea and sepsis. The other with monotherapy had cytopenia.

Conclusion: CD-DST is useful as one of the means to evaluate when we choose the therapeutic drug. Sorafenib is a potential candidate for the therapeutic option of paediatric solid tumors. Further studies are needed to use sorafenib for refractory tumour effectively and safely.

P-0579 | Comparative Analysis of Iron Metabolism and its Adjustment Changes at Cancer Patients in Childhood

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Background/Objectives: Introduction: Studies on various adult cancer types showed that there are changes in levels of ferritin, transferrin receptors, lipokalin-2(LCN-2) and ferroportin that are related to iron metabolism. In our study, proteins related to iron metabolism in various childhood cancers are examined for the first time and results are presented.

Design/Methods: Patients-Method: Part of the study between January 2013-December 2014 included 58 patients who are aged between 1-16y and 17 healthy children at similar age groups. Patients were divided into 4 groups (sarcomas, lymphomas, acute leukaemias, various solid tumors) according to their diagnosis. Serum ferroportin, soluble transferrin receptor (sTFR), transferrin receptor-2 (TFR-2), hepcidin, ferritin heavy chain (FTH-1), ferritin light chain (FTL), LCN-2 levels were examined at diagnosis and in remission using ELISA method.

Results: Results: Levels of FTH-1 was found high in all patients. Levels of FTL was found high in sarcomas and lymphomas, however this was not statistically difference. Levels of LCN-2 was found high (p=0.001) in all patients. TFR-2 levels was found to be higher in all patients and this was statistically difference in lymphomas(p=0.05). Although levels of serum hepcidin found to be higher in all patients, this was statistically difference only in acute leukaemias and lymphomas (p=0.001). It was observed that levels of serum ferroportin were low in sarcomas and leukaemias.

Conclusion: As a result, we found higher levels of ferritin, LCN-2, TFR-2, hepcidin in our study and this made us think that iron deposit could be increased in cancer cells. Increase of hepcidin levels were particularly significant in leukaemias and lymphomas. It is known that hepcidin is related with the IL-6 and IL-6 increase was observed in leukaemia and lymphomas. In the second stage of our study, examination of relationship between cytokine and iron metabolism, and relationship between iron accumulation in tissue and medicine refractoriness is planned.

P-0580 | Anti-Treg Cell is A Potential Treatment for Childhood Neuroblastoma
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Background/Objectives: Neuroblastoma(NB) is a kind of malignant tumour in children, which originated from the primitive neural crest. 50% of patients had metastasis with poor prognosis. CTLA-4(Cytotoxic t-lymphocyte-associated Antigen 4) belongs to the B7 family molecules and Specific expressed in the Treg cells which inhibited the T cell activation. Anti-CTLA-4 was a potential immune treatment in solid tumour. Goal of this research is to investigate the value of Treg cell level in Neuroblastoma and potential use in the immune treatment.

Design/Methods: Patients hospitalized in Beijing Children's Hospital between Jan 2015 and Jun 2015 were included. Meanwhile we also collected more than 200 normal children's peripheral blood as the normal control. We used the Flow cytometry to test the Treg level in both normal child and the NB patients. All the data were collected and analysed by SPSS version 13.0.

Results: Seventy patients were diagnosed NB or developed NB. The median value of Treg cells levels in the normal control was 3.57 (1.4-8.5). And the median value of Treg cells levels in the NB patient was 7.3(3.3-18.9). The result showed the Treg cell of the NB patient was significant higher than the normal child(P<0.01). It suggested that there were a phenomena of immunosuppression in the neuroblastoma. Anti-CTLA-4 was a potential useful way to treat the neuroblastoma.

Conclusion: When the tumour happened, the immune system was suppressed by Treg cell. And the CTLA-4 were expressed on the Treg cell which inhibited the immune system. Anti-CTLA-4 could block the the CTLA-4 on the Treg cell and removed the depression of T cell activation. Blockade of Treg cell provided a theoretical foundation for immunotherapy of neuroblastoma.

NURSING

P-0581 | Reaching into Your Toolbox: Creative and Effective Teaching Strategies to Educate Paediatric Nurses Working in Both Low-And Middle Income Countries and High Income Countries

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Background/Objectives: Pediatric oncology nurses teaching in low-and middle income countries (LMIC) and high income countries (HIC) must communicate information that is relevant and meaningful within the local nursing culture and scope of nursing practice. The purpose of this abstract is to identify the challenges that nurse educators and consultants confront when teaching outside their country and present a toolbox of teaching strategies.

Design/Methods: Nurses are not passive learners and must be involved in the learning process. Although one may think that PowerPoint is the preferred method of teaching the adult learner, it is not always the best way to educate nurses. The challenge is to keep the nurse learners focused and engaged; therefore, it is necessary to have a variety of teaching strategies when teaching both theoretical and clinical knowledge of paediatric oncology nursing in the classroom setting.

Results: It is important to know your audience. The nurse educator must quickly assess the learners and be flexible. By acknowledging that one size does not fit all, the nurse educator has permission to utilize a variety of teaching methods. PowerPoint presentations must use images as well as text with opportunities for interactive activities dispersed throughout a lecture. Examples of this type of learning include videos of a skill or concept such as hand-washing, case studies with small group discussions and/or presentations, individual or group brainstorming sessions. Ask as well as encourage questions. Actual clinical scenarios and role playing activities often demonstrate greater value than textual lectures. Game playing was shown to be an

effective strategy for testing learned knowledge. These approaches engage the learner and create a positive learning environment.

Conclusion: The nurse educator must utilize creativity to draw from an arsenal of teaching strategies. Recognizing that language and cultural differences can be a barrier, the nurse must embrace the challenge to successfully promote learning.

P-0582 | Facilitating Radiotherapy for Children: Technique, Design and Professional Care in Synergy, a Multicenter Intervention Study

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Background/Objectives: There is a lack of comprehensive investigations into how parents and children cope with radiotherapy, such as which tools and strategies are most common and important. The present study aims to evaluate parents' experiences and responses to an intervention that psychologically prepares children and their families for a child's radiotherapy.

Design/Methods: The study was performed as a multicenter baseline/intervention design at three paediatric radiotherapy centers in Sweden. The intervention, a systematic strategy for psychological preparation and distraction, was developed in a multi-professional collaboration with Umeå Institute of Design, radio-oncologists and nursing researchers, using interviews and a Human Centered Design approach. The intervention included age-adjusted information on tablets, stuffed toys and toy models of the CT and RT-machines. For evaluation, a mixed-methods data collection was conducted including interviews, surveys and rating scales. A total of 57 children and their parents were included: N=30 children in the baseline group and N=27 in the intervention group. Results from the parents' data will be presented.

Results: Overall, the parents expressed positive feelings in the interviews. They found the information suitable for their young children on the tablets and saw them finding pleasure and distraction. Siblings and friends were involved and the children used the toy models for play both before and after the radiotherapy. The parents requested technical development of the tablets and more diagnose-adjusted information. They rated their Health Related Quality of life low, but parents in the intervention group expressed less worry and anxiety.

Conclusion: The innovative solutions contributed to parents' positive experiences for their child, siblings and themselves and in addition reduced worry and anxiety. More diagnose-adjusted information might be tested in a future design model.

Acknowledgement: We thank the parents for their participation and The Swedish Childhood Cancer Foundation and Cancer Research Foundation in Northern Sweden for funding.

P-0583 | Audit of Factors Influencing Nursing Staff Leaving Principal Treatment Centres Within the United Kingdom and Ireland, over a One Year Period

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Background/Objectives: The Children and Young People's Cancer Nurse Education Group (CYPNEG), a subgroup of the Royal College of Nursing's (RCN) Children and Young People's Specialist Nursing Forum meet twice a year and regularly discuss staffing as a challenging issue within Principal Treatment Centres (PTC's) across the United Kingdom (UK) and Ireland. The RCN London Safe Staffing report published in 2015 identified that nursing staff simply cannot afford to live and work in London. As the PTCs are based in cities we wanted to explore whether this was a factor for nurses within our speciality, or if there were other similarities causing nurses to leave.

Design/Methods: The group retrospectively collated the numbers of nursing staff who had left the inpatient and outpatient areas within the paediatric oncology setting of their principal treatment centres. They also retrospectively accessed leaver questionnaires/exit interviews and any records that were held which indicated why staff had left.

Results: One hundred and thirteen nursing staff left ward posts within the year of the audit, these were distributed across all bands from 5-8a. The top three reasons for leaving ward posts were Cost of living, lifestyle and impact of shift work and, promotion within the speciality. Stress and pressure of the speciality was also cited frequently. Positively a number of staff left ward areas but to take promotional positions within the speciality.

Conclusion: As a group of educators we are unable to influence the cost of living for staff, however we were surprised at the relatively small number of staff leaving due to this. What we felt important to identify was the number of staff who left due to stress and pressure of the job, and it was positive that staff had feedback that they found access to clinical support, and training whilst learning the speciality of benefit.

P-0584 | Pain and Health-Related Quality of Life in Children with Cancer

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Background/Objectives: Currently, over 79% of children with cancer survive due to more aggressive treatments. The assessment of health-related quality of life (HRQOL) for health professionals is crucial to a valid and accurate diagnosis can sustain an effective intervention in its improvement. This study aimed at correlating pain experiences in children with cancer and their HRQOL.

Design/Methods: Descriptive cross-sectional study that included children aged between 8 and 17 years who had been admitted to two Portuguese paediatric oncology units. Children were selected consecutively. Data were collected on the first day of admission and pain was measured through the use of the Adolescent Pediatric Pain Tool and the HRQOL using the Pediatric Quality of Life Inventory - Cancer Module 3.0.

Results: The intensity of pain reported by 75 children ranged between 0 and 7.9, with a median of 1. About 38 children (50.7%) reported no pain. The number of sites of pain ranged between 0 and 16, with a median of 2 sites. The mean HRQOL was 66.0 ± 13.3. The highest score was obtained in the "perceived physical appearance" subscale (79.0 ± 21.2) and "treatment anxiety" subscale (79.0 ± 27.2), whereas the worst score was obtained in the "worry" subscale (39.2 ± 28.1). The correlation between pain intensity and HRQOL was statistically not significant ($r_{sp} = -0.12$; $p > 0.05$), similar to the correlation between the number of sites of pain and HRQOL ($r_{sp} = -0.09$; $p > 0.05$).

Conclusion: Although pain is a frequent symptom in children with cancer, this experience did not seem to affect their HRQOL. However, further studies are needed to find health care-sensitive areas of intervention that influence the HRQOL of children with cancer.

P-0585 | Development of a Mucosal Barrier Risk Assessment Tool for Paediatric Patients with Oncologic Disease

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Background/Objectives: Mucosal barrier injury is a complication that many paediatric patients with oncologic disease encounter during their treatment. Mucosal barrier injury can be painful to patients and puts the patients at high risk of developing complications. When the mucosal barrier is broken, the patient is at risk of developing severe, life threatening infection. Patients receiving oncologic treatment are often neutropenic putting these patients at an even higher risk of severe complications. Mucosal barrier injury also can prolong or generate a hospital admission. Patients can develop high levels of pain with mucosal barrier injury that may require high doses of opioids to treat the pain, sometimes requiring intensive care treatment.

The ability to recognize patients at high risk of developing mucosal barrier injury can aid in early treatment and may stop the progression of injury or further complications. This quality improvement project is the creation and validation of an assessment tool used to identify patients who are at risk of mucosal barrier injury. The tool can be completed by the patient's nurse and communicated to the provider using strengths of the multidisciplinary team to treat the patient and prevent complications. This tool will provide supportive care for the paediatric patient receiving oncologic treatment.

Design/Methods: Identified possible risks and place a scoring method to the tool.

Use tool on all paediatric patients with oncologic disease receiving treatment who are inpatient and perform a chart review on these patients for 30 days after their assessment was completed to determine if there were complications. This will be compared to a chart review of similar patients who did not have the risk assessment tool used to determine if the knowledge of risk affected patient outcomes.

Results: Note: This study is currently in progress and would have results for inclusion prior to the Conference.

Conclusion: See results note.

P-0586 | Role of Nursing Staff in Out-Patient Management of Paediatric Low-Risk Febrile Neutropenia: A Single Institutional Prospective Observational Study

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Background/Objectives: Febrile neutropenia (FN) is the most common clinical scenarios encountered during treatment of paediatric malignancies. Majority of low-risk FN can be effectively treated on an out-patient department (OPD) basis with the help of nursing staff.

Design/Methods: We have prospectively evaluated all paediatric (≤ 18 years) cancer patients with FN WHO presented in OPD. FN was defined as an oral temperature $>38.5^\circ\text{C}$ or two consecutive readings of $>38.0^\circ\text{C}$ for 2 hour and an absolute neutrophil count $<0.5 \times 10^9/\text{l}$, or expected to fall below $0.5 \times 10^9/\text{l}$. Low-risk or high-risk FN were categorized as per Multinational Association for Supportive Care in Cancer risk index. All patients of low-risk FN were treated with first line antibiotics (intravenous cefoperazone-sulbactam and amikacin) on OPD basis and were followed-up on daily basis by our nursing staff. They consulted the physician in case of no improvement in next 24 hours. Up-gradation to 2nd line antibiotics and use of antifungal agents were made as per institutional guidelines. Baseline blood culture-sensitivity test were sent by our nursing staff whenever feasible.

Results: A total of 514 episode of fever during chemotherapy were encountered between 1st Aug¹⁵ and 29th Feb¹⁶, of which 336 episodes met the definition of FN. One-hundred and five episodes had low-risk FN (31%), out of which 87 episodes (83%) were managed on OPD basis; only 4 required up-gradations to 2nd line antibiotics. The rest 18 episodes (13%) required inpatient care and 17 (94%) got discharged after cure of infection; one patient died of pneumonia. Three out of 51 episodes tested had a growth in blood culture samples.

Conclusion: Majority of low-risk FN can be treated on OPD basis with 1st line antibiotics under active supervision of nursing staff and can reduce the admission rate and cost of therapy, especially in a resource-poor setting.

P-0587 | Haematology/Oncology Hickman Education App

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Background/Objectives: The clinical nurse specialist team in the Haematology/oncology unit have taught parents how to care for their child's Hickman line for many years using a specially adapted doll and written guidelines. A Hickman education DVD was previously designed and used. Most people now access smart phones and tablets so an App would be more user friendly.

Design/Methods: Discussions were held with members of the multidisciplinary team regarding the appropriateness of developing an App. A literature review was completed to ensure current best practise was adhered to. A core group of parents and staff members were consulted during the development stages to ensure information that would suit both parents and health care professionals.

An App development company was contacted and employed.

The App contains written information and video demonstrations, including:

- Practical information on using the Hickman catheter
- Troubleshooting
- Procedures on Hickman catheter care, taking bloods and cytarabine administration
- Contact numbers

An information poster was designed explaining what the App is about and how to download it to specific devices. This was displayed in our inpatient unit and day unit. The App has been incorporated into our current teaching practises.

Results: A questionnaire was devised to ascertain feedback from parents who utilised the app over a 4 month period. An excel spreadsheet to analyse the data was developed.

Feedback from the questionnaire and verbal feedback was very positive. There was some difficulty in finding space on mobile phones to download the App but feedback relating to the content of the App was all positive.

Use of the app has produced a reduction in teaching times of 25% prior to parental sign off in Hickman care competencies.

Conclusion: Integrating information technology into nursing practise is innovative and can be of significant benefit for families and health care professionals.

P-0588 | Electronic do not Resuscitation Documentation as a Means of Improving Communication

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Background/Objectives: Do Not Resuscitate (DNR) status is important information for clinicians in the provision of care to paediatric oncology patients. The state of Tennessee requires a paper document to communicate DNR status, while our facility has transitioned to a predominately paper-free environment. Anecdotal evidence suggests that there is a breakdown in DNR status communication between the physical and the electronic medical records (EMR). An extensive literature search supported efforts to improve coordination of care, but yielded very little pertinent data to either refute or confirm this anecdotal information. The purpose of this evidence-based practice project is to assess the current DNR communication process and identify changes to better meet the needs of the entire interdisciplinary team.

Design/Methods: A survey was distributed to clinical staff to evaluate satisfaction with the current method of accessing DNR status, as well as preferences for alternate locations for this information in the EMR. Follow-up surveys will be conducted at 3 and 6 months following physician education to determine satisfaction with the process changes. Chart audits will be conducted at 12 month intervals to determine compliance with the new process.

Results: A revised DNR communication process was implemented institution wide. The current institutional policy regarding DNR status communication was updated to standardize the inclusion of the DNR status in the EMR. Education regarding the updated DNR communication process will be conducted throughout the facility and a chart audit will be conducted at one year to evaluate compliance with the new process.

Conclusion: Increased visibility of a patient's DNR status within the EMR is expected to improve communication of this sensitive information across disciplines and reduce the likelihood of adverse events relating to resuscitative efforts.

P-0589 | Administration of Subcutaneous Cytarabine in a Home Environment

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Background/Objectives: Children receiving cancer treatment face many disruptions to their normal routines. These disruptions are often caused by frequent hospital visits and can have a significant impact on their quality of life. Developing novel approaches to providing chemotherapy in a home environment supports patient centered care.

The Oncology, Haematology & Blood and Marrow Transplant Program at British Columbia Children's Hospital (BCCH) in Vancouver, British Columbia (BC), Canada, is challenged by its geographical location. Given that BCCH is the only tertiary care center for paediatric oncology within the province, many families travel significant distances to receive cancer care. Recognizing that certain chemotherapy protocols require daily administration of cytarabine, a new approach was sought. Until recently, patients and their caregivers were required to visit BCCH to receive each dose of cytarabine via intravenous push. While these are often relatively short visits, they undoubtedly cause interruptions in daily living, particularly for those travelling to Vancouver from elsewhere across BC.

Design/Methods: An interdisciplinary team of oncology nurses, physicians and pharmacists collaborated to develop and implement an initiative allowing for administration of cytarabine subcutaneously in a home environment. Our aim was to provide education to patients and their

caregivers to safely administer cytarabine via subcutaneous injection themselves in hope of decreasing the frequency of hospital visits and thus increasing quality of life.

Results: The initiative will be evaluated using quality of life indicators and patient/caregiver satisfaction measures, along with a review of feasibility and number of hospital visits.

Conclusion: A diagnosis of cancer has a considerable impact on a child's home life. Developing creative solutions in accordance with treatment protocols, such as administration of subcutaneous cytarabine in a home environment, may improve quality of life for patients and their caregivers who do not reside close to a treatment center.

P-0590 | Promoting Professional Growth of the New Hematopoietic Stem Cell Transplant Nurse

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Background/Objectives: Hematopoietic Stem Cell Transplant (HSCT) is a complex treatment option available to children with a variety of life threatening illnesses including hematologic malignancies, immunological diseases, bone marrow failure syndromes, and genetic disorders. Providing care to children undergoing a stem cell transplant is a distinct and specialized type of nursing, one that requires a comprehensive training program. At Boston Children's Hospital (BCH) we provide a 12 – 14 week orientation program that includes a didactic component as well as hands on experience with a preceptor.

Design/Methods: Our program is designed to meet the Foundation for Accreditation of Cellular Therapy (FACT) education guidelines. We provide general paediatric training concentrating on developing competency in caring for paediatric HSCT patients and their families. Classes are interspersed throughout the orientation. They include central orientation, program specific, and HSCT classes. The HSCT classes address all aspects of HSCT care, conditioning/ablative therapy, administration of human progenitor cells, supportive care, managing complications, and patient family education.

Results: In addition to the classes the new registered nurses' orientation to the HSCT unit includes one-on-one orientation with a preceptor who has attended a preceptor workshop and is competent in the care of the HSCT patient. The unit orientation incorporates all aspects of caring for the HSCT patient. This experience is progressive; assignments are limited and increase as orientation proceeds. During the orientation the new nurse and preceptor care for HSCT patients during various stages of the HSCT process.

Conclusion: Staff development for HSCT nurses at BCH is a continuous process. During orientation the Nurse Manager and Clinical Nurse Educator collaborate with the new nurse and preceptor to confirm that orientation goals are met. Going forward the new nurse will have education goals as part of their annual review as outlined in the RN Clinical Development Expectations as well as continued competency in HSCT.

P-0591 | The Role of the Research Nurse in Enabling Families to Make Informed Decisions Concerning their Children's Treatment in a Digital Age

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Background/Objectives: In the UK there have been a number of cases where parents have wanted non-standard therapy in the treatment of their child; the most notorious of these was a young boy whose parents took him overseas to try and force UK authorities to finance his proton therapy against medical opinion. Whilst this may have an isolated incident the increasing level of information available via the internet - not always accurate or relevant - is influencing the decisions made by parents in relation to clinical trials. This paper will explore the issues concerning gaining informed consent in the digital age with particular reference to the role of the research nurse.

Design/Methods: A literature review has been undertaken which demonstrates a paucity of research and other published high quality data in this area. However there are some opinion papers that discuss specific cases. By including this with related research data, published anecdotal accounts and discussion within wider research team we have drawn together the threads of the argument and made some suggestions for good practice.

Results: Parents gain knowledge concerning their child's treatment and prognosis from a wide variety of sources, these include the information provided by health care professionals, disease related Facebook pages, and of course the ubiquitous google search. The quality of this information is variable. Parents do not always have the background knowledge to judge and appraise the information they discover. As one consultant said "There's a doctor that makes me very afraid and which influences patients. It's Doctor Google".

Conclusion: Research nurses are in a privileged position to help inform parent's decision making processes. They need to understand the changes that are occurring. Social media should be embraced rather than being seen as an enemy. Examples of this are dedicated twitter or Facebook accounts, or the supplementation of information sheets with newer media e.g. YouTube.

P-0592 | Job Analysis of Paediatric Oncology Nurses in Advanced Practice Nurse-Led Integrated Service

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Background/Objectives: About 1,200 children per year were diagnosed childhood cancer and survival rate is rising each year by advanced medical technology in Korea. The consequences of cancer and its treatment are devastating and many patients suffer long-term effects for years

after completion of treatment. The latest trend in childhood cancer treatment has changed from inpatient to outpatient and paediatric oncology advanced practice nurses play a key role in care patients and collaboration with health care team as a control tower. The purpose of this study was to investigate advanced practice nurses' duties as well as effects of an advanced practice nurse-led integrated service that would provide comprehensive survivorship care for children with cancer.

Design/Methods: Pediatric oncology advanced practice nurses classified their nursing activities according to characteristics of specific duty and task and recorded activity frequency based on working log at C university hospital in 2015.

Results: Pediatric oncology advanced practice nurses dealt with 234.4 cases of management of medical record every month. Education for patients and their family recorded 109.2 cases, while screening and confirming chemotherapy order followed with 105.3 cases.

Conclusion: Pediatric oncology advanced practice nurses were in charge of performing medical treatment and returning children to daily life successfully. Furthermore, advanced practice nurse-led integrated service may lead improving quality of life and survivorship in children with cancer.

P-0593 | Effects of Art Intervention Program for Siblings of Paediatric Cancer Patients

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Background/Objectives: Siblings of paediatric cancer patients often experience negative feelings such as loneliness, depression, jealousy, guilt, and grievance. Art intervention is helpful for children to encourage expression feeling and overcome hardships. The purpose of this study is to develop an Art Intervention Program to improve the psychological adaptation of siblings of paediatric cancer patients and to evaluate its effects.

Design/Methods: Art intervention program was conducted with 17 siblings of paediatric cancer patients who aged 8 to 11. Program consisted of 12 sessions which were carried out once a week. The effects of the intervention were assessed in terms of categories of self-esteem, anxiety, depression and problem behavior.

Results: Overall self-esteem was significantly improved after the intervention in comparison with the pretest. Children showed lower score in externalizing problem scale and total behavior problem scale after the art program. However, anxiety and depression were not changed by art program.

Conclusion: The Art intervention program was effective in improving the self-esteem of siblings of paediatric cancer patients, and partially effective in reducing problem behavior. Nursing intervention integrated with art program may be suitable for children to manage psychological problem. Therefore, the Art intervention program will be used as a mediating way to help siblings of children with cancer to improve psychological adaptation.

P-0594 | Evaluation of Simple and Effective Oral Hygiene Interventions in the Prevention of Chemotherapy Induced Mucositis at Indus Children Cancer Center

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Background/Objectives: Oral mucositis is a frequent side effect of anticancer treatments. It impairs the patient's quality of life, aggravates clinical conditions, increases the risk of infection and can delay anticancer treatment. Healthcare Workers (HCW) at the Indus Children Cancer Hospital (ICCH) emphasize on a simple intervention for oral hygiene to prevent such complications for the patients. Proper oral hygiene protocol can reduce the risk of oral ulcers. These study intends to evaluate the effectiveness of simple interventions such as patient family education on children undergoing active chemotherapy at CCH.

Design/Methods: An interventional study was conducted from date January 2015 to December 2015 at CCH. During this period 11% (232/2139) of the children actively undergoing chemotherapy had mucositis of different stages/grades.

Results: According to the analysis in January 2015 almost 14% (25/178) children had oral ulcers from which 80% children were identified at grade 1. Despite interventions till June 2015 the oral mucositis rate were fluctuating from 14% to 18%, and there was no significant change observed in the reduction of occurrence of oral mucositis.

After providing increased Patient Family Education sessions on tooth brushing, use of icy water/ ice chips to rinse oral cavity and the use of bicarb mouthwash, there was a significant reduction in the occurrence of oral ulcers. July 2015 saw a drop in occurrence to 4%. This rate remained constant between 4% to 6% with continuous monitoring, intervention and evaluation. This shows the importance of intervention, which reduced oral mucositis by almost 50%.

Conclusion: The use of proper oral hygiene protocols can decrease the risk of chemotherapy induced mucositis. Majority of the patients at ICCH understand the importance of oral hygiene. Furthermore oral hygiene can decrease levels of oral mucositis and eventually decrease inpatient admissions, delays in treatments and improving the quality of life.

P-0595 | Service Development in the Oncology Day Unit

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Background/Objectives: Southampton University Hospitals is one of 22 designated paediatric oncology primary treatment centres in the UK. The day unit co-ordinates the care of

patients from 12 shared care hospitals including, administration of chemotherapy, intrathecal chemotherapy via 2 anaesthetic lists, arranging investigations, patient reviews, long term follow up and supportive care. The unit liaises with shared care hospital teams to update information on patient treatment to provide safe patient care. Increasing patient numbers and complex protocols over time have reduced the efficiency of the unit with communication becoming less productive.

To modernise the oncology day unit, through the use of technology and changes to working practices, to improve patient and colleague satisfaction, staff morale and attitudes whilst maintaining safe delivery of care.

Design/Methods: Changes were implemented over an 18 month period, including introduction of an online diary system with individual time slots, improvements to nursing and medical paperwork. Chemotherapy and Vincristine clinics enabling even distribution of patients throughout the week. Transfer of patient information via secure e-mail including document scanning. Allocation of patients to distribute workload, designated nurse for shared care hospital links and echocardiogram clinic.

Results: Reduction in phone calls from shared care hospitals requiring information, releasing staff time to spend on patient care. The introduction of ARIA and NHS NET provide a trail for prescriptions and patient information. Positive feedback from colleagues in shared care centres due to improved quality and quantity of information. Shorter waiting times and communication improvements were highlighted in a patient satisfaction survey.

Conclusion: Technology and working practice changes have improved the quality of the patient experience. Staff have positively supported these changes leading to an improved working environment, released time to care and improved attitudes towards communication and service development.

P-0596 | Review of Education Provided to Parents in the Haematology/Oncology Unit, our Lady's Children's Hospital, Crumlin

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Background/Objectives: Education is an integral component of the Haematology/Oncology Clinical Nurse Specialist service. The education of parents empowers them to care for their ill child at home. The aim of this poster is to provide a retrospective review of the CNS parent education programme from January 2012 to December 2014.

Design/Methods: Accessing our CNS electronic database we identified all parents who were educated. The data was audited to determine the total number of parents who were educated, the type of education given and the average time spent providing this service. The teaching provided is given by individual teaching sessions with the aid of our educational tools such as the Passport, Cytarabine booklet and Hickman App.

Results: Five hundred and twenty one children were referred to the Haematology/Oncology service between 2012 and 2014. All of these parents received fundamental education.

The average time spent providing this teaching was 5 hours. 238 parents went on to receive training on caring for their child's Hickman line which represents 45% of parents. This took approximately 6.5 hours. The criteria for eligibility is determined by the CNS. Parents must be deemed competent to carry out a Hickman dressing before they can be taught how to take blood samples from the Hickman catheter. 27% of parents were trained and took approx. 3 hours. 9.5% of parents were taught how to perform a full blood count using a fingerprick technique and took approx. 2 hours.

The administration of Intravenous Cytosine Arabinoside (Ara-C) teaching is given to parents of children who have blocks of ARA-C on their treatment protocol. 31% of parents participated in this learning programme and took approx. 3 hours to teach.

Conclusion: The education programmes provided aim to meet the individual needs of the child and family. We are consistently looking at innovative ways to assist our education programmes.

P-0597 | An Education Programme for Parents to Facilitate Safe Administration of Intravenous Chemotherapy at Home

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Background/Objectives: Intravenous (IV) Cytosine Arabinoside (ARA-C) is a chemotherapy agent used in the treatment of Acute Lymphoblastic Leukaemia and Lymphoma. In 2009, a multidisciplinary Haematology/Oncology Steering Group established an educational programme preparing parents to administer IV ARA-C at home. Prior to this programme patients had to travel to the tertiary hospital, local shared-care hospital or general practitioner to have IV ARA-C administered.

Design/Methods: All parents who undertook the education programme were invited to complete a questionnaire to evaluate the education programme and to identify the benefits and concerns of administering IV ARA-C at home. The questionnaires were audited to determine the activity since its inception in 2009.

Results: Since 2009, 140 parents have undertaken the education programme, representing 52% of all eligible parents. Of these, 108 parents returned their evaluation questionnaires, giving a response rate of 77%. Parents identified several benefits to the administration of IV ARA-C at home, including less travel, reduced hospital visits, less disruption and expense, and improved school attendance. The most frequently cited concern related to fear of making an error. However, of the 2004 doses of IV ARA-C administered to children at home by their parents during the evaluation period, there were no reported dosage, dispensing or administration errors, which is in contrast with the existing literature.

Conclusion: Parents reported that being able to administer IV ARA-C at home resulted in reduced financial and time costs, less disruption to daily routines and less physical and psychological effects. This evaluation has identified the strengths of the programme. A home chemotherapy programme must include effective communication between healthcare providers

and parents, and a robust education process about the medications and the possible errors which may arise. The findings will be used to continue to develop and improve the CNS training sessions.

P-0598 | Improving the Discharge Process for Patients Undergoing Hematopoietic Stem Cell Transplants

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Background/Objectives: The hematopoietic stem cell transplant (HSCT) program at our institution is a regional, national, and international referral center performing about 120 allogeneic and autologous stem cell transplants yearly. Nursing staff on our unit felt that our discharge process could be improved as patient and family education was often rushed, taking place on the day of discharge.

Design/Methods: A focus group of nurses conducted a needs assessment for discharges with the purpose of identifying problems with the current discharge process and prioritizing concerns based on issues that affected patient safety and caused delays in discharges. Nurses shared creative ideas with the goal of making discharges safer and more efficient. The qualitative data obtained from this focus group revealed two areas to prioritize for improvement: central line care and organization of prescriptions.

Results: A task force was established to gather further data from staff and to implement interventions aimed at improving the discharge process. A survey of staff nurses showed that while 76% of nurses felt comfortable providing central line care education for families, only 14% of respondents felt that nurses were teaching parents the same techniques for line care at home. Nurses also wanted to prioritize earlier organization of prescriptions, allowing time to cross-check prescriptions with current orders ensuring appropriate medications for home and to address potential issues in obtaining insurance approval.

Conclusion: In response to these suggestions, a central line education book was created to standardize teaching for patients and families. To organize prescriptions, nurses developed an information sheet for the front of patient charts listing the medications and supplies needed. Providers received a time line of expectations for when scripts needed to be completed. Future goals include initiation of a weekly interdisciplinary discharge huddle to review upcoming discharges in order to ensure teaching is on track and to anticipate any potential barriers.

P-0599 | The Impact of Delayed Diagnosis: A Unit Experience

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Background/Objectives: South Africa is still considered as a developing country where skills and resources are still out of reach for major groups in need for oncology care. This is evidenced by challenges encountered by paediatric cancer nurses in the country, where proper screening, prevention and outreach programmes are not available for the majority, as specializing oncology units and personnel are limited.

To highlight how challenges of nursing patients admitted with advanced disease impact on the nurse's ability to render quality care, job satisfaction, resources and nurses morale.

To encourage peers to acquire knowledge, do research, case management and outreach programmes in spite of all these challenges.

Design/Methods: A prospective observational and cross sectional survey of records from 2012 to 2015 was done. Contributory and related factors were looked into for detailed more insight, at 3, 6, 9, and 12 months intervals.

Results: During the analysis, patient turnover of new complicated patients has not decreased: 2012(42); 2013(52); 2014(42); 2015(46)

Contributory factors ranged from: Delayed consultation (30%) Beliefs and Religion (25%); Denial and disbelief (20%); Lack of knowledge and Socio-economic issues (15%) and Poor referral system (10%), Gender: F (38%), M (62%); Lack of school nurses in the country (100%).

Conclusion: Despite ongoing cancer awareness on media, patients are still referred or sent for consultation at a very advanced stage where the disease process and complications has set in. The system is overburdened and more skilled nurses are still needed to minimize complications.

P-0600 | Evaluation of Diet of 30 Paediatric Oncology Patients from Guatemala

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Background/Objectives: Evaluation of the diet of Guatemalan cancer patients from Unidad Nacional de Oncología Pediátrica; identifying common deficiencies and propose an educational handout on how to improve diet using available foods (trifold).

Design/Methods: The study evaluated 33 caregivers of cancer patients in Guatemala, they were surveyed about their children's diet. Trained dietitians collected the 24-hour dietary recalls and were evaluated using Nutritionist Pro, a food processing software (Identified common deficiencies, and common foods from each food group). Dietary intake was compared with recommended intake for macro and micronutrients for age and gender.

Results: In Guatemala the 68% of the evaluated patients cover their 75 to 100 of their Kcal Goal and 87% of the patients cover their 75 to 100 of requirements of protein.

Conclusion: It was considered all the side effects that chemotherapy produced in oncologic paediatric patients in UNOP, about half of the study's population reflected an optimal calorie daily intake and more than 80% of the population reached daily consumption requirements of protein. This patients receive nutritional support during treatment which is based on timely

delivery of nutritional education as well as nutritional formulas and other foods that help balanced nutrition. The frequency of consumption shows that the staple food of the evaluated patients: eggs, tortillas, beef, black beans, sugar, INCAPARINA. The development of adequate nutritional tool in the sociocultural context of the intended population, is an element for nutrition education. This is important in any strategy that is aimed on improving food and nutrition security to prevent any form of malnutrition, either poor or excessive calorie diet, also serve to mitigate the side effects experienced by paediatric cancer patients and promote the active participation of parents or caregivers in the development and implementation of nutrition programs. Adequate intake of micronutrients corresponds to the high consumption of foods that contain them.

P-0601 | A Study on Preparation Which Utilized a Picture Book at Admission - for 3-10 Years Old

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Background/Objectives: The purpose of this study is to explore how preparation utilized a picture book influences handle ability of the children with cancer in primary care of a hospitalization.

Design/Methods: The design was a method of inductive qualitative approach. Subject of children were 8 (3-10 years old) hospitalized for the first time.

Results: Seven categories were analytically generated. Finding revealed "They made up their mind to be hospitalized by receiving preparation when being hospitalized." "They made an effort in order to get over loneliness which gets away from the family, and in order to get." "They could depend on nurses and spend the hospitalization life." "They spent the hospitalization life by the feeling that they cooled down." "They had time by positive feeling in a hospitalization life." "They met with medical practice by positive feeling." "They had the feeling of achievement." as core category.

Conclusion: Children could avoid their crisis by receiving preparation which utilized a picture book. Nurses may have the necessity for the intervention to notice enclosed in a coward unconscious bur, and to reveal suffering confined in the depths of the mind.

P-0602 | A Model for Interacting with Siblings of Children with Cancer

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Background/Objectives: To develop an interaction model for enhancing the spiritual growth of healthy children with a brother or sister with cancer, based on their experience of confronting the onset of cancer and death of their brother or sister.

Design/Methods: 1. Research Design: We employed phenomenology (Edmund Husserl, 1859-1938) and the Trajectory Equifinality Model (TEM, 2006) as the methods to conduct qualitative research (retrospective and longitudinal study), and a narrative interview to construct the life stories of our research subjects.

2. Data Collection and Analysis: We collected data by interviewing 11 subjects consisting of 4 parents and 7 healthy siblings of children with cancer who attended a group of bereaved families and agreed to participate in this research. Interviews were conducted 1-3 times with each subject. Using the philosophical method of Amedeo P. Giorgi, a phenomenological psychologist who developed the descriptive phenomenological method of research, the obtained data were analyzed employing a qualitative and descriptive approach.

Results: A total of 394 phenomena, 66 constituent elements, and 27 essential elements were extracted from the verbatim records. The experiences were represented as a time sequence to set goals for interventions, and we attempted to develop a model by clearly determining the timing of interventions.

The results clarified how siblings of children with cancer perceived the experience of confronting their brother or sister struggling with cancer as well as their death. Also, the essential experience of siblings and the sequence of events were clarified using phenomenology and the TEM, respectively, suggesting optimal directions of support by describing the appropriate stages and timing of interventions.

Conclusion: Through the experience of confronting the disease and death of their brother or sister, the siblings could achieve spiritual growth by re-establishing a relationship and building new bonds with their family members or other people, as well as discovering new emotions and their meanings.

P-0603 | A Literature Review on Support for Siblings of Children with Cancer - the Current Status and Issues of Psychological and Social Support in Japan and Overseas

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Background/Objectives: To identify the current status and issues of support for siblings of children with cancer in Japan and overseas, and use the obtained results as basic data for establishing a program to support them at medical institutions.

Design/Methods: A literature review using Medline, CINHAL, Ichushi-Web (ver. 5), and CiNii-Web, was conducted, using key words such as "siblings", "support", "child", and "cancer". After excluding duplicates and irrelevant articles, 33 foreign articles published between 2004 and 2014 and 19 domestic articles published between 1994 and 2014 were selected for analysis.

Results: Approximately half (n=15) of the foreign articles were quantitative research reporting: psychosocial interventions to support siblings of children with cancer, the evaluation of psychosocial adjustment and functioning, evaluation of scales, and participation in camp

activities and its assessment. Support for bereaved siblings was reported in 4 articles, and research on donors was observed in 1 literature review study.

Fifteen of the 19 domestic articles were qualitative research. Since Japan has a short history of providing support for siblings of children with cancer, only a small number of articles involved research on their support. Although the necessity of providing it to siblings has gradually been recognized, no study reported interventions, and, as reported in 14 of the 19 articles, support for siblings involved only the provision of patient's information. Research on sibling donors was observed in only 1 article.

Foreign articles involved large-scale studies on interventions, the evaluation of psychosocial adjustment, and development of scales.

Conclusion: The age group-specific characteristics and problems/issues of siblings of children with cancer have gradually been clarified in both domestic and foreign studies. The results indicate the need to establish a program to support siblings of children with cancer at medical institutions, and promote studies on bereavement support, particularly on that for sibling donors.

P-0604 | The Role of a Clinical Research Nurse: A Narrative Review of the Role in a National Paediatric Haematology/Oncology Unit

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Background/Objectives: Our Lady's Children's Hospital Crumlin (OLCHC) is the National Haematology/Oncology and Haematopoietic Stem Cell and Blood Transplant Referral Centre for all paediatric patients who have been diagnosed with a malignant condition in the Republic of Ireland.

The National Haematology/Oncology and Haematopoietic Stem Cell and Blood Transplant department of OLCHC has been participating in multi-centre paediatric clinical trials for over 30 years.

The Clinical Trials Unit (CTU) is comprised of 6 Paediatric Consultants (3 Oncology and 3 Haematology), 1 Clinical Trials Coordinator, 5 Clinical Trial Associates and 2.5 Clinical Research Nurses.

Clinical Research Nurses play a vital role in the initiation and commencement of clinical research studies. Responsibilities includes the selection, recruitment of patients, coordination of clinical trial activity and treatment, patient advocacy ensuring patients are protected and supported throughout their participation in the clinical trial study.

Design/Methods: A descriptive method has been used to provide a detailed review of the role of the Paediatric Haematology/Oncology Clinical Research Nurse within the CTU. The role was highlighted at both organizational and national level, by the initial presentation of a poster within the unit. Posters were presented at both national nursing/medical conferences in Ireland to further educate fellow nursing colleagues and multidisciplinary team members about the role.

Results: The poster presentation highlighted the key role of the Clinical Research Nurse in conducting clinical studies in the National Paediatric Haematology/Oncology Unit, educating fellow nursing and health care professional regarding the various components and extensive responsibilities of the role.

Conclusion: The role of a paediatric Haematology/Oncology Clinical Research Nurse is a central one within a Clinical trial Unit and the multidisciplinary team, requiring specialized knowledge, experience and skills including management and organization, teaching and mentoring, communication and IT skills.

P-0605 | Evaluation of the Biopsychosocial Needs of Young Patients with Cancer by Adapting the Sisom Tool

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Background/Objectives: Children with cancer, go through many painful procedures for a long time, as a part of their medical treatment. Those procedures may even take place in a daily bases and they often result into the appearance of physical and psychological effects, which usually are not noticed by the nurses and do not get treated. Purpose of this study was to prove that the use of an electronic evaluation tool (Sisom) is much more efficient in order to spot the physical and psychological problems children with cancer suffer, during their treatment, in order to improve the care services provided.

Design/Methods: Thirty children, aged 6 – 13 years old were interviewed about the physical and psychological problems they suffer due to their treatment. Also, children were asked to use Sisom, in order to compare the results from using each method and see whether children gave more information during the interview or when they used Sisom.

Results: All thirty children were very excited when they were informed that they were supposed to use an electronic interactive tool while being in hospital. The majority gave more and more specific information while using Sisom and also more children agreed to specify the answers they gave. On the contrary, while being interviewed, most children hesitated to talk about their symptoms during that period of their life and denied to discuss any further on sensitive themes, such as death or the possibility of a relapse.

Conclusion: The use of an electronic, interactive tool is much more effective into having more information about the physical and psychological problems children with cancer suffer, compared to an interview.

P-0606 | Quality of Life in Adolescents with Cancer and Survivors

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Background/Objectives: Adolescents who have been diagnosed with cancer are a particularly sensitive group of patients with increased risk of emotional disorders and decreased quality of life. The aim of the study was to assess the quality of life of adolescents with cancer and survivors as well as the effect of various demographic factors upon it.

Design/Methods: The sample of the study included 82 adolescents aged 13-20 years who had been diagnosed with any form of cancer. 26 out then received treatment and 56 survivors had successfully completed their treatment. Data collection lasted from July 2010 to December 2012 in Children's Haematology-Oncology Unit in Athens. For data collection Minneapolis-Manchester Quality Questionnaire of Life Instrument was used. The quality of life assessment for adolescents undergoing treatment was performed with three (3) measurements and their survivors with one measurement. In order to conduct this research, authorization was preceded from the Hospitals' Scientific Council (Protocol number 7853/04.04.08).

Results: The quality of life of adolescent patients did not significantly change during treatment and they showed a satisfactory quality of life. Boys scored higher than girls ($z = -1.78$, $p = 0.04$ and $t = 2.27$, $p = 0.02$ respectively) as far as quality of life in social relations is concerned ($z = -2.79$, $p = 0.002$ and $z = -2.31$, $p = 0.01$ respectively). Scores on the scale for the quality of life of survivors who completed treatment was 3.91. Survivors showed a higher quality of life than the adolescent patients.

Conclusion: The studied population scored a sufficient quality of life, especially survivors ones. Moreover, their quality of life seemed to be influenced by the stage of treatment, the type of cancer, sex, age, family support, and their level of education.

P-0607 | The Use of Innovative Methods of Sanitary Disposal of the Surgical Unit

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Background/Objectives: The timeliness of the problem is based on the necessity of reduction of the use of cleaning and disinfecting agents, water consumption, and decrease of pressure on medical stuff by using ergonomical inventory and scientifically based organization of cleaning process with the application of innovative technologies.

Design/Methods: From 2013 till the December of 2015 the system of harmless cleaning is applied in the surgical unit, it is used for all the cleanings and disinfections. The inventory is made of polymeric materials, it can stand the use of disinfecting agents and autoclaving and has color coding. Previously dampen expendable cotton materials are used on the strictly defined area, it keeps the constant concentration of disinfection solution what leads to the prevention of cross contamination and also to the prevention of splash of contaminated liquids. As cleaning is over the inventory needs sanitary disposal for its future use. The system can be used with any means which are appropriate for the cleaning of operation unit.

Results: 153 deep cleanings and 2 964 ordinary cleanings are made. The use of the system allowed to reduce the stuff by 67% and to reduce the time of cleaning for 2,6 times. Duly made washouts and inoculations showed negative result in all cases. The quantity of sanitary indicator microorganisms using all the methods of cleaning amounted to 0% whereas the norm before the start of the work is 200 CFU/cm and the norm during the work is 500 CFU/cm. Performed 497 operations in 460 children with solid tumors, from 2013 till 2015 years. Early postoperative complications caused by an infectious process were observed in 7 (1.5%) cases.

Conclusion: The innovative system of harmless cleaning is aimed to the prevention of cross contamination, the spread of hospital infection and infectious post-surgery complications.

P-0608 | Information Leaflet on the Completion of Chemotherapy and Transferring to the Out-Patient Follow-Up Clinics

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Background/Objectives: For patients and families reaching the end of in-patient chemotherapy treatment can bring mixed emotions. It is a time of uncertainty and anxiety for patients and extended family that requires adjustment from a well-defined and structured active treatment regimen/protocol to that of no treatment but rather clinical and radiological follow-up only. The aim of the project is to provide patients and families with written information to assist in the transition from active treatment to out-patient follow-up.

Design/Methods: The information leaflet was developed as a result of the Clinical Nurses Specialists (CNS) identifying a high level of anxiety in the parents of patients approaching completion of treatment, accompanied by similar questions being asked by parents. A task group of CNS was formed with the primary aim being to identify themes of questions being asked and ways in which to answer these in a distributable effective manner. Six themes of the most commonly asked questions were identified: what happens in the follow-up clinic, frequency of scans and results thereof, timing of removal of central venous device, medication duration, vaccinations, what to do if my child becomes unwell. Concise answers for each were constructed, reviewed by the multidisciplinary team and the Haematology/Oncology parent partnership before being presented as a 2-sided A4 information folded leaflet. These leaflets are now being given to each family of a patient approaching completion of treatment.

Results: The leaflets have been well received by parents to date. The leaflet's impact will be evaluated by a formal questionnaire to the multidisciplinary team and parents following a further 6 month distribution period.

Conclusion: These leaflets are intended to assist patients and parents in an informed transition to out-patient based follow-up. It is a time that necessitates support and information. A strength of this project has been the parent involvement in the leaflet's development and evaluation.

P-0609 | Teaching Strategies for Parents of Children Newly Diagnosed with Cancer

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Background/Objectives: When a child is diagnosed with cancer, it is a stressful time for parents. Following the diagnosis, parents receive extensive information while attempting to adjust to the diagnosis. Healthcare providers must employ effective strategies to present this essential education to parents but methods to deliver this information are variable. A systematic literature review was performed to determine best methods of providing education for newly diagnosed paediatric oncology patients and their families.

Design/Methods: A literature search was conducted in MEDLINE, CINAHL, and The Cochrane Library databases with an English language limit but no publication date limit. An experienced medical librarian performed the search using keywords and MeSH terms associated with the purpose statement. Due to the limited results within paediatric oncology, the search was expanded to other paediatric diseases or conditions that required the parent to learn new information and/or skills. The review included 83 research-based articles.

Results: Specific nursing teaching strategies can improve the educational process. These strategies include the use of informal, followed by more formal instructional methods, repetition, role modeling, consistent providers, evaluation of the learner's understanding, and establishment of a partnership. In addition, several factors negatively affect the process of learning including how the information was delivered, emotions, language barriers, relationship with healthcare providers, the child's condition, and social issues.

Conclusion: Effective education has the potential to improve parental understanding of the diagnosis and treatment, increase satisfaction and confidence with care, and improve the quality of life for children newly diagnosed with cancer and their family members; however, best teaching strategies must be recognized and incorporated into daily practice.

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P-0610 | Standardizing Nursing Education for Ambulatory Paediatric Oncology Patients

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Background/Objectives: The oral chemotherapy patient education process is not standardized in the ambulatory paediatric oncology patient setting. A multidisciplinary task force was created at the Dana-Farber/ Boston Children's Cancer and Blood Disorders Center (DF/BC) to improve the safety of the oral chemotherapy prescription process, and to educate paediatric oncology patients/caregivers about oral chemotherapy given in the home setting.

Design/Methods: In an initial pilot, nursing verification of oral chemotherapy prescriptions and patient/caregiver education were implemented in one disease center. Verification was documented using a chemotherapy verification checklist. For prescriptions with an available completed checklist, the electronic medical record (EMR) was reviewed to determine the extent of nursing-provided education to parents/caregivers of paediatric patients prescribed oral chemotherapy for home administration. Documentation was screened for such information as educational barriers, chemotherapy storage, administration guidelines, and safe handling. An educational tool was developed to standardize the education provided.

Results: From February 2016 through March 2016, checklists were available for 32 prescriptions that had been verified by nursing. Documentation of verification of dosing was present for the vast majority of prescriptions. Chart review showed that education was not documented for 26 prescriptions. For the six prescriptions with any chart documentation of education, content was highly variable.

Conclusion: Documentation of nursing education provided to parents/caregivers of patients receiving home oral chemotherapy was not standardized in this subset of paediatric oncology patients. Implementation of a comprehensive educational tool to standardize the elements of education that nurses provide is ongoing and future results will be reported.

P-0611 | Evaluating Well-Known Predictors of Cardiovascular Disease in New Childhood Cancer Survivors

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Background/Objectives: Cardiovascular disease is the leading non-cancer cause of death among childhood cancer survivors, including those with anthracycline exposure. Screening new survivors using low-cost well-known predictors of cardiovascular disease would allow early intervention to prevent or delay its onset. The study objective was to evaluate the feasibility of screening new survivors using two low-cost well-known predictors of cardiovascular disease (e.g., arterial stiffness, vascular inflammation).

Design/Methods: The study uses a prospective observational design. Data are being collected at a single institution during regularly scheduled clinical visits. Consecutive new survivors who meet criteria (aged 7-19 years; 1-4 months post-treatment; anthracycline exposure; no evidence of cardiac disease, diabetes, renal dysfunction or infection) are invited to enroll and consent/assent is obtained. Arterial stiffness is measured by carotid-femoral pulse wave velocity (PWV) using portable, non-invasive technology (e.g., peripheral artery tonometry) in a clinic examination room. Vascular inflammation is measured by high sensitivity c-reactive protein (CRP) in serum obtained during clinically indicated blood sampling. Demographic and clinical (weight, height, blood pressure, treatment exposures, most recent echocardiograph results) data are also collected.

Results: To date, 21 new survivors have been evaluated (mean age 12.28, SD 3.26 years, 57% male, 24% Hispanic, 19% non-White, mean time post treatment 2.52, SD 1.03). Of these, 45% had leukaemia, 25% lymphoma, 30% solid tumour, and 20% received chemotherapy plus radiotherapy. Enrollment, evaluation and data analysis are ongoing. PWV measurements will be compared to child and adolescent reference values. CRP measurements will be compared to established cut-points.

Conclusion: Screening new survivors for known predictors of cardiovascular disease during regularly scheduled clinical visits is feasible and could allow us to identify those who need early and aggressive intervention using cognitive-behavioral and/or pharmacological approaches. These well-known predictors of cardiovascular disease are modifiable and thus they could be used as surrogate endpoints in research to improve cardiovascular outcomes.

P-0612 | A Standardized Daily Oral Care and Hygiene Bundle for Paediatric Oncology Patients

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Background/Objectives: Pediatric oncology patients are at high risk of infection related to ongoing immunosuppression. Consistent oral and hygiene care are critical in prevention of infection. In a large paediatric cancer center, staff observed inconsistent oral and hygiene care. It was reported that patient's and provider's lack of understanding of its importance, uncertainty of proper procedure, and patient's unwillingness contributed to this inconsistency. Duration of treatments expose these patients to develop mild to moderate oral mucositis (OM), bloodstream infections (BSIs) and subsequent potential of life threatening bacteremia. Consistent oral hygiene may reduce the severity of OM and subsequent BSIs. Bundled care has been proven to increase consistency of care. A review of evidence based practice oral care was conducted. The findings led to the development of a practical and affordable oral care bundle.

Design/Methods: In an attempt to mitigate inconsistent care, reduce the severity of OM and subsequent infections; the bundle was proposed to key stakeholders. The bundle includes use of a soft bristled toothbrush, fluoride toothpaste, twice daily brushing, twice daily sodium bicarbonate or dry mouth oral rinse and an optional mouth moisturizing gel. Additionally, a daily bath and linen change was implemented as the hygiene component. A laminated oral care and hygiene bundle checklist was placed in each patient's room to encourage family participation and bundle adherence. The bundle was piloted and now fully implemented for all oncology patients.

Results: Evaluation of the bundle implementation included incidence of mucosal barrier injury-related infections (MBI-CLABSIs), patient family satisfaction and nursing provision of oral care. Previous MBI-CLABSI rates of 2.56/1000 catheter days decreased to 0.99/1000 catheter days with recent results at zero.

Conclusion: The ongoing bundle use maintains effort to improve quality and consistency of daily oral and hygiene care in this vulnerable patient population as we continue to do no patient harm.

P-0613 | The Role of a Paediatric Oncology Rehabilitation Nurse

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Background/Objectives: In Israel, about 450 children and adolescents are diagnosed each year with cancer. Due to new treatments, the majority of children recover from their illness. However, alongside these achievements there are side effects that accompany the treatments from diagnosis for years to come. During the active phase of treatment, a wide array of supportive treatments is offered.

Many patients are unable to complete the recommended regimen of the supportive treatments. Maintaining a regular follow-up schedule is challenging, the treatment phase is completed. At this point, the treatment plan is neglected and many patients fall between the cracks, resulting in delay or lack of rehabilitative care.

The importance of creating a rehabilitation program from the start of treatments is a model that exists only in adults. Research indicates that a structured rehabilitative program improves the quality of life among these patients.

Problem- Review of existing literature, revealed the absence of a model that addresses the role of a paediatric rehabilitation-oncology nurse.

Design/Methods: Purpose: The aim of this presentation is to increase awareness among clinicians to the importance of the role of Oncology-Rehabilitation nurse.

Results: We will present case study reports of two patients that required admission into a rehabilitation hospital due to the development of late side effects. We will describe the challenges related to this unique care.

Conclusion: Recommendation:

- Integrate into the field of paediatric oncology an orientation to rehabilitation.
- Incorporate into the nursing educational program of the oncology advanced course a rehabilitation component.
- Create a nurse case manager role focused on oncology-rehabilitation that will identify the patient's rehabilitative needs.
- Addition of a rehabilitation nurse into the long term follow up clinic will enable close monitoring of the patient's needs.
- Educate the staff of paediatric rehabilitation centers about cancer treatments and its side effects.
- Further research in this area should be conducted.

P-0614 | Identification, Comparison and Clinical Application of Interventions Core to Paediatric Oncology Nursing Based on Nursing Interventions Classification NIC-6th)

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Background/Objectives: To identify the core interventions performed by paediatric oncology nurses and compared them with U.S.'s, and also to know their clinical application.

Design/Methods: The basis of a questionnaire was based on the Chinese translation version of NIC-6th. A 10-member expert panel engaged in a 2-round survey to identify the core interventions of paediatric oncology nursing from 2 aspects: the representation of paediatric nursing and the frequency of application in clinic. The results from the experts consensus were designed to be the items in a questionnaire of application frequency, which applied for 285 paediatric oncology nurses from 5 national wide triaged hospitals on January 2016.

Results: 82 interventions were selected as core interventions to paediatric oncology nursing, 24 of which were same as ones of 42 core paediatric oncology nursing interventions from NIC. The sensitivity and specificity is 57.1%, 65.5%. Chinese and American paediatric oncology nurses both preferred to physiological complex, behavior and family domain. In classes, Chinese paediatric oncology nurses performed more interventions related to patient education (20.7%), risk management (12.2%) and childrearing care (13.4%), while American nurses to coping assistance (14.3%) and lifespan care (14.3%). The application rate of 82 core interventions were from 83.86% to 100%, and 97.56% interventions were applied at least once a day by more than 50% of the paediatric oncology nurses. There are differences between North China and East, West, South China in basic and complex physiology domains, and differences between North China and East China in family domains. As to professional grade, intermediate grade nurses performed frequently in basic physiology domains than other ones. There is no significant difference among departments, positions and education levels in domains.

Conclusion: Pediatric oncology nursing core interventions show similarity between China and U.S. in domains, but significant differences in classes. Core interventions of paediatric oncology nursing are frequently performed in practice, showing difference by the groups of regions and professional grades.

P-0615 | Advanced Nurse Practitioners (ANPS) - an Audit of Services Provided in Tertiary Paediatric Oncology Centres in the UK

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Background/Objectives: The Royal College of Nursing of the United Kingdom declared in 2014 that 'Advanced nursing practice in the UK has evolved significantly over the last 20 years, with the emergence of increasing autonomy, clinical decision making, professional responsibility, nursing research and the expansion of traditional nursing roles. As nursing roles, responsibilities and areas of practice have diversified and expanded some of the boundaries of professional practice and competence have become blurred (RCN 2014)'

Within the field of paediatric oncology in the UK numbers of ANP's have increased but very little research has been done to establish the numbers and the services they provide. There is little evaluation of the role currently including the education students undertake to qualify as advanced practitioners and the impact the role has on service provision and patient outcomes within paediatric oncology.

Within our centre, we are the first to offer this service and a secondary aim of this research was to adapt our service provision by learning from centres where the role is established.

Design/Methods: A survey was undertaken to ascertain which of the tertiary centres within the UK employ or plan to employ ANP's; the educational preparation undertaken to fulfil the role and the core elements of that role. The survey was then sent to all 21 tertiary centres in the UK using well established 'link member' network. Initial results are being collated and analysed and will be presented at SIOP.

Results: Many centres have ANP's in training and early results suggest that the role is rapidly developing, but with wide variation in responsibilities. In the centres where there are ANP's in post, there are common issues and barriers.

Conclusion: These results will be used to guide units developing ANP roles, to allow benchmarking and to move towards creating a national network for ANP's.

P-0616 | The Experience of Parents Caring for Children with Incurable Cancer at the End-of-Life

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Background/Objectives: The purpose of this study was to explore the lived experience of parents caring for children with incurable cancer at the end-of-life.

Design/Methods: This phenomenological study was designed to understand the lived experiences of parents caring for their child with incurable cancer at the end of life. Ten parents with cancer children were recruited using purposive and snowball sampling methods. Data were collected through in-depth interviews, guided by a *semi-structured interview guide*. Data were then analyzed using phenomenological method.

Results: The findings contained three themes: **confrontation with the disease and struggling with heart, wish to extend their child's life, and perceived children's life-limiting**. Additionally, the factors influencing parents' without using active treatments when their children at the end-of-life were: without suffering in children, respecting children's decision-making, the prior experience of parents' facing death, gaining full information, and counting on religion.

Conclusion: The findings showed deeper understanding of the lived experiences of parents caring for children with incurable cancer at the end-of-life. The results also facilitated health-

care professionals better understanding parents' feeling and thought when their child at the end of life. For that reason, the healthcare professionals could provide more complete information to assist parents with similar situations when caring for their very ill children. And hopefully there is no regret for children and parents at the end of life.

P-0617 | Evaluation of Nursing Care Guidelines for Children with Cancer and their Families in Japan

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Background/Objectives: We developed "Nursing Care Guidelines for Children with Cancer and Their Families" to standardize childhood cancer nursing in Japan. The guidelines consist of the following 13 chapters; 1) Establishing a trust relationship, 2) Telling children about the disease and treatment, 3) Hospital environment, 4) Procedural pain management, 5) Symptom management, 6) On hematopoietic cell transplantation, 7) On relapse, 8) End-of-life care, 9) On discharge, 10) Support for outpatients, 11) Long-term follow-up, 12) Mental health for nurses, 13) Nursing role in multidisciplinary team.

The purpose of this study is to evaluate and improve the guidelines.

Design/Methods: Sixty-eight nurses participated in this cross-sectional survey about the guidelines.

We made questionnaire of a 46-items Likert Scale based on the contents of the guidelines, and asked expert nurses who were in charge of caring children with cancer and their families to see how much important they think each item is, and how often they and their colleagues bring them into action in their daily nursing. In addition, we asked 14 open-ended questions related to difficulties, problems and challenges in their wards.

Results: More than 90% of nurses said "important" in almost all items. There were significant correlations on 28 of 46 items between frequency of practices and degree of importance. In other items, the nurses pointed high score on importance, but low score on the frequency of practice in their wards. Especially, "Support for Siblings" and "Grief care for Families" were very low score on practices. In responses to the open-ended questions, they described difficulties in supporting children when parents refused permission to tell the diagnosis to children.

Conclusion: Many nurses realize each items in the guidelines are important, but it seems that there exists some barriers when they bring it into practice. We need to further discuss the background factors. These findings will contribute to building more practical guidelines and improve care for children with cancer and their families in Japan.

P-0618 | Correlation of Triage Evaluations Conducted by Nurses and Physicians: Experience in the Emergency Room of the Hospital Infantil Teleton De Oncologia (HITO)

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Background/Objectives: Strategies for better attention in emergency rooms have become essential for the proper functioning of these services. According to literature, well trained nursing staff can reduce service times and make more efficient use of hospital resources.

Objective: To compare and correlate Triage evaluations given by doctors and nurses to paediatric cancer patients presenting to the emergency room of a paediatric oncology hospital: Hospital Infantil Teleton de Oncologia.

Design/Methods: A cross-sectional study including all records registered between December 2013 to July 2015 in emergency room of a monothematic model paediatric oncology hospital was performed. Assignments triage level according to the Emergency Severity Index (ESI) was compared by evaluating the interobserver correlation between the two assessments. Participants were instructed to assign the level of triage in each case, using the scale of five levels of triage (1 = emergency, 2 = urgency, 3 = stable requiring more than one resource, 4 = stable requiring one resource 5 = stable not requiring resources) and report whether there is any difference between the two evaluations.

Results: A total of 1551 ratings, of 146 patients were recorded. Differences between records given by nurses and doctors in the emergency department of our hospital were analyzed with a correlation of 0.9051 to 0.9245 ($p < 0.0001$ Spearman 95%) between both evaluations. There was no difference between the two groups of scores given by doctors and nurses (Mann Whitney $p = 0.91$). There was agreement on evaluations in 88% of interobserver records and mismatched ratings, 72.4% were scores given in stable patients (Triage 3, 4 and 5).

Conclusion: There is a correlation between the scores given by doctors and nurses and there is no significant difference between the scores of both groups. Therefore, you should consider train nurses for assessment of Triage in emergency rooms also in a nationwide multicenter study.

P-0619 | Central Venous Catheter (CVC) Care and Maintenance: A Practical Training Session Promoting Cooperation and Building Support among Professionals

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Background/Objectives: It is important that health professionals feel comfortable using CVCs (Central Venous Catheters) when taking care of children with cancer. Our regional network is a partnership between two University Hospitals and five other smaller hospitals. It develops a training program, believing that consistent CVC care is essential to minimize unnecessary risk factors and improve care, as well as quality of life of children with cancer and their families.

Design/Methods: Paediatric oncology units nurses from University Hospitals, with the support of our regional network coordination team, organize four hours workshops in general paediatric units of each smaller hospitals. This workshop is based on a practical approach where participants are encouraged to perform on mannequins. It includes CVC care, maintenance, recognition and management of complications (for every type of device). This program is especially designed for nurses who are not frequently involved in children with cancer care (Hospitalization and Emergency units). In order to strengthen peer to peer support within the paediatric unit, they are invited to participate with their colleagues from the ambulatory day treatment area (where children with cancer usually stay) who are more comfortable with the use of CVC.

Results: Nurses skills and knowledge of CVC clinical practice guidelines were evaluated using a pre-self-assessment/post-self-assessment. Results show that this program improved nurse's knowledge, self-confidence, and skill performance. Moreover satisfaction questionnaires show that this peer to peer collaboration facilitates training as well as mentoring between expert and novice nurses, supports information sharing, and improves outcomes.

Conclusion: As CVC is also cared for by home care nurses we plan to extend and adapt our workshop to their needs.

P-0620 | Changes in Body Composition of Children with Cancer Admitted to A Paediatric Intensive Care Unit in Brazil

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Background/Objectives: The nutritional status of paediatric critical patients affects their clinical evolution, and protein-energy malnutrition contributes to increased mortality in intensive care. Sepsis and systemic inflammatory response syndrome lead to metabolic changes such as accentuated lipolysis and increased protein catabolism, which may result in loss of muscle mass. Body composition assessment is a good way to monitor these changes in order to establish nutritional interventions targeted to reducing their impact. The objective of this research is to investigate changes in body composition of children with cancer during hospitalization in a paediatric intensive care unit (PICU).

Design/Methods: Patients with cancer from 0 to 18 years old who were admitted to a tertiary paediatric haematology -oncology hospital's PICU in Sao Paulo, Brazil were included. To assess body composition we collected mid-upper arm circumference (MUAC) and triceps skinfold (TSF), and calculated arm muscle area (AMA). The first assessment was done up to 72 hours from admission in the PICU and the second 7 days after the first. Normality was tested with the Shapiro-Wilk test and either paired t test or Wilcoxon matched-pairs signed rank test was used to verify differences between the first and second nutritional assessments. Statistical significance was set at 5%.

Results: Thirty seven patients (n=37) were evaluated (mean age: 6.6±4.9), 46% were female. Because of clinical complications, it was only possible to collect TSF on both analyzed moments from 11 of 37 patients (30%). The median MUAC dropped from 17.5 to 16.5 (p=0.005, n=37), TSF from 8 to 7 (p=0.797, n=11) and the mean AMA from 17.3 to 16.3 (p=0.272, n=11).

Conclusion: All body composition parameters decreased in the first week in the PICU, although only for MUAC there was statistical significance, perhaps because of the bigger sample size. Our results indicate possible loss of muscle mass in this population.

P-0621 | Exploring Perceptions and Experiences of Stakeholders about Clinical Components of a Nursing Diploma Programme in Nairobi

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Background/Objectives: Nurse training includes a theoretical and clinical education component. Clinical education is vital and impacts on patient outcomes. Clinical education prepares student nurses for professional role, facilitates integration of theory to practice and develop student nurse competencies for licensing and registration with the Nursing professional regulation bodies.

Student nurses are core to the clinical education process and many stakeholders collaborate to ensure that the goals and outcomes are achieved.

The study explored perceptions of stakeholders involved in a nursing diploma programme regarding the integration of theory into practice and their views on clinical assessment tools utilized in the programme.

Design/Methods: This qualitative study used semi structured interviews and focus group discussions. Purposive sampling of stakeholders included: student nurses ((3rd year), Charge nurses, preceptors and nurse lecturers. Data collection was by means of interviews and focus group discussions. Transcribed data was analysed for themes. Ethics approval was obtained from the institutional research and bio-ethics committee.

Results: The student nurses perceived clinical education offers student advocacy; peer reciprocity; self-directed learning and theory practice disparity. For preceptors it signified role overload; identification of teachable moments and relationship builder.

Nurse Lecturers identified ownership of clinical learning; complexity of clinical learning environment and theory practice disparity. Charge nurses perceived their role to be leaders and educators; collaborators; and ward culture moderators.

Overall the participants reported that the assessment tools were limited in scope and objectivity, primarily focussing on psychomotor skills.

Conclusion: There is need to train preceptors on clinical teaching and assessment methods to bridge the perceived theory practice gap and to realign clinical tools to evidence based practice like objective competence assessments.

P-0622 | Comparison of Interventions Core to Paediatric Oncology Nursing between China and America

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Background/Objectives: To explore differences and similarities on paediatric oncology nursing practice through comparing core nursing interventions between China and America.

Design/Methods: Using the classic four steps of comparative pedagogy developed by Bereday G, the interventions core to paediatric oncology nursing were described, interpreted, collocated and compared between two countries.

Results: Chinese and American paediatric oncology nursing core interventions show differences in the methodology, numbers of interventions and classes, but similarities in domains.

Conclusion: The further development of Chinese paediatric oncology nursing core interventions rely on refining interventions, expanding items related to "family-centered" care, and to be sustainable and with Chinese characteristics.

P-0623 | Paediatric Oncology Patients' and their Mothers' Enteral Nutrition Experiences: A Qualitative Study

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Background/Objectives: Background: Enteral nutrition is a method commonly used in the clinical treatment of malnutrition in paediatric oncology clinics.

Objectives: The aim of the present study is to reveal children's and their mothers' views and experiences related to enteral nutrition, which is the most frequently performed nutrition delivery method in paediatric oncology.

Design/Methods: The present study was carried out at the Clinic Inpatient Service of an University Paediatric Oncology using the phenomenological research method, one of the qualitative research methods. A total of 3 children and 14 mothers participated in the study between January 2015 and June 2015.

Results: The analysis of the data was conducted according to Kolcaba's Comfort Theory. The findings at the conclusion of the qualitative analysis were explained under four main themes; (1) physical: includes the inability to be fed orally, NG tube intervention, comfort due to feeding, medication administration, and satisfaction; (2) psychospiritual: includes anxiety, fear, distorted body image, and compliance; (3) sociocultural: includes conflicts with the child about feeding and advice on feeding via the NG tube to other parents and children; and (4) Environmental: includes unrestricted / freedom of feeding.

Conclusion: Both parents and children should be given a "NG feeding education" on potential decreases in feeding through oral intake due to cancer treatment-induced side effects.

Implications for Practice: Oncology professionals can also provide basic counselling and resources to children and parents about the importance of maintaining an optimal weight and of enteral nutrition.

OTHER

P-0624 | Home Urine Sampling as a Research Methodology in Longitudinal Biological Research Studies in Children with Cancer - Patient, Parent and Scientific Perspectives

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Background/Objectives: Sequential sampling is essential to identify longitudinal changes in biomarkers, especially considering in vivo studies collecting fluids and liquid biopsies from children with cancer. Children receiving chemotherapy rarely spend prolonged periods of time admitted to hospital, instead attending hospital frequently for both treatment and management of side effects, impacting on quality of life. Asking for visits solely for the collection of research samples is therefore unfair and unethical. Missing sampling points across a cohort may however allow changes in biomarkers to go undetected, missing events such as late rise or peak changes. Home urine sampling offers a methodology to allow the capture of these research samples without hospital attendance.

Design/Methods: From a cohort of 60 paediatric cancer patients recruited to a longitudinal research study exploring changes in urinary and serum markers of nephrotoxicity, perspectives were gained from patients about the utility and acceptability of obtaining urine sampling at home. The stability of the biomarkers of interest was investigated. Published literature was reviewed for similar qualitative and quantitative data.

Results: Home urine sampline is acceptable to patients and their families, including temporary storage and subsequent dispatch and transport to hospital. Parents report feeling empowered and as though they were participating actively in research to the potential benefit of future patients. Stably data in the biomarkers of interest was acceptable.

Conclusion: Home urine sampling offers a simple methodology to increase the number of time points at which urinary research samples can be collected, to give a more complete data set for longitudinal, observational biological studies. This will reduce the potential to miss significant changes in the levels of biomarkers of interest. Furthermore, it is a method of sample collection that is acceptable to both patients and their families, and has received research ethics committee approval for our study.

P-0625 | Ethical Dilemmas and Moral Distress in Global Paediatric Health Programs: A Survey of Paediatric Haematology/Oncology Professionals

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Background/Objectives: Ethical dilemmas and concomitant moral distress frequently occur in medical settings within high resource countries. Ethical dilemmas likely occur in global health projects but with unique factors that complicate the management of these circumstances (e.g., constrained resources, cross-cultural differences). A web-based survey of professionals working on international paediatric Haematology/Oncology projects was conducted with the aims of characterizing the nature, frequency and impact of ethical dilemmas in these projects and collecting recommended management strategies.

Design/Methods: Members of the International Society of Paediatric Oncology engaged in international projects were invited to participate in an anonymous survey including the following elements: 1) professional and project demographics (e.g., applicable degrees, country or region of projects), 2) Likert-scale ratings of frequency and impact of dilemmas and distress, 3) free-text descriptions of significant dilemmas, attempted strategies and recommendations based on experience. Data analysis used both quantitative and qualitative methods.

Results: Results indicate that ethical dilemmas are prevalent, substantially impact projects and generate significant moral distress for professionals. This presentation will include a description of the major themes of ethical dilemmas and methods found useful in managing these situations.

Conclusion: It is anticipated that the characterization of predictable, high-impact ethical challenges will help prepare and support professionals working in global settings. Institutions will be able to incorporate the findings in established educational and/or support structures. For example, the Texas Children's Hospital Global HOPE (Haematology/Oncology Programs of Excellence) Center has an ongoing case conference titled Reflective Practice and Global Leadership for faculty and staff in international placements. The conference provides a disciplined approach to problem analysis and planning for strategic action in challenging circumstances. The survey data has helped us develop a more rigorous approach to ethical analysis and decision-makings as well as provide additional support in contending with moral distress.

P-0626 | Design and Implementation of Comprehensive Inpatient and Outpatient CPOE in a Paediatric Oncology Centre

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Background/Objectives: Computerized Provider Order Entry (CPOE) has been shown to reduce chemotherapy-prescribing errors and potentially increase clinical efficiency. Despite these potential benefits, implementation remains a significant challenge given the complexity of paediatric oncology regimens. We sought to safely implement CPOE in tertiary paediatric oncology setting.

Design/Methods: In the spring of 2014, our organization implemented CPOE with a commercial Electronic Health Record (EHR) in almost all elements of inpatient and ambulatory care, with the exception of chemotherapy. A multidisciplinary project team was then formed to design chemotherapy order sets. Consultation with staff and review of past adverse and 'near miss' events suggested particular areas of concern including outpatient to inpatient transitions, regimens requiring specific timing of medications and laboratory tests (such as High Dose Methotrexate), the need to ensure proper verification of pre-treatment laboratory and diagnostic testing prior to administration and variable dosing based on age and weight. Furthermore, we reviewed evidence based Clinical Practice Guidelines suitable for incorporation to standards of care. Selection of plans and regimens for building were made on the basis of standards of care of common malignancies and also clinical trials anticipated to be open at the time of 'go live'. Following its' initial creation, each plan was reviewed by 2 independent bodies to ensure the content validity.

Results: Over a 20-month period, approximately 280 order sets were created. All plans included anti-emetic prophylaxis as per the guidelines published by the Pediatric Oncology Group of Ontario (POGO). The plans were thoroughly tested with particular attention to accuracy of drug, dose and timing. Following extensive provider, nursing and pharmacy testing, the system was implemented in the spring of 2016.

Conclusion: Despite the complexity of paediatric oncology treatment regimens, implementation of CPOE with a commercial EHR is feasible with the careful efforts of a multi-disciplinary team.

P-0627 | How does PET-MRI Apply to Paediatric Tumours?

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Background/Objectives: To study the usefulness of PET-MRI versus MR alone in Pediatric Oncology.

Design/Methods: We have collected the data of patients from the Pediatric Oncology and Haematology Unit who had one or more PET-MRI between November 2014 and March 2016.

Results: 34 patients have been included (16 males and 18 females, aged between 19 months and 17 years). 55 procedures studies were performed. The diagnoses were: CNS tumors (13), lymphoma (6), rhabdomyosarcoma (4), neuroblastoma (4), histiocytosis (3), osteosarcoma (1), Ewing sarcoma (1), retinoblastoma (1) and PEComa (1).

In 12 procedures the result of MRI was positive with negative PET, corresponding to 3 patients with rhabdomyosarcoma on chemotherapy, 5 patients with CNS tumors after surgical partial resection, 3 patients with Hodgkin lymphoma after chemotherapy and 1 patient with neuroblastoma after receiving chemotherapy. In one procedure, and only in a limited area, the result of PET was positive with a negative RMI, corresponding to 1 patient with a high grade CNS tumour. In two patients, both MRI and PET were positive, and an infection was subsequently confirmed. In the remaining 40 studies the positive correlation between MRI and PET due to active tumour origin was confirmed.

Conclusion: MRI has a high sensitivity for the initial diagnosis of paediatric tumours. The combination with PET may be useful in some situations:

- To assess the metabolic status of tumors that have not been resected and have been treated with chemotherapy or radiotherapy.
- To assess the metabolic status of stable lesions on MRI.
- To differentiate tumour lesions of infectious or inflammatory lesions.

PET-MRI has the obvious advantage of lessening the radiation exposure in the child with cancer as compared to the standard PET/CT. The main disadvantage is the longer time needed to perform a PET-MRI versus PET/TC especially in small children that needs general anesthesia.

P-0628 | Posterior Reversible Encephalopathy Syndrome (PRES) in the Course of Oncologic Treatment in Children

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Background/Objectives: Posterior reversible encephalopathy syndrome (PRES) is a clinical syndrome of various etiologies with similar neuroimaging findings and clinical symptoms. PRES is characterized by acute neurological symptoms of brain dysfunction such headache, convulsions and visual disorders and MRI abnormalities in parietal and occipital lobes of brain. Underlying mechanism of PRES is not clear, but hypertension and low magnesium concentration may play a role. The purpose of this study was the assessment of predisposing factors of PRES based of clinical and radiological picture of this syndrome in the course of oncologic treatment in children.

Design/Methods: The study comprised 6 children with cancer aged 3,5-15 years, diagnosed as having: ALL, hepatoblastoma, nephroblastoma, granulocytic sarcoma, neuroblastoma and PNET. We analyzed the clinical and radiological manifestation and the course of PRES, electrolytes concentrations and blood pressure observation cards.

Results: In our study group all patient presented both clinical and radiological picture of PRES. In clinical presentatoin dominated headache (6pts) and convulsions (5 pts) Most of them (5 pts) had a history of hypertension (RR> 99pc), and electrolytes concentration abnormalities, mainly hypomagnesemia. MRI picture revealed characteristic white and grey matter of the parietal and occipital lobes oedema in all study group (6pts). All patients were given symptomatic therapy. Durations of PRES clical symptoms 1-2 weeks, radiological abnormalities persisted 2-4 weeks.

Conclusion: PRES may complicate oncologic treatment in children. Hypertension is the most important risk factor of PRES. Knowledge of the clinical and MRI presentation of PRES can be helpful to differentiate it from other neurological complication.

P-0629 | A Novel Technique for Chromatin Immunoprecipitation from Frozen Tissue

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Background/Objectives: Traditionally, fresh tissue or cultured cells are the substrates for chromatin immunoprecipitation (ChIP), a technique used to study the interaction between proteins and DNA. Availability of fresh tissue or cell lines may however be limited. We investigated whether the profiles of histone post-translational modifications are maintained following snap-freezing of tissue.

Design/Methods: Fresh and snap-frozen thymus were homogenized in parallel, followed by fixation in formaldehyde. Fixed tissue was stored in SDS buffer with protease inhibitors. After resuspension in IP buffer, chromatin was sheared to yield DNA fragments with a bulk size of 200-1500bp. Lysate was pre-cleared by addition of blocked beads. Samples were incubated with antibodies overnight. Immune complexes were recovered by adding blocked beads, and incubated at 4°C. These beads were washed and to elute, ChIP elution buffer was added followed by incubation at 65°C. The beads were pelleted and the supernatant incubated overnight at 65°C. DNA was phenol/chloroform-extracted. qPCR was performed using SYBR Green detection system.

Results: Comparison of the profiles of histone post-translational modifications (PTMs) in fresh and snap-frozen tissue shows that these are comparable across these tissue substrates. Thus, the binding profiles of direct DNA-associated proteins are maintained in snap-frozen tissue.

We found that the profiles of indirect DNA-associated proteins are similarly maintained in snap-frozen tissue. Higher gene enrichments were observed in snap-frozen compared to fresh tissue ChIPs. These results suggest that protein-DNA interactions are slightly better preserved in snap-frozen tissue.

Conclusion: We have developed a novel technique for ChIP from snap-frozen tissue, and shown that the profiles of direct and indirect DNA-associated proteins are retained in snap-frozen tissue. Where availability of cell lines or fresh tissue is a limiting factor, this novel method importantly allows for wider use of this valuable technique on archived frozen tissues to generate credible results.

PSYCHOSOCIAL (PPO)

P-0630 | A Change in Childhood Cancer: Protecting the Rights of a Child in a Hospital Setting

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Background/Objectives: Statement of Need: The hospital stay changes the whole life of the child having cancer. As most of the hospitals are not well equipped to cater the child's needs, they face many uncomfortable situations during their treatment. According to the "United Nations Convention on the Rights of a Child" a child has the right for a full and decent life including access to equal opportunities for educational, cultural, artistic, recreational, play and leisure activities.

Design/Methods: Cankids ensures the rights of a child who is hospitalized by engaging them in play and recreational activities appropriate to their age, provides counseling, Play, Art, Music and Relaxation Therapy, Hospital Medical Dolls and Story Telling. We also ensure the emotional well-being of the child by doing Child Friendly Wards so as to provide a happy and cheerful environment in the hospitals and providing non formal education interventions.

Results: The child and the family showed better psychological and emotional well-being on receiving these interventions and were more cooperative during the treatment.

The feedback of the hospital staff showed that the children are less fearful, more comfortable and enjoy their stay. Parents become visibly relaxed as they see their children less stressed. The hospital staff also reported higher motivation on seeing the child in a better condition.

Conclusion: We not only take care of a child's right during treatment but also aim to spread awareness about the current situation experienced by a child in a hospital setting. The rights of a child ensure the quality of life of every child undergoing treatment. Cankids strives to ensure that no child is deprived of his or her right of access to such health care services. By advocating those rights we hope to make the hospital stay as suitable as possible and to make a change in childhood cancer.

P-0631 | Building Capacity: A Psycho-Oncology Training Program for a Multi-Disciplinary Team

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Background/Objectives: Statement of Need: Psycho-oncology now has a recognized role through clinical care, research, and training. In a low economic country, there are limited resources and high demands for professionals to minimize the emotional and psychological distress experienced by a child having cancer. The development of the professionals suffers due to financial constraints. Hence training on psycho-oncology issues for multidisciplinary professionals is imperative.

Design/Methods: To overcome these constraints, Cankids has initiated a Training model in Psycho-oncology. It is an ongoing training program for multidisciplinary team of Psychologists, Social Workers, Support Groups, students and Medical Professionals through didactic lectures, Videos, role-play exercises, group and field work. We had also organized a ten day course in Pediatric Psycho-oncology focusing on Counseling at different stages of cancer, Group and Supportive Therapies, Child Life, Palliative & Bereavement Care, Research, Program Management and Implementation. This kind of specialization will lead to more competent Psychologists in the Psycho-oncology field.

Results: The staff is empowered to deal with the children and their families in an effective way by understanding coping skills, communication, dos and don'ts of counseling and learning management skills. These training programs are proven to be a cost effective way to ensure the quality and effectiveness of our emotional support services. Primary outcomes included self confidence; knowledge and attitudes which helped them function better. As a secondary outcome there is a significant reduction of job-related stress and burnout in the Multidisciplinary Team.

Conclusion: This psycho-oncology training program has significantly improved the confidence and knowledge regarding care for patients with psycho-social problems hence the children and their families can get better psychological support. The future goal of Psycho-oncology Training Program includes developing a full-fledged Psycho-oncology course accredited by a University, strengthen research as well as improve access to psycho social knowledge and services worldwide.

P-0632 | Integrated Approach: An Alternative Pain Reduction for Children Having Cancer by Non-Pharmacological Interventions

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Background/Objectives: Children having cancer experience various physical pain and psychological distress not only from their illness, but from the many painful procedures such as cannulation, bone marrow aspiration, lumbar puncture and even simple dressing changes. This leads to several behavioral changes causing an aversion to hospital which makes cancer care even more difficult in the long run. Our purpose is to introduce an "Alternate pain reduction and management approach" for children through non-pharmacological interventions.

Design/Methods: This model empowers parents and professionals through active participation and shared understanding to reduce procedural pain among children. An assessment of needs, a cancer center pilot project plus literature review led to the development of our "Non Pharmacological Intervention Model" as an alternate pain reduction among children. The model can be used alone or as an adjunct to pharmacological management and is a combination of various environmental, positional, behavioral, psycho-therapeutic and educational approaches.

Results: This approach has successfully proven to reduce procedural pain and promote coping in children. It also helps in reduction of anxiety and gives the children a sense of mastery over stressful situations. It empowers parents to take an active role in their child's cancer care thus helping them cope with and improve their experience with cancer treatment. As a Mutual Participation Model, it also trains hospital staff to bridge the gap between the patients and Cankids palliative and supportive care services thus strengthening working partnerships.

Conclusion: The procedural pain experienced by the children can be reduced with the use of a non-pharmacological approach such as this. This alternate approach in local cancer centers provides informational and educational tools and training to the parents and staff members. Through this model, we aim to educate and empower families, hospital professionals and staff in effective pain management.

P-0635 | The Impact of Creating A Child-Friendly Hospital Environment in Paediatric Cancer Patients and their Families in Comprehensive Cancer Center at King Fahad Medical City

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Background/Objectives: Hospital admission can be scary for a child, most especially for hospitalized paediatric cancer patients, but studies show that there is growing evidence that environmental modification has a great impact in patient experience and health outcomes.

Majority of paediatric cancer patients and their family was not satisfied with the unit environment. The aim of this study was to explore the impact of creating a child-friendly hospital environment in paediatric cancer patients and their families.

Design/Methods: General surveys were conducted. Performance improvement team studied the result of the surveys, a specific survey was formulated. Relevant data were collected.

After studying the results, suggestions for improvement were considered. Contributing factors for their dissatisfaction were also analyzed in a form of Cause-and-Effect Diagram. A post-intervention survey was conducted.

Results: Result of general, specific survey and repeated focus group discussion showed that we need to create a child friendly hospital environment. Series of interventions applied like Wall posters designed to mimic a "ZOO", play rooms designated for certain age groups, quiet patient rooms for families to rest, an attractive waiting room and plasma televisions with kid channels.

Post intervention satisfaction survey have shown an increase satisfaction rate of 90% from the pre-intervention satisfaction data which was 68%, with around 95% of hospital staff interviewed were very positive with the effects of the interventions to the patient's journey of stay in the hospital.

Conclusion: A hospital or healthcare setting needs essential tools to improve the quality of care continuously for their patient population to enhance comfort for the patient and the entire family. A small initiative to address the emotional needs of the patient can bring a huge difference in their health condition; thus, giving positive health outcome and an excellent journey of patient experience.

P-0636 | The Use of 5-HTT and BDNF Polymorphisms as Biomarkers to Study the Resilience of Children and Adolescents During Treatment of Acute Lymphoblastic Leukemia

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Background/Objectives: Why are some children more likely than others to develop resilience in the face of similar levels of trauma exposure as compared to others who do not. It is increasingly clear that there are critical roles for predisposing genetic and environmental influences in differentially mediating psychological risk. Resilience differs from traditional concepts of risk and protection in its focus on individual variations in response to comparable experiences. Here, we tested the hypothesis that anxiety and depression as well as neural repair and plasticity related polymorphisms may partly account for the difference in resilience observed during treatment for acute lymphoblastic leukaemia (ALL).

Design/Methods: Fifty patients (1-18 yrs old) diagnosed with ALL were enrolled in two centers (protocol AIEOP-BFM-2009) and genotyped for 5HTT and BDNF (val66met). Patients were subjected to a short screening battery (including the PAT2.1) and a specific assessment of their resiliency during treatment. The resiliency scale was composed of three subscales: Sense of Mastery (MAS), Sense of Relatedness (REL), and Emotional Reactivity (REA).

Results: Patients with the SL allele of 5HTTLPR had a more compromised score in some areas of resiliency than patients with the LL allele; the presence of the S allele most affected emotional reactivity REA and sense of mastery MAS. Furthermore, age was an important factor, as younger children displayed a reduced trust and tolerance versus their surroundings. This then

contributed importantly to an overall reduction in their overall resiliency. Also, resiliency was reduced one year into therapy while vulnerability was significantly enhanced.

Conclusion: Genes regulating susceptibility to stress, such as 5HTTLPR and BDNF, may help to predict susceptibility towards the development of resiliency in children and adolescents treated for cancer, and may play a critical role as a predisposing factor in differentially dealing efficiently with the emotional risks related to cancer and its treatment.

P-0637 | Use of Psychotropic Drugs for Acute Psychiatric and Behavioral Problems in Paediatric Oncology: A Multi-Center Study

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Background/Objectives: Children and adolescents diagnosed with cancer are forced in the most unexpected way to cope with an extraordinary, highly unlikely event. Such an experience can be extremely disruptive. When symptoms become pathological and impair a child's development and functioning, early intervention is warranted. Given that severe childhood and adolescent adversities may negatively impact adult mental health, our aim was to critically examine, the advantages and disadvantages of acute symptom management and (short-term) psychopharmacological interventions in these severely ill patients.

Design/Methods: Twenty-one patients (1-18 years old) diagnosed with cancer were enrolled in five centers. Categorical variables were analyzed with descriptive statistics and open-ended questions were examined qualitatively. Because of the importance of developmental phase, patients were divided in three age groups: 1) aged 1-6; 2) >6-11; and 3) >11-18. Variables included age, gender, the type of cancer, treatment protocol, oncologic treatment applications, the use of corticosteroids, methotrexate and vincristine, first onset of psychiatric symptoms, treatment approach to symptoms, and the possible presence of side effects due to psychotropic drugs.

Results: The development of psychiatric problems differed according to tumour type and treatment protocol. Also, age was an important factor: younger children (< 6 years) and adolescents (>12) were more vulnerable, especially when the CNS was directly or indirectly involved. Finally, the necessity to use psychotropic drugs was related to treatment phase (the first six months of treatment), and to treatments involving corticosteroids.

Conclusion: Psychotropic drug use in children is still extremely controversial, and seems like a catch-22, in which a true solution or desired outcome is almost impossible. However, efficient and prompt management of mainly acute behavioral or psychiatric symptoms during treatment might help improve quality of life as well as psychological, functional, and medical outcomes for a child or adolescent who is trying to handle their cancer.

P-0638 | The Psychosocial Assessment Test 2.0 is Sensitive to Context, Type of Cancer and Risk Management in Children and Adolescents Diagnosed with Cancer and their Families

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Background/Objectives: Some children and families are more likely to display psychosocial problems in the face of trauma exposure as compared to others. Therefore, evaluating risk at diagnosis will allow prompt intervention. Given this, the aim of this study was fourfold: 1) test its validity in an Italian sample; 2) test the context sensitivity of the PAT; 3) evaluate its sensitivity to stress caused by different types of diagnosis; and 4) evaluate whether stratified interventions reduce the overall impact of specific risk factors on psychosocial wellbeing during therapy.

Design/Methods: A multicenter prospective study was performed and 254 children and adolescents (1-18 yrs old) diagnosed with cancer were enrolled in four centers. Parents were asked to complete the PAT within the first month after diagnosis. After initial PAT score analysis, a nested design was employed testing: 1) the sensitivity of the PAT to type of diagnosis or 2) the effect of stratified management strategies.

Results: In Italy PAT scores are differently stratified than in other countries: the universal level contains significantly less patients (40%) than the targeted level (51%); the clinical level contains 9%. PAT scores are also sensitive to the type of diagnosis: both patients with ALL and those subjected to transplant displayed markedly higher scores for stress reactivity and patient problems. PAT scores, furthermore, scores progressively diminished during treatment, reducing the percentage of cases in the targeted level to 30% and enhancing cases in the universal level to 60%.

Conclusion: The PAT is an extremely useful instrument in the Italian Pediatric Oncology setting and helps to define initial psychosocial risk of the child and its family, and is sensitive to their socio-cultural context and type of tumour. The PAT also represents a critical instrument

to monitor the effectiveness of stratified interventions that deal differentially with psychosocial risk.

P-0639 | Usability Testing of a Digital Child Experience Measure for Children with Cancer

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Background/Objectives: There is a lack of validated measures for young children with cancer that captures their views of hospital care and whether services meet their needs. A multi-professional working group developed a digital application (app) to measure the experience of being in hospital for children with cancer, ages four to twelve. The app was tested for usability with children.

Design/Methods: Children, aged four to twelve years, currently being treated in hospital for cancer were invited to take part in usability testing. Participant demographics regarding the age and gender of the participant, as well as the length of time spent in hospital were recorded. Usability testing allowed for the app to be tested for ease of use, level of engagement and level of understanding. As part of the testing, each child completed the app with the support of a data collector. Children were also asked additional questions regarding particular sections that they liked or did not like, and the aesthetics of the measure. Time taken to complete the measure and whether it was fully completed was also recorded.

Results: Feedback was obtained from the children by data collectors about the app's usability. This was used to make adaptations to the measure, to improve validity, make it more child-friendly and functional to be used with children. It also provided insights into the role children play in usability testing and the development of this type of software.

Conclusion: Usability testing was employed to collect feedback from potential users of the app. We will present the design challenges in the development of this interactive tool and discuss how the usability testing influenced further development of this app.

P-0640 | Analysis of Organizational Climate in a Paediatric Haematology-Oncology Department

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Background/Objectives: Hospitals organization requires continuous adaptation to optimize the use of resources for the promotion and protection of individual and collective health status. The mandate of cost containment leads to changes that affect not only health delivery, but also the organizational climate. Within the Department of Paediatric Haematology and Oncology, we assessed the organizational climate to study the delicate area of management of human resources, based on individual levels of analysis about the capable of embracing uncertainty and the ability to cope with change.

Design/Methods: All of the physicians and nurses that work in the Department (150) were enrolled. The assessment was anonymously carried out through the following tools: Questionnaire about uncertainty (Clampitt & DeKoch, 1999) at individual and organizational level, Resilience Scale (Wagnild & Young, 1993) and Psychological Well-Being Scale (Ryff, 1988). The data analysis was performed using U Mann-Whitney and Kruskal-Wallis tests.

Results: Completed questionnaires were received from 94 subjects. The median age was 41.9 years. Questionnaire analysis revealed that 54.3% of subjects experience a "status quo" level about organizational climate. The uncertainty is significantly higher among younger workers (PB=0.006). The 50% of sample shows a medium level of resilience (26.6% higher level). Males show a higher level in self-acceptance than females (P=0.009); the establishment of quality ties to other and the pursuit of meaningful goals and a sense of purpose in life are higher among younger workers (PB=0.022; PB=0.028).

Conclusion: Throughout the analysis we made the assumption that within the department staff there is a substantial homogeneity in organizational climate. The "status quo" prevailed: workers reported a moderate level of investment. Younger workers reported a disturbing climate, but they are not able to use the uncertainty to develop a dynamic one. The older workers hold up the "status quo" as a model to control emotional burden.

P-0641 | Foreign Mothers of In-Patient Children with Cancer: Needs and Expectations

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Background/Objectives: Over the last decades we have experienced a continuous increase in the number of patients coming from countries all over the world. For a great deal of the immigrant parents of very sick children, treated in our department, it is difficult to follow roles and style of life which it is necessary for immunosuppressed patients. Their cultural backgrounds, as well as the difficulties related to communication are barriers towards building a good compliance with therapy. The purpose of our investigation is to build a link between health professionals and foreign family with the aim to improve their coping skills and attitudes towards their children's health.

Design/Methods: We developed an instrument of investigation, QoL-str, involving the quality of life, expectations, needs, and satisfaction of foreign mothers who are hospitalized with their sick children. A total of 57 variables were collected by interviewing 182 mothers of inpatient children, focused on the description of the child, quality of life of the mothers and their opinions on life in hospital.

Results: We developed an instrument of investigation, QoL-str, involving the quality of life, expectations, needs, and satisfaction of foreign mothers who are hospitalized with their sick children. A total of 57 variables were collected by interviewing 182 mothers of inpatient children, focused on the description of the child, quality of life of the mothers and their opinions on life in hospital.

Conclusion: Our results emphasize the need to use a family-centered approach in order to achieve a better quality of life for the sick children and for their mothers. The task of health team is to help them to communicate and to cope with their new life in hospital and to create a therapeutic alliance based on trust and confidence, allowing them to achieve an acceptable quality of life based mostly on bonds of intimacy and trust.

P-0642 | Socio-Demographic Factors and Psychological Distress in Platinum-Treated Childhood Cancer Survivors

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Background/Objectives: Survivors of childhood cancer treated with platinum-based chemotherapy are at risk of treatment-induced ototoxicity. To date, there is limited knowledge of the effect of the ototoxicity on socio-demographic factors and psychological distress.

Design/Methods: We included 54 platinum-treated childhood cancer survivors treated between October 1958 and March 2004 with completed surveys including socio-demographic data, such as insurances, education and employment. All survivors included a questionnaire consisting of the Dutch version of the Distress Thermometer (DT), measuring the severity of distress. The DT was measured in two ways, but all DT were recoded to a 0 (no distress) – 10 (extreme distress) scale. The Hospital Anxiety and Depression Scale (HADS) was used to study the psychological distress whereby a score ≥ 15 is indicative for clinically significant distress. For this study, we included 54 platinum-treated childhood cancer survivors after cessation of therapy. Analysis were stratified by result of pure tone audiogram performed with a median time of 8.4 years after cessation of platinum-treatment (range: 0.0-23.0 years). Definition of serious ototoxicity was Münster score $\geq 2b$.

Results: Median HADS score of survivors who suffered from serious ototoxicity ($n=22$, median score: 4.5, range: 0.0-29) was not significantly different from the platinum-treated group who did not suffer from ototoxicity ($n=32$, median score 5.5, range: 0.0-11, $p=0.482$). In addition, the DT was also not significantly different between both groups ($p=0.317$). Median DT in the survivors with ototoxicity was 2.0 (range: 0.0-8.0) and median DT in the survivors without ototoxicity was 1.5 (range: 0.0-6.0). There were no differences in problems obtaining insurances, highest education achievement and (un)employment between the two groups.

Conclusion: Survivors of childhood cancer who suffer from ototoxicity do not encounter more socio-demographic problems and psychological distress than survivors who do not. As our study includes a limited study population further investigation has to be done.

P-0643 | The Impact of Amputations on the Quality of Life in Children with Cancer

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Background/Objectives: Adaptation to the physical, psychological and social consequences after a limb amputation in children can be very difficult and requires a multidisciplinary approach.

Aim of the study: evaluation the role of the multidisciplinary team in improving the quality of life in amputated children with cancer of the extremities (retrospective study).

Design/Methods: Twenty two children (8 girls, 14 boys), age 5-18 with limb amputation (20 of lower limbs, 2 shoulder disarticulations) for osseous tumors (19 patients) and soft tissue sarcomas (3 patients) treated in the Paediatric Oncology Department of the Institute of Oncology in Bucharest between 2004-2015 by a multidisciplinary team (doctor, nurse, psychologist, play therapist, kinesiologist) who were observed for at least 4 months after the amputation. We identified and studied the factors that influence the quality of life: pain at ≥ 7 days post-op, regaining motor skills, the psychological impact of the amputation on the amputee and his family.

Results: Pain at ≥ 7 days post-op: nociceptive pain – 50%, combined pain – 50%, intensity VAS ≤ 7 in 19/22 patients; the complete resolution of pain was at 4 weeks post-op. Some emotional reactions of the amputees/their families in the process of readaptation: fear, anxiety, panic, sadness, denial, anger, negotiation and, finally, acceptance and adaptation in all cases. Acceptance of the new body-image was difficult for the patient and his family. Motor independence was partially regained at 3 months after amputation. Readaptation in the family was easier than in the collectivity. Psychological intervention regarding stigmatization/discrimination had some limits due to perceptions and attitudes of the social background.

Conclusion: 1. Limb amputations can severely influence the quality of life in children and their families. 2. Psychological impact is profound. 3. A multidisciplinary team is required to improve the quality of life. 4. It is necessary to change the attitudes of the community towards amputated children.

P-0644 | Interventions for Promoting Participation in Shared Decision-Making for Children with Cancer: Update of a Cochrane Review

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Background/Objectives: Children with cancer generally prefer to be involved in shared decision-making (SDM) and therefore it is important to know what interventions are most effective in promoting children's participation in SDM. In this update, we included randomised controlled trials (RCTs) and controlled clinical trials (CCTs) of SDM interventions for children with cancer aged four to 18 years. The types of decisions were: treatment, health care, and research participation decisions. The primary outcome was SDM as measured with any validated scale.

Design/Methods: For this update we searched the following sources from the period of 23rd September 2012 to 29th February 2016: Cochrane Central Register of Controlled Trials (CENTRAL), The Cochrane Library; PubMed; EMBASE; CINAHL; PsycINFO; ERIC; ProQuest Dissertations and Theses; Sociological Abstracts, trials register and conference proceedings.

Results: The authors identified 2290 potentially relevant documents from only the electronic databases, of which 2289 were excluded by reviewing titles and abstracts. Of the remainder, we retrieved one full text publication for more detailed screening. Hollen et al, 2013 tested a decision aid for cancer surviving adolescents related to engaging in substance abuse behaviors and measured decision-making as an outcome using a decision-making quality scale. Although Hollen conducted an RCT on SDM with children, it was excluded because the children did not have cancer but were cancer survivors. The focus of this review is on children who currently have cancer and how SDM impacts on decisions related to their cancer care or even end of life care. The issue of decision-making for cancer survivors is a very important issue but it requires a separate protocol and new review.

Conclusion: It remains unclear what factors promote the SDM approach and what interventions are effective and suitable for children. Based on the currently available evidence it is not possible to give recommendations for clinical practice.

P-0645 | Protecting Through Research Rather Than from Research: Supporting Children and Young People's Participation in Clinical Research

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Background/Objectives: Researchers are often concerned about carrying out research with children and young people, because of the particular ethical challenges associated with such research. Yet, if children and young people are not given the opportunity of taking part in research, it is very difficult to obtain the evidence needed to improve the treatment provided for them.

Design/Methods: The Nuffield Council on Bioethics explored the involvement of children in clinical research through an expert Working Party, supported by a stakeholder group involving young people and parents. Throughout the project, input was sought widely from young people, parents and professionals concerned with clinical research, in the UK and beyond. Views and experiences were sought through web-based surveys, an open 'call for evidence' and face-to-face meetings; through school projects in the UK and Kenya; through community engagement in Kenya; and through networks of research professionals working in low and middle income countries from South East Asia to Latin America.

Results: The report, Children and clinical research: ethical issues, was published in May 2015.

This paper will illustrate how a child's or young person's can input into a decision about research participation using three distinct paradigm cases or scenarios. The key issues that researchers need to think about for carrying out clinical research with children or young people will be explained. The process of dissemination (magazine and an animated film) which will be shown and explained.

Conclusion: We argue that high quality research, that addresses questions of importance to the health of children and young people, should be seen as intrinsically good: part of the 'core business' of a health service. The key recommendations have been made more accessible for children through a magazine version and animated film and for professionals via a e-learning course <https://globalhealthtrainingcentre.tghn.org/children-clinical-research/>. All the Council's materials are available free of charge from its website.

P-0646 | www.clicsargent.org.Uk/Relationships - How CLIC Sargent Developed An Online Tool to Help 16 to 24-Year-Olds Manage the Impact of Cancer on their Personal and Sexual Relationships

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Background/Objectives: In 2014 CLIC Sargent's Information team consulted with 16 to 24-year-olds who have or have had cancer, in order to identify their information needs in relation to sex and relationships.

Design/Methods: Consultation was carried out through an online survey collecting both qualitative and quantitative data over a range of key topics including emotional and physical impact, self-esteem and communication issues. Recruitment was through care professionals and social media.

Results: Significantly more young people than anticipated responded – 125 overall – indicating how important this topic is to young people with cancer. The survey found that young people are more than twice as likely to have questions about relationships and sex after being diagnosed. The results also suggest that many questions about the impact of cancer on relationships and sex are going unanswered, with respondents finding it over twice as difficult to find answers to questions after a diagnosis, compared to finding answers to queries they had when they were well. Key concerns include whether a partner would still find them attractive, worries around starting a new relationship, not feeling like sex and embarrassment around talking to their doctor.

Conclusion: CLIC Sargent developed a youth-centric resource which recognises that young people, due to their life stage, are likely to have questions and concerns in this area prior to diagnosis, and that cancer can exacerbate these as well as bring new worries in this area. The

resource provides honest, direct advice, with the aim of increasing young people's confidence in communicating about these issues. The information is delivered across different channels – written content, video and 'Ask the expert' online sessions – thereby increasing accessibility. Furthermore, it is also marketed to health and social care professionals as a tool they can use to help them raise these issues with young people with cancer.

P-0647 | Uncertainty in Parents of Children with Cancer: The State of the Science

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Background/Objectives: Evidence suggests that parents of children with cancer are prone to high levels of uncertainty, post-traumatic disorder, and stress symptoms as a result of their child's diagnosis, treatment, and unpredictable outcomes. This vulnerability may impact how parents perceive their child's health-related quality of life (HRQOL). However, there's a dearth of evidence explicating the linkage between parental uncertainty and HRQOL in this population. Thus, the purpose of this systematic literature review is to identify the gaps in literature addressing parental uncertainty and HRQOL in children with cancer. The Roy Adaptation Model and Mishel's Uncertainty guided this systematic literature review.

Design/Methods: CINAHL, PubMed and Academic Premier were searched for research findings using the terms: *parental uncertainty, children and cancer, quality of life, uncertainty*, published between January 2005 and September 2016 in English language. Exclusion criteria were non-research articles and literature reviews. Data were extracted from included studies and content analyses were done to synthesize the results of the review.

Results: Ten articles met the inclusion criteria. The literature suggests that high levels of uncertainty are prevalent in parents of children with cancer particularly in the first 6 to 12 months of a child's diagnosis and can persist overtime. High levels of PTSS symptoms were associated with parental perception of the child's HRQOL. Parents who experience PTSD symptoms report higher symptom burden in their children and are more likely to experience high uncertainty and high distress level themselves compared to the parents without PTSD symptoms.

Conclusion: Uncertainty is a major psychological and psychosocial stressor in the lives of children with cancer and their parents. It is important to explicate the linkage between parental uncertainty and HRQOL in order to inform future interventions that will reduce uncertainty in parents, which will ultimately improve HRQOL in this vulnerable population.

P-0648 | Survival from Tumours of the Central Nervous System in Danish Children: Is Survival Related to Family Circumstances

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Background/Objectives: Due to diverse findings as to the role of family characteristics for childhood cancer survival even within Europe and particularly little knowledge on central nervous system (CNS) tumour survival, we explored a nationwide, register-based cohort of Danish children with CNS tumours.

Design/Methods: All children born between 1973 and 2006 and diagnosed with a CNS tumour before the age of 20 years (N=1,259) were followed until 10 years from diagnosis. Adjusted Cox curves and Cox proportional hazards models estimating hazard ratios (HR) and 95% confidence intervals (CI) were used to assess the impact of various family characteristics on overall survival from CNS tumours.

Results: HRs for all CNS tumours combined, did not point to strong associations between survival and family characteristics. Somewhat worse survival was observed for children living in provincial cities and rural areas compared to children from greater Copenhagen area. Analyses by CNS tumour type showed statistically significant worse survival for children with glioma when living outside of Copenhagen (HR 1.59; CI 1.05, 2.42). For embryonal CNS tumours, the association between survival and place of residence was not confirmed. However, having full siblings was significantly associated with worse survival from embryonal tumours (HR for 3 or more full siblings 3.25; CI 1.25, 8.44). A tendency of inferior glioma survival was seen for children of very young fathers whereas, based on small numbers, a tendency of better survival from embryonal tumours was observed for children with parents of younger age at child's diagnosis.

Conclusion: Despite free and uniform access to health care services, family circumstances may effect survival from certain CNS tumours in Danish children. Further research is warranted to elaborate the pathways of those survival inequalities as well as to gain further knowledge on the impact of family circumstances on childhood cancer survival in other populations.

P-0649 | Cope with Pain in Children/Adolescents with Malignant Hematologic Cancers

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Background/Objectives: Pain is a multifaceted issue and a challenging concern in paediatric patients with hematological malignancies. Pain can originate from several sources, including diagnostic and treatment procedures, underlying malignancy, or other factors not associated with the disease process. In the light of the multiple dimensions involving the phenomenon of pain in children and adolescents with cancer, this study aims to present the ways that children and adolescents with acute leukaemia or lymphoma cope with pain. The study focused specifically on aspects pain-related coping during phases of treatment.

Design/Methods: Ongoing multicenter observational study of 34 children: 19 male and 15 girl (range age 7-14 years; M=8.2, SD=3.1) with Acute Lymphoblastic Leukaemia (ALL), Acute Myeloid Leukaemia (AML) Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). Rating of intensity of pain and pain-coping traits were assessed using VAS and Pediatric Pain Coping Inventory, to identify systematically children's pain coping.

Results: Children reported low present pain intensity [M=1.29, SD=1.85] but their rating of prior pain (average of all pain in hospital) were reported as moderate to severe [M=6.94, SD=2.44]. The phase of treatment was related to the coping strategies used for pain management. Children in an active phase of treatment (induction, consolidation, re-induction) used fewer overall coping strategies than children in the maintenance phase (maintenance, bone marrow transplant, stop) [F(1,32) = 10.332; p = 0.003; partial η^2 = 0.244]. The regression analysis confirmed that phases of treatment predict overall pain-coping skills [β = 0.494, t = 3.214, p = 0.003].

Conclusion: The active phases of therapy in this group of patients with malignant hematologic cancers were related to less effective coping strategies. These results highlight the importance of better identifying particular treatment phases, which will help improve the support offered to children and adolescents and hopefully lead to better adjustment when coping with pain.

P-0650 | The Relationship between Parent Perception of Child Pain & Parent Psychological Distress: An Exploratory Analysis of Rumination

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Background/Objectives: Research examining psychosocial outcomes of paediatric cancer has largely focused on the child, despite findings that caregivers are at risk for concomitant psychological and physical health declines. Current research also supports an association between parent and child psychosocial adjustment. To better understand predictors of both parent and child adjustment to paediatric chronic illness, current research has turned toward exploring illness-specific and non-specific variables. Thus, the aim of the current study was to conduct preliminary analyses on parental adjustment, focusing on the illness-specific variable of parent perception of pain, and the non-specific variable of rumination.

Design/Methods: Caregivers (N=19, M_{age} = 36.82 years, SD=7.7 years) of children diagnosed with cancer (M_{age} = 8.47 years, SD= 5.10 years) completed measures of rumination, psychological distress, and parent report of child cancer specific quality of life as part of a larger ongoing study assessing adjustment in families with youth newly diagnosed with cancer.

Results: Parent perception of child physical pain (a common side effect of cancer and inherent concern for parents) predicted the amount of psychological distress reported by parents. The relationship between parent perception of child's pain and parent's psychological distress was mediated by parent rumination (R²=.81, β = -.53, 95% CI = -1.31 to -.023); such that parent's subjective rating of child pain had an indirect effect on parent psychological distress through rumination. Child age, gender, ethnicity, and cancer type were included as covariates.

Conclusion: The illness-specific variable of parent perception of child pain was significantly associated with greater rumination and greater psychological distress. Since child pain during the course of cancer treatment cannot be eliminated, this study indicates that parent rumination could be a potential target for future intervention. Reducing parents' repetitive thinking would facilitate the alleviation of psychological distress among parents of children newly diagnosed with cancer and could even reduce children's concomitant distress.

P-0651 | The Rating Scales for Stress and Depression in Children with Cancer are Lower Than in Healthy Children: Objective Assessment of Art Technique

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Background/Objectives: We assessed the perceptions of depression, ego, aggression, lethargy, death, stress through 'draw-a-story' (DAS) technique and post-traumatic stress syndrome (PTSD) tests in childhood cancer patients and compared with those items in their parents and healthy children.

Design/Methods: Childhood cancer patients as well as their parents and healthy friends were included during winter camp. The participants were asked to perform a PTSD tests and draw a picture and tell a story according to Silver's technique. Three art therapists contributed to this study by scoring or judging response drawings.

Results: The DAS rating scale was from the score of 1 to 5 points. There were no significant differences of PTSD scores in childhood cancer patients (n=12) compared to their parents (n=10) and healthy children (n=14). Interestingly, in DAS technique, the scores of depression (2.33±1.22 vs 4.33±0.86, p=0.0023) and stress (1.16±1.52 vs 3.66±1.08, p=0.0049) were significantly lower in childhood cancer patients rather than in healthy children. Furthermore, all 6 items of emotional disturbances did not showed any significant differences between childhood cancer patients and their parents.

Conclusion: Our results suggest that supportive programs for hospitalized childhood cancer patients can bring positive emotional development and helps to correct their self-perception, and also patients and their parents seem to share their values of life.

P-0652 | The Relationship between Parental Distress and the Presence of Emotional and Behavioral Problems in Children with Cancer

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Background/Objectives: The level of parental psychological distress can influence the psychological well-being that children with cancer may experience during active chemotherapy.

The purpose of this study was to investigate the relationship between the level of parental psychological distress and the presence of emotional and behavioral problems in children with cancer. The ecological purpose of the study is to improve and adapt the psychological intervention for the patient and his family.

Design/Methods: A cross-sectional descriptive study was designed using the Profile of Emotional Distress to measure the parental distress level and the Child Behavioral Checklist to identify emotional and behavioral issues of children with cancer. Fifty eight subjects were recruited from the Oncology Institute of Bucharest and Fundeni Clinical Institute of Bucharest: 29 hospitalized children with cancer undergoing active chemotherapy, (average age=13.9, SD=3.3) and 29 attending parents (average age=41, SD=7.5).

Results: Spearman's rank correlation coefficient revealed statistically significant correlations between parental distress level and depression ($r=0.5$, $p<0.01$) and anxiety symptoms ($r=0.41$, $p<0.05$) and social problems ($r=0.43$, $p<0.05$) of the children. The partial correlation analysis revealed that considering the existence of the brothers/sisters variable, greater significance was shown for anxiety symptoms ($r=0.52$, $p<0.05$), social problems ($r=0.6$, $p<0.01$) and less significance for depression symptoms ($r=0.47$, $p<0.05$).

Conclusion: The findings indicate that the social-psychological intervention should focus on the relationship between parent and patient, on decreasing depression, anxiety symptoms and social problems and on the involvement of the extended family in the therapy process. This adapted intervention could lead to an improvement in the quality of life of children with cancer and their families.

P-0653 | Enhancing Nurse/Physician Collaboration in Ethical Issues in Paediatric Oncology

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Background/Objectives: A Nordic Working Group on Ethics (WGE), consisting of paediatric oncology nurses and physicians, was established in 2008. Until now this is the only inter-professional working group in the Nordic Society of Pediatric Haematology and Oncology and the Nordic Society of Pediatric Haematology and Oncology Nurses (NOPHO/NOBOS).

Nursing care versus medical cure of children and adolescents with cancer often creates challenging discussions. Physicians and nurses agree that the goal is the child's best interest. However, there is often a difference of opinion concerning what this best interest involves. Diverse opinions between the professions regarding ethical questions in childhood cancer treatment has been a recurrent theme in the work of the WGE. This discrepancy in opinions is a potential cause of conflict. The objective of this presentation is to explore how this difference can be transformed from conflict to strength.

Design/Methods: A search through the literature was performed.

Results: Theoretical background of nursing is based on an urge to care for the patient, whereas the medical goal is to cure disease.

The search through the literature revealed the existence of conflicts, especially related to introduction of new experimental treatment, truth telling, resuscitation, intensive care treatment as well as end of life care and decisions.

Conclusion: There is a need for improving the dialogue between the two professions to promote a more holistic approach of care and treatment in paediatric oncology. Recommendations structuring the collaboration between physicians and nurses will possibly transform the difference in views from conflict to strength.

P-0654 | Canteen Ireland- Nationwide Support Group for Young People with Cancer

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Background/Objectives: As there is no teenage cancer unit in Ireland, they are either treated in adult or children's wards. Often a teenager would never get to meet another teenager with cancer. A diagnosis of cancer is a very frightening experience at any age, but especially so during the adolescent years. Cancer disempowers young people. They are more dependent on their parents, and can be ostracised from their peers. It is often when the young person leaves hospital that they feel more alone and isolated than ever.

CanTeen Ireland is a nationwide support group for young people between the ages of 12 and 25 years who have or have had cancer. Membership currently stands at 260. It is a testament to the success of the group that many of our members are now volunteer leaders including our current chairperson. Our aims are to support, empower and develop young people with cancer. CanTeen Ireland provides an opportunity for young people who have been affected with cancer to meet up in a relaxed and informal setting.

We have 7/8 weekends away per year along with 5/6 day meetings. We go to various activity centres throughout Ireland. These activities challenge the young person's perceptions of their own abilities and helps build their self-esteem. During these meetings we talk about cancer, and how it has affected them. By providing these opportunities, a young person with cancer realises that there are not alone, and that the feelings they have are in fact very common. They meet up with other teenagers who have "come through the other side of their treatment" and now lead normal lives.

We also produce a biannual newsletter which is written by our members, and sent out to everyone on our mailing list. CanTeen Ireland is "run by young people for young people".

Design/Methods: N/A.

Results: N/A.

Conclusion: N/A.

P-0655 | Supporting Parents Who Have Lost A Child to Serious Illness: Combining Bereavement and Therapeutic Recreation Models of Intervention

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Background/Objectives: The aim of this paper is to describe and discuss a supportive intervention for families who have lost a child to serious illness including cancer, which combines the principles of therapeutic recreation (TR) and bereavement support.

Design/Methods: This action research study included a documentary analysis (with researcher reflection), a mixed methods exploration of parents' experiences of the programme, and a qualitative study of staff views of the programme. Data collection included interviews and observation, while analyses included frequency, content and thematic analysis. Central to the interpretation of the data was the integration and identification of higher level themes across the elements of the study.

Results: The findings suggest that the intervention model creates fellowship and shared experience, addresses isolation and offers a place to come together as a family. It creates a support network where children can be remembered and celebrated and family members can also reinvest in themselves and each other. The residential nature appears to create a safe space and allows families to reconnect with their child and each other. Overall, the findings suggest that this programme has potential to support families who have had a child die from serious illness. The study highlights implications relating to the combination of bereavement and TR models in understanding the experience of bereaved families and informing a therapeutic programme.

Conclusion: This research has implications in a number of areas. It considers the impact of the loss of a child following serious illness on the family. The study also captures parents' and professionals' thoughts on the supports needed by this group. The findings of this exploratory study highlight the potential contribution of a combined bereavement/TR model for supporting families who have had a child die from serious illness.

P-0656 | A Multidisciplinary Intervention to Tell Children about the Parent's Cancer: Preliminary Results

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Background/Objectives: It is well known that children of parents with cancer are at increased risk of developing emotional and behavioral problems. Different studies highlight the importance of an open communication with children about the parents' cancer to reduce distress in the family. Parents with cancer, however, may be reluctant to talk openly with children about their illness.

The intervention aims to inform or improve children's knowledge of their parent's cancer, to facilitate their coping with the illness, to enhance parents' competence and communication about cancer inside the family.

Design/Methods: The most peculiar characteristics of this intervention, dedicated to patients with cancer diagnosis and with underage children, are the collaboration of different specialists (oncologist, paediatric hemato-oncologist and psychologist) and the direct involvement of children. At the beginning of cancer treatment the psychologist explains the project to the parents. If the parents accept to participate in the intervention, the paediatric hemato-oncologist and the psychologist, without the parents present, explain to children, with the support of metaphors and images, the parent's disease and try to understand their needs. Then counseling sessions with the parents are organized to improve their attention to their children's needs and their ability to satisfy them. In order to evaluate the intervention, a specific questionnaire has been realized that describes the family atmosphere, the parents' satisfaction, the level of communication in the family and the children's psychological conditions after the intervention.

Results: Since 2012, 43 families have participated in the program. Preliminary quantitative analysis underline the increase of communication in the family, the family satisfaction and the absence of severe psychological symptoms in the children.

Conclusion: The project shows the advantages of the direct engagement of children in the communication of parent's cancer to facilitate the relationship, to reduce family distress and to open communication inside the family.

P-0657 | Breaking Bad News in Paediatric Oncology: Methasynthesis, New Protocol- Empathy

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Background/Objectives: To review the literature on breaking bad news to gain a better understanding of this processes in paediatric oncology.

To create a protocol for disclosing unfavorable information in paediatric oncology (responding to the needs of children and their parents and suitable for wide dissemination).

Design/Methods: Methasynthesis.

Systematic review of qualitative studies that focused on the patients and doctors experiences and points of view about breaking bad news in paediatric oncology. Electronic searches were conducted in four databases. Thematic analysis was used to identify key themes and synthesize

them. The most consistently mentioned recommendations were examined, sorted into discrete categories, and summarized.

A group of 107 patients and parents filled an anonymous questionnaire about their needs and their preferences when receiving bad news about their health or the health of their child.

The creation of protocol EMPATHY.

Evaluation of the protocol:

- protocol has been evaluated by 28 psychooncologist in an anonymous questionnaire.
- an anonymous written survey was administered to 238 medical students immediately after the course: "What do you remember about the EMPATHY protocol?"

Results: Conveying bad news is a key moment in the doctor - patient relationship and one of the more difficult tasks in paediatric oncology.

Protocol EMPATHY dedicated to paediatric oncology has been created.

Protocol emphasized the importance of: empathy, truth, hope, advance preparation and patients and their parents empowerment.

In an anonymous questionnaire 100% psychooncologist expressed a positive opinion about the protocol.

Studies have shown that 89% of the students remembered all the essential elements of the protocol EMPATHY after a single hearing his principles.

Conclusion: Breaking bad news is a difficult and challenging process which affect medical outcomes in cancer care.

Learning friendly protocol EMPATHY may be helpful in paediatric oncology.

Controlled trials are needed to assess the effectiveness of the guidelines in changing paediatric oncology practice to identify the most effective strategies.

P-0658 | Social Stigma Associated with Diagnosis of Childhood Cancer in a Developing Country and its Impact on Quality of Life

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Background/Objectives: Human beings have an inherent quality of attaching a stigma to unknown. Stigma can result in psychosocial stress leading to poor quality of life and abandonment in patients with childhood cancer. The purpose of this study is to measure the levels of social stigma in childhood cancer patients and to measure the quality of life of children.

Design/Methods: The present single arm prospective study was conducted in the Department of Pediatrics of a tertiary care centre in Punjab, India. All patients undergoing treatment in the Pediatric oncology unit whose parents gave consent were included in the study. The social stigma was assessed using cancer stigma scale (CASS) and multidimensional scale of perceived social support (MSPSS). PedsQL cancer module was used to assess the quality of life of patients.

Results: Twenty patients between the age of 2- 17 years (mean age = 7.6 years) were included in the study. Male: female ratio was 2.33:1. The mean score of oncology patients on six dimensions was : Severity 19.3, responsibility 7.3, awkwardness 8.35, avoidance 4.95, financial discrimination 8.15, policy opposition 6.6. Patients scored highest on severity indicating negative attitude towards the diagnosis and least on avoidance indicating they would like to help patients suffering from cancer. MSPSS was used to assess the support received from significant others, family and friends as perceived by patients and parents. They perceived high support from family and moderate from significant others and friends. In the quality of life module patients scored highest on the cognitive ability indicating that there has been no negative impact of the therapy on the cognitive functions. Procedural anxiety score was the lowest indicating high level of anxiety during procedures.

Conclusion: Patients in our setup get moderate support from society and do not face discrimination and stigmatization that could result in poor quality of life.

P-0659 | Racial and Socioeconomic Impact on Paediatric Oncology Outcomes in Mississippi

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Background/Objectives: The investigation into the impact of race and socioeconomic status on survival and relapse in paediatric oncology has provided mixed results. The aim of the current study was to investigate the impact of race and socioeconomic status on survival and relapse in a roughly equal number of Black and White children diagnosed with cancer within the state of Mississippi.

Design/Methods: Participants were 196 children with cancer (Mean age at diagnosis = 7.4 years; 43.4% female; 49.0% White, 51.0% Black). 33.7% of children had ALL/AML, 20.9% CNS/brain tumour, 12.2% lymphoma, 26.5% solid tumour, and 6.6% other cancers. Caregivers provided demographic information. Chart review obtained medical diagnosis, age at diagnosis, time survived, and time to relapse. Kaplan-Meier analysis examined survival curves using SAS software, Version 9.4. Racial differences were further assessed using a log rank test while controlling for family income level, Cox proportional hazard ratios (HR), and 95% confidence intervals (CI).

Results: Across cancers, Black children did not have a reduced 5-year survival [$\chi^2(1) = 0.40$, $p = 0.53$] nor a reduced 10-year survival [$\chi^2(1) = 0.71$, $p = 0.40$] compared to White children. Black children also were not more likely to relapse [$\chi^2(1) = 0.01$, $p = 0.91$]. Contrary to expectations, family income above the poverty level was associated with reduced 10-year survival [$\chi^2(1) = 4.28$, $p = 0.04$]. The interaction between race and family income was not significant.

Cox regression analyses showed a similar pattern, with higher family income marginally associated with reduced 10-year survival [HR = 0.291 (CI 0.084 - 1.012), $p = 0.05$].

Conclusion: Contrary to other research, we did not observe Black race to be an independent predictor of survival or relapse. The relationship between race, socioeconomic status, and survival appears complex and is likely influenced by a multitude of both medical and social factors.

P-0660 | Summer School for Children with Cancer in Istanbul

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Background/Objectives: Summer school programs are wonderful experience for kids with cancer and their families. Although these programs are available in USA and West Europe, they are not common in developing countries.

Design/Methods: "The summer school for kids with cancer and their families" project, in Istanbul, Turkey, was first planned in 2014 and coordinated by Izzet Kebudi, who was then a senior in high school who had previous training/experience of a summer school program for children in a limited-resource area in Turkey. The positive feedback from patients/families stimulated the team to continue the project in 2015. The summer school was free of charge. Volunteers of the Childhood Cancer Love and Support Society (COKSEV) supported the project.

Results: 50 children with cancer, their siblings and parents joined the program. Half were coming from other cities or countries. Most families had poor socioeconomic resources. The major theme was "To learn about our environment". A one-week program was done. Each day education in English for beginners, painting, outdoor excursions in Istanbul were done. Some were, historical tour of Istanbul, an openair museum, a Bosphorus boat tour, Aquarium, outdoor picnic. Every day breakfast and a full lunch was served to all. The kids and families were very happy to join such a program and expressed their wish to join further programs. The pictures drawn by the children were further used by consent of the families in the yearly calendars produced by COKSEV. The donations received from the calendars were used for the children as well. Thus, resources for the continuation of the project were planned.

Conclusion: The Summer School Project was very successful and gave the patients, siblings and parents a chance to be together, have fun and to open up and helped them to better cope with their treatment process.

P-0661 | Reiki for Alleviation of Physical and Psychological Distress in End of Life Care in Children with Cancer in Pakistan

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Background/Objectives: End of life care has been seen as a field fraught with challenges and according to the American Psychological Association, much research is required to make this part of life easy on the children dying from cancer and the caregivers who watch their slow and painful death.

Design/Methods: Complementary alternative medicine is something that has slowly been gaining a foothold in alleviation of physical and psychological distress. Reiki, a Japanese complementary alternative energy therapy, is used for alleviation of stress, anxiety, increasing relaxation and improvement of the overall quality of life. Sixty patients were enrolled in the study on whom Reiki was carried out. The method involved the laying of hands on key points where the patient pointed out as painful spots till the patient would report a reduction in pain.

Results: It was found over a period of 3 years with patients on end of life care, that Reiki was an effective medium of pain alleviation. Of the sixty patients on whom Reiki was carried out, 90% of them reported a reduction of physical and psychological distress.

Conclusion: The children would call the laying of hands over affected areas as 'magic', and as something that helped alleviate their suffering and give them respite from the constant excruciating pain that they suffered. It was concluded that Reiki needs to be offered as an option for the alleviation of physical and psychological distress of children with cancer.

P-0662 | Secondary Trauma Faced by Health Professionals Giving End of Life Care to Children with Cancer in Pakistan

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Background/Objectives: End of life care in paediatric oncology, involves providing support to the child and the parents, which involves alleviating physical and psychological pain. Children experience trauma, and find it difficult to express it especially when they see their parents in pain, parents in turn want to hide the prognosis from the child which creates a vicious circle. This also creates many challenges for the health professionals such as doctors, nurses and counselors who are providing care at this time.

Design/Methods: 25 health professionals were enrolled in workshops which entailed role play and presentations on end of life care. Post workshop evaluation questionnaires were filled out by participants and questions were asked pertaining to their state of mind during the workshop.

Results: Qualitative analysis of the data was derived from 25 health professionals, which included doctors, nurses and counselors. The themes that were identified in workshops with health professionals were feelings of helplessness, repression of their emotions, anger and an aversion to noise and crowds. A need for respite from long working hours was also mentioned as well as vacations more than once a year to recharge.

Conclusion: Quality of life and emotional well being were factors that were adversely affected as health professionals carried the aftermath of the effect of end of life care into their personal lives and professional relationships. The participants stated that they needed stress and anxiety reduction techniques and counseling to deal with the secondary trauma that they

faceted. A better program of self care needs to be incorporated into the health professionals schedules as well giving them flexible timings and vacation leaves so that they can recuperate from trauma thus preventing burnout.

P-0663 | Cold Pack for Pain Alleviation in Children with Cancer, Resulting in Reduction of Distress

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Background/Objectives: Children with cancer not only have to deal with pain associated with the disease itself, but also the physical distress or discomfort associated with the medication given during the treatment. Cold alleviates pain and stinging sensations, by numbing the skin and flesh to discomfort. After interviewing nurses, doctors and patients it was found that the medicines causing the most distress during administration were Vincristine which causes a burning or a cold sensation; Levofloxacin and Vancomycin which cause itching, and Potassium Chloride which causes pain.

Design/Methods: A clinical trial was carried out on a 100 children in Indus Children Cancer Hospital (ICCH), who were administered cold pack therapy. This was done by applying a cold pack on the painful site till the child had reported reduction in physical distress.

Results: It was found that cold pack application while the medicines were being administered caused significant reduction in physical distress. The application of an ice pack made it easier for the child to bear the physical discomfort and the ensuing psychological distress of child and caregiver was alleviated, thus increasing treatment compliance. This in turn made the children less anxious during administration of medication during treatment of cancer.

Conclusion: Therefore cold pack application should be accessible to all children while medicines are being administered which would help in treatment compliance across the board. Especially those who are being given medicines intravenously which cause pain, burning, itching or any other kind of physical discomfort.

P-0664 | Stress Reduction through Play for Health Professionals in Paediatric Oncology in Pakistan

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Background/Objectives: Health professionals be they doctors, nurses or counselors, are constantly dealing with trauma in the field of paediatric oncology, and suffer from increased levels of stress, which in turn lead to a sub-optimal performance at work. Play is the simplest means of enhancing physical, mental and emotional well being of health professionals thereby optimizing their productivity. From Plato to Anna Freud play has been touted as a means to help people reach their optimum potential.

Design/Methods: Play was used as an intervention for which activities such as musical chairs, blowing bubbles, clay or play doh, and coloring were designed for 30 health professionals which included doctors, nurses and counselors. This was carried out in small groups in the form of workshops in Indus Children Cancer Hospital in Pakistan.

Results: Post intervention evaluation forms yielded results that showed enhanced physical and mental energy levels as well as increased feelings of well being with an increased demand for play therapy workshops. Participants reported significant reduction in their stress levels. There was laughter and camaraderie among them as they played.

Conclusion: Play is a simple yet effective way to enhance skills such as creativity, abstract thinking, problem solving, conflict resolution, leadership and social cognition. It also provides therapeutic benefits such as stress reduction and renewed vigor and physical well being. It is important to use diverse strategies to create an environment, for people working in high stress fields such as paediatric oncology, which helps them not only alleviate their stress but also help them optimize their performance at work and create a more amiable environment.

P-0665 | Mindfulness Meditation for Physical and Emotional Wellbeing in Healthcare Professionals in Paediatric Oncology

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Background/Objectives: Prolonged periods of stress are a significant factor leading to decreased productivity, mistakes and early retirement from the health field or switching of jobs and may lead to burnout eventually. One of the simplest ways to manage stress is through mindfulness meditation, a strategy which was derived from ancient Buddhist meditation practices by Jon Kabat-Zinn. Compassion, patience and acceptance are taught to individuals to view their inner and outer experiences with, thereby creating emotional and physical well being. As mindfulness meditation calms the mind it reduces stress thereby reducing stress related aches and pains.

Design/Methods: Fifty healthcare professionals from Indus Children Cancer Hospital were given training in mindfulness meditation, through workshops which incorporated mindful breathing practices. They were instructed by counselors trained in mindfulness meditation, through the relaxation breathing process while keeping their minds tuned into the present.

Results: It was found through anonymously filled evaluation forms, from the participants after the workshop that there was a significant reduction of distress and that they felt calmer and ready to take on their duties. Many reported that they felt their mood lift and were in a happier state of mind than before. Others reported a relaxation of muscles and reduction of aches and pains.

Conclusion: There was a demand for more frequent mindfulness meditation workshops during the week, by the healthcare professionals as they felt that it helped them experience physical and emotional well being. Mindfulness meditation proved to be an effective method of improving mood and a significant increase in efficiency in practice, in healthcare professionals. It is

recommended that mindfulness meditation should be taught as an integral part of self care for healthcare professionals in paediatric oncology.

P-0666 | Self-Reported Worries of Childhood Cancer Survivors in Korea

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Background/Objectives: Adolescents and young adults who experienced childhood cancer may have a broad range of concerns and worries after experiencing a life-threatening illness. However, the various worries of childhood cancer survivors, and the correlates of their worries, were not fully understood. This study examines the effects of sociodemographic factors, cancer-related factors, and self-esteem on self-reported worries of adolescent and young adult survivors of childhood cancer in Korea.

Design/Methods: Questionnaires from 145 respondents were collected in 2013. About 52.4% of participants were male and the average age of the participants was 19.3 years. The average age of the participants at diagnosis was 9.2 years and the average time since diagnosis was 10.1 years. About 70.3% were diagnosed with hematological cancers. The Rosenberg Self-Esteem Scale was used to assess the survivors' self-esteem, and the Self-Reporting Worry Questionnaire was used to assess their various concerns. Hierarchical regression analyses were conducted to examine the effects of demographic variables, cancer-related variables, and self-esteem on worry.

Results: The most common concerns reported by childhood cancer survivors were about parents' health status and financial burden. The sociodemographic factors (age, gender, and household income) accounted for 13.4% of the variance in the total worry scale in the first step and the cancer-related factors (time since diagnosis and late effect) accounted for an additional 6.1% of the variance in the second step. Self-esteem accounted for an additional 7.7% of the variance in the final step ($p < .001$). Older age, female gender, lower income, longer time since diagnosis, having late effects, and lower self-esteem were associated with higher levels of worry.

Conclusion: Understanding factors that predict worries of childhood cancer survivors enables us to provide appropriate services to meet survivors' needs. This study could help oncology social workers identify long-term cancer survivors who are at risk of developing anxiety and distress resulting from cancer experiences.

P-0667 | Speleca: A French Study about the Evaluation of Parental Stress (PS) in Children with Acquired Brain Injuries (ABI)

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Background/Objectives: Pediatric cancers, in particular brain tumors (BT), and severe traumatic brain (TB) generate clinically significant levels of parental stress (PS). The prognosis of ABI in children is associated to the type of pathology (BT, TB) and to sociodemographic factors (parental psychological distress, educational level). Importantly, the effect of PS on children's recovery is well-established: PS is associated with children's own distress and to the therapeutic alliance. Therefore, it is relevant to evaluate PS in children with ABI, especially in order to measure the efficiency of interventions. However, measures aimed at evaluating PS and validated in the French population are currently unavailable.

The first aim of our study was to validate the PIP (Pediatric Inventory for Parents) questionnaire on a French sample.

The second aim was to compare PS in children diagnosed with either BT or TB.

Design/Methods: Forty mothers were recruited in a French rehabilitation unit of acquired neurological pathologies in children.

Inclusion criteria were paediatric ABI (BT and TB) and time since diagnosis ranging from 1 to 18 months.

Other medical information included the type of tumour (for BT), the Glasgow score (for TB), medical treatment, motor sequelae and cognitive deficits. *

Each mother filled three questionnaires: the 1) PIP, the 2) State-Trait Anxiety Inventory (STAI) and the 3) Family Assessment device (FAD).

Results: Preliminary results showed that mothers displayed high levels of PS in both groups. PS was correlated to mothers' anxiety, as well as to communicational characteristics of the family.

Data of PS in both groups (BT and TB) is presently being analyzed.

Conclusion: Our findings on PS in a French sample of children confirmed results from previous reports.

However, several research questions remain to be explored, such as if data regarding PS should be obtained indirectly through a parental questionnaire *versus* a direct interview.

P-0668 | Creating A Multi-Stakeholder Organization Representing Parents, Survivors, Clinical and Basic Research, and the National Childhood Cancer Registry to Improve the Situation of Children and Adolescents

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Background/Objectives: No national organization was taking care of all issues related to Childhood Cancer in Switzerland and representing the different stakeholders (parents,

survivors, clinicians, researchers, and institutions funding research). The need for such a representation towards national and cantonal governments and authorities became more evident over the years and the lack of an existing body resulted in insufficient participation of the childhood cancer community in legislative and health care projects. Objectives were to improve the situation of affected persons by establishing an organization which is raising awareness, participating in political processes, raising funds for research and projects and supporting survivors.

Design/Methods: Case report.

Results: Roundtables started 2010 with six national or regional childhood cancer organizations, 2012 a Memorandum of Understanding declaring the intention of establishing a new organization was issued, in 2014 the project for the founding process started and February 15th, 2015 the launching event took place in the Swiss Capital. In March 2015 the office started its operations and since then a team is taking care of public relations, lobbying, fundraising, new projects for survivors and coordinates activities among the members organizations. A website has been implemented, presenting activities and projects of the organization and including a platform (www.suivinet.ch) dedicated to survivorship topics.

Conclusion: The creation of this national organization opened new opportunities. The public sector (companies and private persons) and government bodies reacted positively and welcomed the fact that they would have one unique partner for all issues regarding childhood cancer. The member organizations got a better understanding of the different actors in the field. Ideas could be transported more easily from one language region to others. The cooperation with other existing health organizations (in paediatric and adults) remains challenging, due to limited resources. Overall, the process opened new opportunities and the paediatric cancer topics are becoming more visible. www.childhoodcancer.ch.

P-0669 | Purchases of Antidepressants after Cancer at Young Age in Finland – A Nationwide Study

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Background/Objectives: Childhood and young adult cancer survivors are reported to be prone to psychiatric and physical late-effects. The aim of this study was to explore, whether cancer survivors in various diagnostic and age groups have increased risk for purchasing antidepressants compared with siblings.

Design/Methods: Medication purchases of 7,093 (47% male) cancer patients (0-34 years at cancer diagnosis) and siblings (N=13,061, 51% male) were retrieved from the Social Insurance Institution of Finland. Cancer patients were identified from Finnish Cancer Registry and siblings from the Population Registry Centre. The first purchase of antidepressants was assessed from the cancer diagnosis made from January 1st 1994 to December 31st 2011. The hazard ratios (HR) were computed with adjusting for birth year, gender and age at the start of follow-up.

Results: In patients aged 0-11 years or 12-19 years at cancer diagnosis, the HR for purchasing antidepressants was comparable to siblings (HR0.9 and 1.0, respectively). In patients aged 20-34 years at diagnosis, the HR was increased (1.3, 95%CI 1.1-1.5). Remarkable was that in the youngest age group, each one year increase in start of the follow-up elevated significantly (p<0.0001) the risk for purchasing antidepressants. Female cancer patients in all age groups had significantly higher HRs for buying antidepressants than the males. YA patients with bone tumour [HR 2.4, 95% CI (1.5-3.7)], brain tumour [HR 1.6, 95%CI (1.3-2.0)], and leukaemia [HR 2.7, 95%CI (2.0-3.7)] had significantly higher risk for antidepressant medication purchases than siblings.

Conclusion: YA cancer patients seem to buy antidepressive medication more often than siblings and, thus, also their need for psychological support should be properly assessed. Similarly, later support for those treated for cancer in childhood should be organized. Females are more prone to depression than males, and certain diagnostic groups among adults may need more support than the others.

P-0670 | Youth Survivor Initiative – Connect, Share, Support Bringing Teenage Survivors of Childhood Cancer Together

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Background/Objectives: The effects of cancer and cancer treatment can adversely affect the quality of life of teenaged survivors. The non-medical results of treatment can include poor social skills, low self esteem and challenges developing and maintaining friendships with peers. Overall quality of life moving forward can ultimately be negatively impacted.

Design/Methods: In May 2015, Candlelighters membership included 42 survivors aged 13 – 18 years of age, who were each invited to participate in the Youth Survivor Initiative (YSI), a quarterly get-together with a focus on having fun, sharing experiences and building friendships.

Results: The inaugural gathering garnered 26% participation (12 individuals) in which the group attended an exciting stadium football game. A decrease in that number occurred for the second event, with 14% participation from the initial pool of qualifying participants. Positive feedback, however, included expressions of “being glad” to be invited, having “had a great time” and “looking forward” to the next outing. Seven teens have connected on a newly established, closed Facebook Page, which Candlelighters Program Coordinator monitors and encourages involvement in. A number of the participants report texting between outings with some of their new friends.

Five outings/events have been planned for 2016, based on feedback and input suggestions from the group itself. Candlelighters overall membership will be reviewed for additional participants who fit the qualifying criteria of 13 – 18 years of age, a minimum of one year off treatment. Ongoing evaluation will take place informally with a year-end formal on-line survey evaluation planned.

Conclusion: Advances in cancer treatment mean that today almost 80 percent of children diagnosed with cancer are alive at least five years after diagnosis. The teenage years are often considered a particularly challenging time in growth and development.

Bringing teenaged survivors together for social recreation helps them develop social skills and personal relationships, gaining independence and self-knowledge.

P-0671 | Providing Access to A Variety of Educational Opportunities at No Cost to Parents Decreases Stress in Families of Childhood Cancer Patients

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Background/Objectives: The childhood cancer journey has many transitions, each one requiring adjustments and understanding. Managing information is an important piece in parenting childhood cancer patients and is a valuable strategy for coping with stress.

Design/Methods: Candlelighters provides families with numerous resources including books, access to online information and education days to combat feelings of helplessness, enhance understanding of what is happening to their child, and ease the adjustment to these changes.

Books provided at the time of diagnosis range from “Living with Childhood Cancer” and “The Essential Cancer Treatment Nutrition Guide and Cookbook” for parents, “Chemo, Crazyness & Comfort My book about childhood cancer” for patients (age appropriate) through a variety of disease specific resources including, but not limited to “Childhood Cancer A Parent’s Guide to Solid Tumour Cancers” The Lymphoma Foundation of Canada’s “Lymphoma Patient Resource”, “Autologous Stem Cell Transplants ~ A Handbook for Patients”. Also provided are resources for siblings and grandparents, produced by the Children’s Cancer and Leukaemia Group out of the UK and when appropriate, a number of palliative and bereavement books for parents, siblings in different age groups and grandparents are also given.

Education Day, a one-day workshop, gives parents and sometimes adolescent patients and young adult survivors, an opportunity to hear from a variety of health care professionals (including paediatric oncologists, neuropsychologists, psychiatrists, radiation oncologists, naturopathic doctors) on a variety of topics that are of interest to them. Speakers are chosen based on feedback and input from the membership.

Results: Parents within the Candlelighters membership consistently report through program evaluation surveys and general feedback that they place high value (in the top 5 of 21 programs and services offered) on the resources that are provided by Candlelighters.

Conclusion: Empowering parents and patients, increasing knowledge and confidence has a positive effect on a family’s childhood cancer journey.

P-0672 | Child Life Supports for Patients with Retinoblastoma Highlight Disparities and Enhance Quality of Life and Service Delivery in Canada and Kenya

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Background/Objectives: Child Life (CL) provides engaging play-based and expressive arts experiences that educate, prepare and support coping of infants and children from diagnosis through treatment. We integrated CL approaches into daily care of patients with retinoblastoma (Rb) aged 0-5years+ within Canadian and Kenyan programs. We describe similarities and differences between CL coping supports in these countries, and impact of psychosocial supports on quality of life, clinical outcome and service delivery.

Design/Methods: Through 8 years of annual CL training in Kenya, and constant mentoring, we integrated culturally appropriate patient supports into daily practice. Comparison of CL supports in Kenya and Canada is gathered from case studies documented in daily practice logs.

Results: CL supports are unique to the child’s needs no matter where they occur in the world. There are similarities and differences in delivery across Canadian and Kenyan cultures. In both countries, patient coping and overall healthcare experience is enhanced. Canadian, patients are primarily infants (0-2yrs). Developmentally appropriate CL supports include sensory activities, infant massage, parent education and positions for comfort. Survival is above 98% in this group. While age at diagnosis is decreasing in Kenya due to awareness campaigns, most patients are over 24 months. CL supports are adjusted for older children and include more medical play, preparation for procedures and parent education. Survival is improving, but remains comparatively low, primarily due to delayed diagnosis and treatment. In both countries, supported children heal faster, are discharged sooner, require less sedation and fewer nurses to complete procedures, and manage pain with less medication.

Conclusion: CL supports vary based on age, stage of development, disease progression, treatment and the child’s needs. CL strategies enhance the child’s well-being and support effective application of limited resources. Integrating CL supports can improve service delivery and quality of life for children with cancer in diverse healthcare settings globally.

P-0673 | Relationship between Personal and Social Resources to Quality of Life, Distress and Future Orientation: Comparison between Jewish and Arabic Mothers of Children Diagnosed with Cancer

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Background/Objectives: The study attempts to assess the stressful situation, and the adaptation of Jewish and Arabic mothers of paediatric cancer patients. It investigates the contribution of mastery and social support as personal and social resources of these mothers, respectively, to the appraisal of the stressful event, the child’s illness, while evaluating how these factors affect their quality of life, feelings of distress and future orientation.

The hypotheses of the study were: 1. Jewish mothers would report a higher level of mastery than Arabic mothers 2. Jewish mothers would report a lower level of social support than Arabic mothers. 3. Mothers with higher levels of personal and social resources would experience less distress, higher quality of life, and less concerns about the future.

Design/Methods: The sample was composed of 197 mothers, 97 Jewish and 100 Arab. The participant mothers had a child under 18 who was going through active treatment. The mothers answered the following questionnaires: demographic data, sense of Mastery, Social Support, Brief Symptom Inventory to assess distress, Quality of Life, and Future Orientation.

Results: It was found that Jewish mothers had more social support than Arab mothers and similar levels of mastery. The findings of the path analysis showed that the more resources that were available, the higher quality of life and the more hope for the future and the lower the distress level and fear from the future.

Conclusion: The findings contribute to the body of knowledge in the field of parents coping with their child's cancer. They can also be used in the investigation of cultural differences in coping with paediatric oncology patients.

It seems important to have intervention programs that help mothers develop personal and social resources that will enable them to cope more efficiently with crisis situations.

P-0674 | The Costs Experienced by Caregivers of Children Being Treated for Cancer in New Delhi, India

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Background/Objectives: The allocation of time and other resources is essential to enable the treatment of children with cancer. Existing research from high income countries indicate that families incur significant variable costs impacting their finances and lifestyle substantially. However, there is no research examining the costs of childhood cancer from families in India, which may impact families' decision to abandon their child's treatment.

Design/Methods: A qualitative descriptive study was carried out in one private and one government-run hospital in New Delhi. Semi-structured interviews were conducted with caregivers of children with cancer in English or Hindi. Interviews were transcribed verbatim, translated into English, and analyzed using a thematic approach.

Results: In total, 26 caregivers of 25 children diagnosed with cancer participated in the study. Caregivers described various direct, indirect and psychosocial costs associated with their child's cancer treatment. The primary sources of direct costs were hospital admissions, medications, food and travel expenses. Indirect or time costs involved managing their child's treatment and its side effects. Work hours, time spent with other family members and sleep were most affected by this commitment to caring for their child. Psychosocial costs included coping with the uncertainty caused by a cancer diagnosis, feelings of guilt and sadness as well as having to watch their children suffer. Family members, healthcare professionals, other caregivers and employers were named as sources of support for families. Cutting back on routine expenses and negotiating treatment options were described as strategies for coping with the financial burden of treatment. No families abandoned treatment or indicated that they intended to do so.

Conclusion: The results of this study provide avenues for healthcare professionals and institutions to develop interventions aimed at reducing the costs associated with cancer treatment. Further research into the relationship between direct, indirect and psychosocial costs and treatment abandonment is needed.

P-0675 | Traditional and Complementary Medicine Therapies used with Curative Intent in Childhood Cancer: A Systematic Review

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Background/Objectives: Traditional and complementary medicine (T&CM) therapies are frequently used in paediatric oncology worldwide. There is no published systematic review evaluating the effectiveness of curative T&CM therapies in paediatric oncology. The current review aims to systematically identify studies that have examined the impact of T&CM strategies used with a curative intent on mortality and morbidity.

Design/Methods: MEDLINE, AMED, EMBASE, Global Health, PsychInfo, CINAHL, CDSR and ProceedingsFirst were searched from date of database inception through to February 20, 2016. Records identified were screened for inclusion by two authors. Inclusion criteria were studies involving patients <18 years of age with cancer, in which T&CM strategies were used with curative intent. Articles were excluded if no paediatric-specific outcomes were reported, or authors used non-human or ex vivo paradigms. There was no limit by language or study type. Two reviewers abstracted data using a predetermined, piloted form.

Results: A total of 3,755 articles were screened for inclusion. Eighty-five full text articles were reviewed and 34 studies met inclusion criteria. Most studies were case reports or case series (N=17). Leukaemia/lymphoma was the most commonly evaluated disease type (n=20). Traditional Chinese Medicine was the most frequent treatment modality, utilized in 12 studies. Data were reported from nine different countries, the most common being China (N=15), Germany (N=6) and the United States of America (N=6). Fifteen studies (44%) were in English; other languages included German, Danish, and Mandarin. Outcomes were inconsistently reported across studies.

Conclusion: T&CM strategies are commonly used with curative intent in paediatric oncology. There is limited published data to support their use. The majority of published studies are not

reported in English. International collaboration will strengthen our understanding of the utility of these strategies.

P-0676 | Assessing Public Opinion of Abandonment of Conventional Treatment for Traditional and Complementary Medicine in Paediatric Oncology: Methodology of a Grey Literature Review

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Background/Objectives: Abandonment of conventional cancer therapy for children in high-income countries is rare. These cases often involve child protection authorities and legal proceedings. Patient confidentiality typically precludes publication in the academic literature, but these cases are often heavily covered in the news media. The objective of this study is to develop a protocol to examine the content and tonality of reports of children abandoning conventional cancer treatment for traditional and complementary medicine therapies (T&CM).

Design/Methods: The media database Lexis Nexis Academic will be searched for cases of children abandoning conventional cancer therapy for T&CM since 2002. Inclusion criteria will comprise children <18 with any cancer, who attempted to abandon or successfully abandoned treatment deemed lifesaving or essential by the treating team, for any T&CM. Exclusion criteria will include adult patients, non-oncologic diagnoses, and non-life saving, palliative-focused or non-essential treatments. Once cases have been identified, a second iteration search will be executed using Google News Archive to encapsulate all published news and magazine articles.

Results: Analysis of cases will examine both the outcome of all identified cases and the tone of each reported article. Tone will be assessed by a qualitative analysis by two reviewers who will ascribe the terms "positive", "neutral" or "negative" to each article. A subsequent analysis will use sentiment mining to apply a numerical score to the tone of each article. A subset of articles will be analyzed from a grounded theory perspective to identify common themes among cases.

Conclusion: News media reports of cases of conventional childhood cancer therapy abandonment for T&CM strategies provide case descriptions, and an understanding of the breadth of concerns held by the general public. A novel approach to the analysis of media reports will assist healthcare providers in counselling patients on T&CM therapies and provide context for these important discussions.

P-0677 | Young People with Cancer Peer-To-Peer Support Intervention: Process Evaluation of a Two Day Residential Conference

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Background/Objectives: When diagnosed with cancer, young people experience psychosocial effects that can include isolation, poor peer relations, anxiety and depression. Following treatment these can remain and be accompanied by fear of recurrence, increasing the risk of reduced psychological wellbeing and health post-treatment. "Find Your Sense of Tumour (FYSOT)", is a two day residential conference which brings together young people with cancer (13 to 25 years old) for educational presentations, peer-to-peer support and social activities. The conference is split into an under 18s and over 18s event. This paper aims to explore the outcomes and processes related to participating in FYSOT.

Design/Methods: Participant observation of activities and participants during the over 18's conference followed by semi-structured interviews (n=25) with professionals attending FYSOT and steering committee members were conducted. Key themes and concepts were identified using framework analysis.

Results: The outcomes identified for young people participating in FYSOT included: increase positive attitudes (including increased sociability, confidence), feeling they were not alone (including feeling accepted, understood), recreation (including balance between having fun and talking about their concerns); and increased knowledge (including the educational talks and interactions with other young people). Processes that facilitated these outcomes were organized in three levels: the conference/intentional programming (including a culture of acceptance, openness and fun; spatial and social proximity to others); the support and guidance from professionals accompanying young people (including discussions with young people about their concerns); and being with other young people (including developing friendships, sharing experiences and learning coping strategies).

Conclusion: This in-depth process evaluation identified key mechanisms and outcomes of the conference. Being in a safe, relaxed and fun environment with other young people facilitates the development of peer support networks, and increases young people's confidence and knowledge. This is informing a longitudinal quantitative evaluation.

P-0678 | Making Psychosocial and Peer Support Accessible: An Evaluation of the Canteen Online Support Service for Young People Living with Cancer

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Background/Objectives: Young people (12-24 years) impacted by their own or a family member's cancer experience significant distress and psychosocial unmet needs and have reduced capacity to seek support. Cancer can also be a profoundly isolating experience at this life stage and needs for peer-support are high. The CanTeen Online Support Service (COSS) was developed to provide young people living with cancer (YPLWC) with greater accessibility to age-appropriate information and resources, peer support and access to online and phone-based

counselling. We sought to describe COSS user activity, identify drivers of activity and explore the psychosocial impact of participating in COSS.

Design/Methods: Analysis of site activity (April 2014–December 2015), satisfaction and drivers of activity was undertaken. Measures of distress and unmet needs completed by 404 COSS users across Australia prior to and after joining COSS were descriptively analysed.

Results: COSS had 898 registered users, primarily offspring whose parent has/had cancer (39.5%). Service usage appeared related to external events, with rates of forum posts, blogging & shared personal stories noticeably increasing following, for example, a media awareness campaign (July 2015). Users rated ease of use and helpfulness very high (81.0–85.7%) and 90% indicated they would use the service again. After using the service, the proportion of patients, survivors, siblings, offspring and bereaved siblings and offspring with high or very high levels of distress decreased by between 6.1% and 17.2% and levels of unmet need decreased by between 8.2% and 15.4%.

Conclusion: COSS provides engaging, self-directed information, peer-support and professional counselling to YPLWC, increasing their opportunities for accessing age-appropriate, evidence-based assistance. The growing client-base of registered COSS users and reductions in distress and unmet psychosocial needs evident in those surveyed suggest this is an effective service. Evidence that service usage was driven by external events will inform future decisions regarding staff resourcing and promotion.

P-0679 | AlphaBeatCancer: The Alphabet Against Cancer

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Background/Objectives: AlphaBeatCancer is an educational game about cancer and treatment designed to serve as a tool for learning for children diagnosed with the disease. The project's main goal is to provide information through challenge and recreation, using the principles of information technology through design, usability, gamification and user experience.

Design/Methods: The content of the game came from *Beabook* - an educational booklet consisting of oncologic terms from A to Z - compiled by patients, caregivers, physicians and health professionals. All the material was based on information architecture and design, making use of accessible language, appropriate illustrations and optimistic texts.

The game uses linear narrative, presenting and following the path of treatment: symptoms, diagnosis and the treatment itself, counting on logical support of time, space and characters. After participating in each phase, terms are *unlocked*, becoming accessible in a glossary, which can be consulted at any time.

At the same time the users takes over the patient, they also control procedures such as biopsies, application of radiotherapy and patient care in order to encourage identification with the character and his own treatment, reducing passivity and encouraging control over the situation.

Results: AlphaBeatCancer is being implemented and it is in the process of collecting data of theoretical approaches. However, we can already point out the great enthusiasm of patients, caregivers and health professionals who participated in the development and are following the project. The first results will be available in September 2016.

Conclusion: With so many portable entertainment options today, the attention of children becomes highly disputed, especially when you need to talk about something that maybe they do not want to hear.

We believe providing information in a fun matter, we will be able to educate, empower and, mainly, show children and young adults how to improve their quality of life while dealing with such "grown up" disease.

P-0680 | First Counselling of Childhood Cancer Diagnosis: The Indian Perspective

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Background/Objectives: "...sympathy and understanding may outweigh the surgeon's knife or the chemist's drug"

- Hippocratic Oath

Breaking the bad news is the most uncomfortable yet inevitable duty of a paediatric oncologist. Though there are a few articles on the recommendations for breaking bad news, the quality of communication is solely determined by the listener. Due to workload and lack of time, not many physicians dedicate time for this daunting task. In a multiethnic society like India's, cross-cultural communication pose difficulties to paediatricians and oncologists in conveying bad news.

Design/Methods: The families of 50 children who were recently diagnosed with cancer at Sri Ramachandra Medical University, Chennai, were interviewed with a validated questionnaire, about the quality of the initial counselling on diagnosis of cancer.

Results: All of them preferred a dedicated counselling room and a repeat counselling. Ninety-three percent of families wanted a numerical value for the prognosis and 83% wanted to compare the status of their child with a similar child. Sixty-nine percent did not want their child's school administration to know about their child's condition while 66% wanted their primary physician to be informed. Eighty-two percent wanted to know about treatment facilities available at other centers. A large number (94%) were able to recollect the words of support and confidence given at the time of counselling. The majority of the families did not want to reveal the diagnosis to their children.

Conclusion: First counselling influences the family's decision on further planning, either pursuing treatment or abandonment. Patients and their families have a right to compassionate

counselling and the responsibility falls on the primary oncologist to balance the physiological basis and treatment of the disease with the psychosocial side of medicine while counselling the family on childhood cancer diagnosis.

P-0681 | A Randomised Controlled Trial to Examine the Effectiveness of Reflexology for Reducing Symptoms in Children/Adolescents with Cancer

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Background/Objectives: Children and adolescents with cancer are at risk of experiencing distress as a result of necessary but uncomfortable procedures, the cancer diagnosis and cancer treatment (Woodgate & McClement, 1998).

Reflexology is a form of massage which is usually applied to the hands and/or feet in order to bring about a state of relaxation. Research in adults with cancer suggests some beneficial effects of reflexology on symptoms, particularly breathlessness, fatigue, anxiety and pain (Wilkinson *et al.*, 2008). No such studies have been carried out in children/adolescents with cancer.

The purpose of this study is to examine the effectiveness of reflexology for reducing symptoms (primarily distress levels) in children/adolescents with cancer aged between 8 and 16 years of age. An exploration of the child/adolescent's experience of the intervention (reflexology treatments/sham reflexology) and of their parents/guardian's will also be undertaken.

Design/Methods: A prospective, single centre, randomised controlled trial (RCT) study using a mixed between group repeated measures (2 Group x 8 Time) design (based on CONSORT principles) will be conducted. All eligible children and adolescents receiving cancer treatment at a national paediatric hospital and their parents/guardians will be invited to join the study. A sample size of 80 (with a ratio of 1:1; 40 in the intervention group and 40 in the control group) is determined as appropriate to detect a change in number of symptoms between the intervention and control group following completion of the intervention. However, to allow for an attrition rate of 20%, 96 children/adolescents will be recruited over an 18 month period. Data on the acceptability and satisfaction with the intervention will be obtained through a series of interviews with the children/adolescents and their parents/guardians. Ethical approval for this research has been received.

Results: Pending.

Conclusion: This study will provide empirical data regarding the impact of reflexology in a paediatric oncology context.

P-0682 | There's A Worm in Your Head: Illness Metaphor and Working with Families Around the Psychosocial Aspects of a Paediatric Cancer Diagnosis

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Background/Objectives: The diagnosis of cancer in a paediatric patient is inherently difficult and challenging to patients and to their families. Medical teams often struggle to adequately support families as they respond to a diagnosis of paediatric malignancy. We set out to explore methods of fostering effective communication around these issues.

Design/Methods: Based on a review of child psychiatry consult cases within the paediatric oncology service at the Hospital Fundación Santa Fe de Bogotá, in Bogotá, Colombia, this project describes some of the culturally sensitive ways that the mental health provider may effectively liaison between patients, their families, and other paediatric specialties in supporting patients and their families through serious health events.

Results: In addition to adapting to the implications of diagnosis and treatment, families often struggle to find ways of disclosing diagnosis and treatment to the child. These methods should be age-appropriate and help the patient to understand some aspects of what is happening to him or her. The role of the paediatric mental health teams in these situations can go beyond reacting to psychological crisis as they arise, and should include proactively assist patients and their families in finding a developmentally-appropriate language to allow for discussion of diagnosis, treatment, prognosis, and the emotions which surround each of these complexities.

Conclusion: While news of a paediatric cancer can be devastating to patients and their families, there are ways in which the healthcare team can effectively foster communication and improve emotional outcomes, by both fostering a developmentally appropriate level of patient autonomy and by giving patients and their families the tools to emotionally adapt to adverse events.

P-0683 | Evaluating 'Peer': A New Residential Camp Program for Youth Living with Cancer

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Background/Objectives: Cancer can significantly impact the lives of young people. Therapeutic camp programs which provide a supportive peer environment, opportunity for psychosocial support and skill development, and time-out from daily stresses, are effective interventions for youth (12-24 years) living with cancer. This study reports on the development, implementation and outcomes of a therapeutic camp program aimed at enhancing the resiliency and wellbeing of youth living with their own or a family members' cancer diagnosis, or the death of family member from cancer.

Design/Methods: Reviews of: oncology and chronic illness therapeutic camps literature and evidenced-based psychosocial youth manualised programs, an audit of program documentation and consultations with experts in youth development informed the development of a manualised residential 4-day camp program. Program fidelity was ensured through training,

measuring youth engagement, and recording activities completed. The program was piloted using validated and program-specific measures. Quality of supportive peer relationships, coping (active, emotional, instrumental, planning), sense of belonging, self-kindness, and quality of life were measured at three time points (prior, post and two months follow-up). Feedback on facilitators' and participants' experiences was captured.

Results: Eighty-one youth participated in the pilots (age M=16.1 years, SD=2.6; 45.7% male). Significant findings were found for supportive relationships, emotional coping, instrumental coping, planning coping, sense of belonging, self-judgement, and satisfied with life. Facilitator and participant feedback was very positive; 99% of participants would recommend the program. Youth engagement was high (M range = 7.1-9.0; 0-10 scale).

Conclusion: The current results highlight the benefits of the PEER program for youth living with cancer regardless of their cancer experience. Along with plans to roll-out the program nationally in Australia, consideration will need to be given to sustaining the beneficial impacts of the program in the longer term.

P-0684 | Audit of Psychosocial Problems Faced by Childhood Cancer Survivors

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Background/Objectives: After Completion of Therapy (ACT) Clinic for childhood cancer survivors (CCS) (>2yrs after cessation of Rx & disease free) was started at Tata Memorial Hospital (TMH) in 1991 to improve the standard of care of survivors by regular risk based follow up by multidisciplinary team. Medical, physical & psychosocial aspects are covered through this comprehensive care.

Gunvati J Kapoor (GJK) Medical Relief Charitable Foundation a partner NGO of TMH. GJK foundation provides para medical support staff in various departments of TMH with the aim to help improve the QOL of patients on treatment & post treatment. The main objective of working in ACT clinic is to identify problems & provide motivational counselling.

The Present Study was undertaken by GJK foundation to understand the problems faced by CCS in relation to age.

Design/Methods: The data collection is through structured interview by Medical Social Worker of GJK foundation with the survivors in ACT clinic from Jan 2015- December 2015. A total of 590 survivors were seen at ACT clinic of which participants are 160(27%) across age group of 11-40yrs.

Results: Of 160 survivors, 116(72%) are male & 44(28%) females with median age 27yrs. The most common problems reported by entire cohort are fear of relapse (23.13%), body image issue (9.37%), stress, anger, anxiety (7.5%), cancer as stigma (7.5%).

In age group 11-20 yrs, 26.25% had problems with education. 23.75% in age group 20-30 yrs had difficulty in making career decisions. 2.5% in age group 30-40 feel dejected finding life partner &/or child bearing.

Conclusion: The problems that are identified in the survivors are age related and reflect priorities in life at that juncture. However, fear of relapse is uniformly present in all age group. It is very important to provide ongoing psychosocial support and the platform where the survivors can share their problems, fears to decipher the stress & improve quality of life.

P-0685 | What is Stressful about Childhood Cancer? Stressful Events Reported by Children with Cancer and Their Healthy Peers

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Background/Objectives: Although traumatic stress models have been widely used to examine adjustment to childhood cancer, recent research demonstrates that the diagnosis of childhood cancer is not associated with elevations in posttraumatic stress, and that many children do not identify cancer as their most stressful life event. Research is needed to understand what is stressful in the lives of children with cancer, including both cancer-related and non-cancer-related events.

Design/Methods: Children with cancer (N=254) and demographically matched healthy peers (N=211) completed a structured diagnostic interview for posttraumatic stress disorder (PTSD). As part of this interview, children spontaneously identified what they considered their most stressful or traumatic event (without orientation to cancer) and their responses to it. These responses were examined qualitatively using structured Q-sort and thematic analysis to generate broad categories of stressful events.

Results: About half (54%) of patients identified a cancer-related stressor as their most stressful life-event. A subset (15%) described the overall cancer experience, but others pointed to specific elements, which could be reliably categorized into 6 broad content areas: diagnosis; acute effects of treatment; family/social impacts; pre-diagnostic stressors; late effects; and death-related concerns. In the subset of patients (46%) who identified non-cancer events and the healthy comparison group, the non-cancer events were reliably categorized into 10 content areas, and ranged from severe (sexual abuse; death of parent) to relatively minor (changing schools) events. These events were generally reported in similar frequencies in both groups.

Conclusion: Overall, a portrait emerges of cancer as a stressful, but not necessarily traumatic life-event for children and adolescents. Aspects of the cancer experience that youth find stressful are variable and range from the specific (hair loss) to the broad (death, impact on the family). Findings are discussed in relation to the changing A-criteria requirements for PTSD in the DSM-V.

P-0686 | Hope for Parents of Children with Cancer - Development and Evaluation of a Group-Based and Web-Based Self-Management Intervention for Parents of Children with Cancer

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Background/Objectives: Every day in the UK 10 children are diagnosed with cancer. Parents of children with cancer often face despair, grief, shock, isolation and long term financial and psychological consequences following diagnosis. There is a need to provide parents and caregivers with a specialised support intervention to help them address these challenges. Interventions aimed at similar population groups, such as parents of children with autism have shown positive outcomes, providing parents with the skills, and resilience to support a positive environment for the family. The aim of this project is to develop and evaluate a group-based (HOPE) and web-based (iHOPE) self-management programme to meet the psychosocial needs of parents of children with cancer.

Design/Methods: A co-creation workshop will be conducted with stakeholders (parents, clinicians, and charity representatives) from the Coventry and Warwickshire area. The findings will be used to develop tailored content for the HOPE and iHOPE self-management interventions. A mixed methods design will evaluate the interventions for their acceptability and usefulness. Parents will complete outcome measures (e.g. depression, anxiety, resilience) before, immediately, and 3 months attending the intervention tests will be conducted on all outcome variables to determine whether any differences between the time points are statistically significant. A sub-sample of parents will be interviewed about their experiences of participating in the interventions. Interviews will be analysed using thematic analysis.

Results: The co-creation workshop is planned for April 2016 and the group-based HOPE and iHOPE web-based interventions will be delivered between May and August 2016. We plan to present the mixed methods results at the conference.

Conclusion: Parents of children with childhood cancer experience high levels of anxiety, stress, despair and isolation and currently receive little support. We plan to involve parents to co-create and to develop an acceptable and useful group-based and web-based intervention to meet their psychosocial needs.

P-0687 | Treatment Decision Making for Young People with Cancer and Their Parents

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Background/Objectives: Families of children diagnosed with cancer are faced with difficult treatment decisions, including radiation therapy, fertility preservation, and enrolling in research studies. Many patients and parents find it difficult to understand the rationale and implications of treatment options. They may also be at risk of experiencing decisional anxiety and conflict, uncertainty, and distress. The aim of this study is to qualitatively explore the decision making process of parents and young people when faced with a treatment decision, including the decision making process for participating in psychosocial research, and clinical trials.

Design/Methods: Adolescents and young adults (AYAs) (n=20), and parents of children (n=20), diagnosed with cancer within the past 3-12 months will complete a semi-structured interview. The interview will ask about aspects of treatment that families found easy or difficult to comprehend, information modality preferences, their decision making process, and about enrolling in psychosocial research and clinical trials (via a hypothetical scenario if they were not offered participation in either). Interviews will also explore decisional anxiety and conflict associated with medical treatment decision making. Interviews will be audio-recorded and transcribed verbatim. Emergent themes will be examined using Miles and Huberman's framework.

Results: This study is currently recruiting. Interview data and thematic analysis will be presented at SIOP 2016.

Conclusion: These findings will help to develop a resource to assist families when considering various treatment options. This study will also provide further understanding of an under researched area regarding parents and AYAs decision making processes, and their involvement in treatment decisions.

P-0688 | Risk for Prescription of Psychotropic Drugs among Parents of Childhood Cancer Patients: A Danish Population-Based Cohort Study

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Background/Objectives: Each year, 200 children are diagnosed with cancer in Denmark. Cross sectional studies have shown that experiencing cancer in a child may cause severe psychological distress. Knowledge about the impact on parents using objective measures, however, is lacking. The aim of this study is to investigate the risk for prescription of psychotropic drugs including antidepressants, anxiolytics and hypnotics as an indicator of psychological stress among parents of children with cancer.

Design/Methods: In a nationwide register-based study, we will include all parents to children diagnosed with cancer below the age of 18 years between 1995 and 2014, excluding those with previous use of psychotropic drugs. For each patient, ten cancer-free children matched by sex and age will be identified and their parents will be included as a comparison group. Using Cox proportional hazard models, hazard ratios for first prescription of antidepressants, anxiolytics and hypnotics in the parents will be estimated according to the child's cancer status. In sub-analyses including only parents of children with cancer, associations between disease characteristics, sociodemographic factors and risk for prescription of psychotropic drugs will be examined.

Results: We expect to be able to estimate the risk of having psychotropic drugs prescribed in approximately 7600 parents of children diagnosed with cancer compared with 76,000 parents of cancer-free children. Preliminary results on the risk of parental use of psychotropic drugs after cancer in a child will be presented.

Conclusion: If parents of childhood cancer patients have an increased risk of psychotropic drug use, this will be important knowledge for health care professionals, which has to be taken into account in the care and support trajectory. If we identify vulnerable sub-groups of parents, this knowledge will help to identify the families that are in high risk in order to offer appropriate psychosocial support tailored to their needs.

P-0689 | Medical and Emotional Issues of Transition in Paediatric Oncology: What do Paediatricians Say about Them?

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Background/Objectives: While treatment protocols and monitoring are highly structured, time of the transition to medical care in adulthood appears much less supervised and occurs often late. The separation between the young patient, treated for childhood cancer, and "his" or "her" paediatrician is rarely simple.

This qualitative study, addressed to paediatricians, aims to better understand the specific medical and emotional issues about transition in paediatric oncology.

Design/Methods: Eighteen semi-structured interviews with most of the paediatricians from paediatric oncology centres in Paris area have been conducted and then transcribed and analysed anonymously.

A traditional thematic analysis was conducted to identify common issues around this significant time of transition. We also used the Edicode instrument, which analyses the shaping of subjective experiences across the organization of the speech. This methodological choice proceeds from theoretical models of Attachment and Narrativity, particularly relevant here.

Results: Eleven women and seven men participated. Interviews generally lasted from 30 to 60 minutes.

Many issues seem to influence the transition process like the paediatricians' representations of the disease and its after-effects on the body, the altered perceptions of temporality after the shared experience of life-threatening illness and finally the difficulties faced by paediatricians to describe the relationship that binds them to these young people and to plan the separation.

Thus how to let the adolescents' processes emerge and therefore how to better anticipate the splitting with paediatrics and the transition to adult medicine?

Conclusion: The transition forces doctor and patient into measuring together the cost of the cure, especially through the late effects of cancer treatments. Certain ideals at work within the paediatric vocation are also highlighted at that time. Finally, in these particular wards, disappearances related to the deaths of children and adolescents must be also considered as they influence, for the paediatricians, the separations linked to the transition of young patients towards the adult medicine.

P-0690 | Cankids Parent Support Group – A Model of Empowerment, Livelihood and Reintegration

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Background/Objectives: In developing countries where resources are scarce, a well trained and empowered Parent Support Group member-PSG can become an effective patient navigator and advocate, provide emotional support to families and serve as a health worker as well.

The Cankids Parent Support Group model encourages parents of survivors or those who have lost their children to cancer to become Full time, Periodic or Voice members, trains and empowers them, teaches them to be patient navigators in the very hospital where their own child was treated. They are able to guide and inform a new family. The more literate Parent member learns to administer the YANA-You are Not Alone program as the first bridge building interaction with the family of the newly diagnosed child.

Design/Methods: Every new family is assigned a PSG member under the YANA Hold my Hand program to be with the family through the cancer journey, to help prevent abandonment and for follow up. They are taught the basic principles of emotional support and to identify who may need psychological intervention. They voice their feelings through the PSG Forums and Sharing Caring sessions and advocate for their rights. PSG members are reimbursed expenses through stipends, based also on number of days committed each month and years of volunteering. The aim is to have at least 3 trained Parent Support group members in each Cankids Hospital Support Unit.

Results: Over 12 years the Cankids PSG has grown from 2 members to 183 members across the 44 cancer centers. Since then they have become a vital member of every Social Support Team in the treating Centers.

Conclusion: As the Parent Support Group members learn and gain experience and confidence they become eligible for employment, both within the organization and potentially in other similar support organizations. This becomes a source of livelihood for many.

P-0691 | A Comparative Study on the Level of Anxiety of Paediatric Haematology and Oncology Patients with & Without Exposure to A Hospital-Based Child Life Program

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Background/Objectives: Children with chronic illnesses face numerous long-term visits to hospitals and are at a greater risk of developing mental health or social adjustment problems (Clark, 2003). Hospital-based child life programs are often present to focus on the psychosocial, emotional, and developmental needs of children, providing developmentally appropriate interventions that minimize the stress and anxiety experienced, assuring optimal growth and development. This study aims to compare the levels of anxiety of forty children diagnosed with hematologic and oncologic illnesses who received routine, standard care and with exposure to the services of a hospital-based child life program for at least six months against those of forty children of the same age range with hematologic and oncologic illnesses who received only routine, standard care.

Design/Methods: This quantitative, quasi-experimental study employing a posttest only group design used purposive sampling to select eighty paediatric patients, ages six – eleven years old, with hematologic and oncologic illnesses, assigned to either the control or experimental group. Informed consent and assent were given. Child Drawing: Hospital (Clatworthy, 1999), a validated and reliable tool used to provide a measure of the anxiety level of the child as expressed by the child himself. Independent t-test was used to analyze the data. After the gathering of data, children from the control group were provided with therapeutic play activities, as well.

Results: Results show a *significant difference* on the levels of anxiety between the two groups. Children who have access to hospital-based child life services experienced significantly lower levels of anxiety as compared to their counterparts who did not.

Conclusion: The results support the value of hospital-based child life services and, as such, should be considered an integral part of quality paediatric health care and essential in family-centered care and best-practice models of health care delivery for children.

P-0692 | The Development, Implementation and Evaluation of a Holistic Needs Assessment Tool for Children with Cancer and Their Families

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Background/Objectives: Cancer in childhood has social, practical and emotional consequences in addition to the effects on the child's physical health. In the UK, guidelines state that keyworkers (who are usually Specialist Nurses) should assess and document these needs, and address them through multi-disciplinary working and signposting. Patients' key concerns can be assessed through a Holistic Needs Assessment (HNA). To date, the HNA tools used in cancer services are adult-focused and tailored to individuals. There was a need to design a child-focused tool that recognises parents' and siblings' needs, and to provide training to nurses using the tool. A pilot project was undertaken at Great Ormond Street Hospital to meet this need.

Design/Methods: A child-focused Holistic Needs Assessment tool was developed. Specialist cancer nurses were given a tailor-made training course to introduce them to the tool, enhance their communication skills, and practice using the tool in vignettes with actors. They then piloted the use of the tool with recently diagnosed children and their families. The tool was evaluated through interviews with 15 families about their experience of having HNAs carried out.

Results: Qualitative analysis of interview data found that families value the process of HNAs as well as the resulting actions. It is important to families that these are carried out by someone they know well and not as a "one-off" exercise.

Conclusion: Training specialist nurses to carry out Holistic Needs Assessments can equip the service to better identify and meet the emotional and social needs of children with cancer. The role of keyworkers in addressing families' holistic needs, and the structure that supports these being meaningful conversations, must be better recognised by the wider organisation.

P-0693 | Support Group - Initiative: A Ray of Hope and the Magic Wand of Perseverance

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Background/Objectives: Diagnosis of a child with cancer is a life changing event for parents. Parents are left to deal with numerous difficult issues like opting for or out of treatment, financial implications, social disconnect and sibling negligence. Support Group sessions help such families to interact with each other and cancer survivors, exchange notes, gain confidence and hope to continue this difficult journey.

Design/Methods: A Support group meet was organised by our unit for families of cancer-children on treatment and cancer-survivors. The agenda included sharing of experiences and success stories, talk by the Unit Head, a Nutritionist, a Psychiatrist and an art-therapy session with the Psychology team. This was followed, a month later, by a one-to-one discussion with one parent of children on-treatment regarding any change in their perspective about coping with diagnosis, management, psychosocial and financial issues.

Results: 40 families (families of survivors-17, families of patients on-treatment-23) attended the meet. The succeeding interview (a month later) revealed that the aspects on which they benefitted were: motivation to continue treatment-23/23, relief of stress by having a talk with psychiatrist-17/23, avenues to overcome caregiver-fatigue by speaking to survivors and other families-23/23, improvement in dietary habits of cancer-children by bringing innovations in the limited food options-15/23; alleviation of child's fear of hospital visits-20/23.

Conclusion: Support Group initiative opens avenues where families can interact among themselves and also the cancer-survivors, gain insight into possible ways to deal with psychosocial

stress and imbibe motivation to continue the battle to cure. Art therapy sessions remove the fear of hospitals and make it a fun place to be in for the patients themselves.

P-0694 | Social Support and School Engagement of Young Survivors of Acute Lymphoblastic Leukemia

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Background/Objectives: The purpose of this study was to further understand how social support facilitates the psychosocial adaptation of young survivors of acute lymphoblastic leukaemia (ALL) in the area of their lives in which they invest themselves most once cured: school. Specifically, it aimed to describe and explore the influence of social support on school engagement of young ALL survivors.

Design/Methods: Fifty-three young survivors of ALL (7 to 17 years) completed a measure of school engagement and a qualitative interview focusing on the support offered by four groups of relations associated to school: parents, siblings, friends, and other non-professional relations. Classical content analysis was used to code interview responses and describe the perceptions that survivors have of the types of social support they receive with regard to school. Correlations examined if there was a significant association between the number of groups of relations whose support was perceived and school engagement scores. Analyses of variance evaluated if the presence/absence of support perceived from each group of relations predicted school engagement scores.

Results: Parents were perceived to be the primary source of informational and emotional support, with support also provided to a lesser extent by friends, siblings, and extended family. Inferential analyses indicated that survivors report higher school engagement scores when support is perceived from a greater number of groups of relations, especially from friends or siblings.

Conclusion: These findings encourage adopting a bio-ecological perspective (Bronfenbrenner, 1979, 2001) to support young ALL survivors' school engagement by recognizing and accompanying their various groups of close relations. While this perspective agrees with existing recommendations from key programs and orientations related to school interventions aimed at young cancer survivors, these results also highlight the importance of broadening the sources of support to be considered as intervention partners in both short and long term after cancer treatment.

P-0695 | AYA Cancer Survivors Narrate Their Stories: Predictive Model of Their Personal Growth and Their Follow-up Acceptance

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Background/Objectives: In the last years, the number of childhood cancer survivors that has become adolescents or young adults has fortunately increased. Attention has been paid to the identification of the adverse effects of cancer treatment and a few studies captured the unique ways in which cancer promotes the growth and development of adolescents and young adults (AYA) cancer survivors. The aim of this study is to assess their quality of daily life, post traumatic growth and follow-up perceptions adopting a narrative approach.

Design/Methods: Participants consists in 100 north-east Italian AYA cancer survivors, mean age at diagnosis of 9.26 years old (SD=4.29), 51 treated for haematologic disease and 49 for solid tumours, off therapy from a mean of 8.19 years (SD=2.62). A new version of in-depth interview EFI-C (Tremolada et al., 2013) took place in the DH of the Onco-haematology clinic during their medical controls.

Results: The EFI - version AYA cancer survivors - resulted psychometrically reliable and solid with the extraction of 12 good internal consistency general dimensions from 102 items. Post-traumatic growth was predicted directly by age at the assessment and, indirectly, by the mediation of the following factors: Hospitalization memories and narrating capacities and by Relationship with the hospital staff during the illness; Positive well-being towards follow-up visits was predicted by the relationship with the health staff during the illness (Chi-Square=2.87; df=3, p-value=0.41; RMSEA=0.0001).

Conclusion: Older childhood cancer survivors that established a strong relationship with health professionals at the clinic have a better capacity to narrate their stories, a positive comprehension of their illness experience and accept the follow-ups. The narrative technique allows AYA cancer survivors to reorganize and give a frame to their traumatic experience.

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P-0696 | Factors Contributing to Mental Health and Quality of Life among Adolescents Who Lost A Sibling to Cancer

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Background/Objectives: The aim of the study is to investigate mental health and quality of life among adolescents who lost a sibling to cancer. The study will emphasize health promoting factors where the focus will be to explore and describe the impact bereavement has on adolescent siblings. In order to do so the study will assess adolescents resilience, quality of life, and mental health, as well as their perception of social support from family members and professionals, both in health care and in the school environment.

Design/Methods: A cross-sectional Norwegian nationwide study, which will include approximately 300 brothers and sisters, aged 17-22 years, who lost a sibling between the years 2009-2014. This study also include a control group. The Resilience scale for adolescents, The Pediatric Quality of Life Inventory (PedsQL), and a study-specific questionnaire will be used to assess brothers and sisters resilience, quality of life, as well as their mental health. Interviews with 12 participants will first be conducted as a face-to-face validation of the study-specific questionnaire.

Results: Will be gathered through the standardized questionnaires as well as the pilot study.

Conclusion: The anticipated findings of the study will focus on the areas where interventions can be established for bereaved brothers and sisters to promote good mental health and quality of life, as well as to prevent psychological problems.

P-0697 | Psychological Functioning of Preschool-Aged Children with Cancer

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Background/Objectives: The majority of children with cancer are diagnosed in early childhood, with the most common diagnoses— brain tumors, leukaemia – associated with increased risk for the development of psychological late effects. Developmental psychologists cite the early childhood years (≤6 years) as critical to later development. During this time, children achieve milestones in a number of domains – physical, social-emotional, motor, speech/language, problem solving – that are essential for later development. Unfortunately, little is known about the early psychological functioning of preschool-aged children with cancer.

Design/Methods: Psychological data from 98 preschool-aged children with cancer (M=5.19 years old, SD=0.55; 53.1% male) who completed a clinically-driven assessment between 2011 and 2015 were abstracted. Indicators of cognitive, adaptive, pre-academic, and emotional/behavioral functioning were collected and collapsed across individual measures.

Results: Children were 30.69 months from diagnosis (SD=17.95, range 0-63 months) at assessment. Diagnoses were varied and included brain tumors (69.8%), solid tumors (13.5%), and leukaemias (16.7%). Most were off-treatment (78.1%), though children with leukaemia were more likely to be seen while on-treatment (X²=13.28, p<.01). Mean IQ scores were significantly below expectations (t(93)=-15.56, p<.001, M=84.4, SD =18.02, range 43-129). There were no differences between diagnostic categories, treatment status or gender. Adaptive functioning (t(72)=-18.60, p<.001, M=81.4, SD=19.37) and pre-academic skills (t(74)=-2.61, p<.001, M=7.39, SD=3.54) were also significantly below expectations. Measures of internalizing (M=54.2, SD=11.80) and externalizing (M=51.4, SD=10.92) behavior were within normal limits.

Conclusion: Young children with cancer are at significant risk for deficits in intellectual, adaptive and pre-academic functioning. While our sample is biased by those who were referred for clinical evaluations, the severity of deficits highlights the vulnerability of young patients, even before most have entered formal school. Interventions – such as hospital-based preschool programs to increase pre-academic skills – must be designed that explicitly target preschool-aged children and focus on a wide range of domains.

RADIATION ONCOLOGY (PROS)

P-0698 | Use of Intensity Modulated Radiotherapy in Children: Report from the Montpellier Cancer Institute

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Background/Objectives: Intensity modulated radiotherapy (IMRT) is widely used in adult population though it is not often used in paediatric population, despite its theoretical interest. This study relates 9 years of children IMRT experience in the Montpellier Cancer Institute.

Design/Methods: We reviewed all children treated by IMRT from 2007 to 2016 whatever the tumour type. IMRT was delivered with a 6MV linear accelerator (Varian, France). Doses were delivered according to international protocols.

Results: Fifty-three patients were included in our study. Mean age was 12 years (range 4-18 years). Median follow up was 25 months (range 1-80 months). Tumour types were intracranial (n=32), head and neck (n=11), abdominopelvic (n=8) and others (n=2). Intracranial tumour group represented a wide variety of cancers including astrocytoma (n=4), ependymoma (n=3), germinoma (n=5), glioma (n=5), medulloblastoma (n=6). Head and neck group was represented by carcinoma of salivary gland (n=2) and rhabdomyosarcoma (n=8). Eight patients died due to disease progression: 5 by local failure and 3 due to out-of-field evolution. Acute toxicities were reported but were manageable by usual care and did not delay radiotherapy treatment. Grade 2 chronic toxicities occurred in 12 patients, especially treated for cerebral localizations. No chronic xerostomia was observed in head and neck patients.

Conclusion: IMRT can be used in paediatric population. It results in a better sparing of surrounding critical organs. Longer follow-up is warranted to support our preliminary experience.

P-0699 | First Experience of Monitoring Radiological Response Using MRI During Proton Irradiation of a Paediatric Chordoma

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Background/Objectives: Chordoma is a very rare disease in paediatric patients. Proton therapy (PT) has become the gold standard in the treatment of this tumour for the very high deliverable dose with maximum sparing of the nearby healthy tissues.

The aim of this work is to monitor morphological changes, if any, of the lesion during the treatment, to evaluate therapeutic response and safety in terms of possible re-planning.

Design/Methods: A 10-year old girl affected by skull base chordoma was treated with PT at the Trento Proton Therapy Center. The patient had been previously received three surgical interventions; a residual macroscopic bilateral disease on the tooth of the epistropheus and a left nodular lesion in the lateral medullary-spine junction with compression and shift of the spinal cord were present. The treatment was performed after the comparison of proton plan with an IMRT photon plan. The total dose delivered was 73.8 Gy (1.8 Gy RBE per fraction, 5 times a week).

Four MRI were performed (without contrast, with T2weighted sequence) during the course of the treatment at the dose of) 32.4, 54 Gy, 64.8, and 73.8 Gy, respectively.

Results: The bony lesion around the tooth of the epistropheus did not change in volume or morphology whereas the nodule component showed a progressive dimensional change from 2.323 cm³ before the treatment to 2.829 cm³ (at 32.4 Gy); 2.051 cm³ (at 54Gy); 1.045 cm³ (at 64.8Gy and 73.4 Gy) for a 63% reduction allowing the decompression of the spinal cord.

Conclusion: The monitoring of the evolution of chordoma during PT can permit to observe changes in volume and morphology of the lesion in a disease usually considered a very slowly responding tumour, allowing also the possible evaluation of the usefulness of a re-planning of the treatment.

P-0700 | Initial Experience with Spot Scanning Proton Therapy for Paediatric CNS Tumors at First Italian Proton Therapy Center

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Background/Objectives: The dosimetric advantages of protons which substantially decrease the radiation dose to normal tissues, allow important clinical benefits in childhood cancer survivors, by maintaining tumour control, while decreasing the deleterious late effects of radiation therapy and improving the quality of life. In the following work we report our very early experience in the treatment of heterogeneous Central Nervous System (CNS) paediatric malignancies.

Design/Methods: Between June 2015 and March 2016, 17 paediatric patients have been treated using active beam delivery with spot scanning technique. The mean age was 11.2 years (range, 2-20) and the histology was: high-risk medulloblastoma (3), high-grade glioma (1), glioblastoma (1), chordoma (3), pure germinoma (2), non -pure germinoma (1), low-grade glioma (1), diffuse gliomatosis (1), craniopharyngioma (2), ependymoma (2). Nine patients were males, eight females. Four patients were treated under sedation. 15 patients have already completed the program; two are still under treatment. For all patients photon backup plans were prepared.

Results: In general, compliance was excellent and treatment was concluded without breaks for all patients. According to Common Terminology Criteria for Adverse Events (CTCAE) version 4.0, one patient developed G2 skin reaction and 8 patients G1 acute toxicity as mucositis (1), alopecia (8), dermatitis (3), fatigue (5). There were no grade 3 or higher acute side effects.

Early magnetic resonance imaging in the follow up time is available for 9 cases showing complete radiologic response in six patients, stable disease in two and disease progression in one patient (contralateral disease progression) without significant imaging changes consistent with treatment-related CNS injury.

Conclusion: Compliance was excellent while acute side effects related to PT were rare and mild without treatment breaks. These very preliminary data confirm the safe delivery of PT at the newly opened Trento facility.

P-0701 | Proton Pencil Beam Scanning for Craniospinal Irradiation in Fully Grown Paediatric Patient: A Case Report and VMAT Dose Comparisons

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Background/Objectives: Proton therapy (PT) is increasingly regarded as the gold standard for cranio-spinal irradiation (CSI) particularly in paediatric patients thanks to the potential benefit by reducing late side effects and the risk of secondary malignancies.

Design/Methods: CSI is delivered by active scanning with three isocenters using two lateral cranial opposed beams with couch angle $\pm 15^\circ$ to minimize the overlap between the cribriform plate and the lens and an additional posterior beam and two postero-anterior spinal beams. Single-field-optimization of the three equally-weighted beams is performed. Cranial and caudal field junctions are planned by the ancillary-beam technique. A total dose of 36Gy in 20 fractions to the brain and thecal sac including the nerve roots is prescribed following international radiation guidelines for high risk medulloblastoma. The PT technique and the beam arrangement is described and compared with VMAT plan performed at our Center for dosimetric comparisons. The VMAT plan was performed with six arcs (two for any isocenter).

Results: The following D98% (Gy), D95% (Gy), V98% (%), V95% (%), V106% (%), D1 (Gy) parameters were evaluated for PTV and in-field organs (i.e. chochlea, brainstem, spinal cord) and V5Gy (%), V10Gy (%), V15Gy (%), V20Gy (%), V30Gy (%), V36Gy (%), D1% (Gy), D mean (%) were recorded for esophagus, heart, kidneys, liver, lungs, thyroid, lens, bowel, spleen, trachea. PT improved normal tissue sparing while also providing more homogeneous target

coverage than VMAT; a very significant sparing (PT near to zero for all 60 parameters evaluated) of all organs at risk placed anteriorly to the vertebral bodies were obtained with PT.

Conclusion: CSI was excellent without treatment breaks for this fully grown patient. Superior dose distributions were accomplished with the use of PT.

P-0702 | Performance Changes Associated with Platelet Aferesis Irradiation Obtained in the Blood Bank of Hospital Infantil Teleton De Oncologia (HITO)

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Background/Objectives: Graft versus host disease (GVHD) is present in 5% of all blood transfusions, and the irradiation is the only known method to prevent this disease. The paediatric oncology patients have more predisposition to present GVHD because they are immunocompromised plus the use of chemotherapy. Blood irradiation is the only method used to prevent transfusion associated GVHD.

Objective: to know if the irradiation influences the platelet performance in the apheresis obtained from a blood bank.

Design/Methods: We quantified the platelet concentration in fifteen apheresis before and after the irradiation. We used an ELEKTA SINERGY LINEAR ACCELERATOR and every package was irradiated with 25 Gy. We used for platelet count a BECKMAN COULTER ANALYZER.

Results: We obtained $5.7X10^{11}$ platelets in the apheresis previous to the irradiation and $5.2X10^{11}$ twenty four hours after the irradiation. We only found a reduction of 8.7% that is equivalent only to $0.5X10^{11}$ platelets.

We also diminished the white blood cell count from $0.02X10^3$ to zero.

Conclusion: It is possible to eliminate white blood cell count to zero 24 hours after irradiation with 25Gy using a linear accelerator without reducing performance platelet.

With this results we have the certain that our paediatric oncologic patients received platelet transfusions with almost any white cells without affecting the platelet performance.

RARE TUMOURS

P-0703 | Rare Childhood Tumors: A Tertiary Care Centre Experience from India

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Background/Objectives: Rare (Orphan) Tumors account for approximately 5% of all childhood cancers. They are defined as those malignancies having an annual incidence of <2/million population. Due to lack of specific guidelines their treatment is usually individualized posing further difficulties in developing countries. Aim of this study is to investigate the frequency, profile and Outcomes of Rare Tumors at our Centre.

Design/Methods: Retrospective analysis of Patients upto the age of 12 years suffering from Cancer confirmed by HPE and IHC was done between 2008 to 2016. Patients clinical profile, histopathological type, treatment and outcomes were recorded.

Results: Out of total 465 cases, 23 were diagnosed with Rare tumours in a span of 8 years. Frequency was 4.9%. Age range was 1 day to 9 years. Male:Female ratio was 2:1. Out of 23, 14 were Malignant and 9 were Benign. They were Adrenocortical carcinoma (4), Infantile Neuroectodermal Tumour (1), Optic Glioma (3), Choriocarcinoma of 3rd Ventricle (1), Pleuropulmonary Blastoma (1), Renal Cell Carcinoma (1), Undifferentiated Sarcoma (1), Pseudo Inflammatory Tumour of Bladder (1), Chordoma (1), Infantile fibromatosis (4) and Juvenile Xanthogranuloma (3), Inflammatory Pseudotumor of Liver (1), Focal Nodular Hyperplasia (1). Most common was Adrenocortical Carcinoma (4). Two of them had metastasis at diagnosis and were given chemotherapy with surgery, out of which 1 expired due to progressive disease while other is stable. 2 had localized disease, both of which underwent surgical resection. Infantile Neuroectodermal Tumour, Undifferentiated Sarcoma was operated and received chemotherapy. All Optic Glioma had NF-1.2 of them required treatment. RCC underwent surgery. All Infantile Fibromatosis, underwent surgery but only 1 had recurrence. Out of 3 JXG, 2 required treatment. IPT responded to steroids. Overall 2 patients expired, 2 were lost to follow up, 3 are on treatment and remaining are stable on median follow up of 2 ½ years.

Conclusion: Our study shows less frequency of rare tumors as compared to western countries. This can be attributed to delayed access to Pediatric Oncologist, lack of resources and financial constraints in developing countries. High degree of suspicion and vigilance will result in efficient management of these condition.

P-0704 | Desmoplastic Small Round Cell Tumors with EWS-WT1 Transcript Expression: A Comparative Study between Children and Adults

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Background/Objectives: Desmoplastic small round cell tumour (DRSCT) is an aggressive sarcoma occurring in the young, teens and adult population. The objective of this study is to compare the differences of clinical, initial tumour presentation, therapeutic management and scalability of DRSCT in paediatric vs. adult patients, in order to define if these 2 populations may have different strategy approaches.

Design/Methods: Multicenter retrospective study of 81 Franco-Belgian medical files with DRSCT and EWS- WT1 transcript was set-up to evaluate the differences between children and adults: Pediatric group (P) under 18 years vs. Adult group (A).

Results: Median age was 21.7 years [3-58]. P included 42 patients, and A 39 patients. No notable differences (P vs. A) were found between the two groups P and A on initial symptoms, location and presence of metastasis at diagnosis. The therapeutics used were significantly comparable in both groups: neoadjuvant chemotherapy (78.6% vs. 79.5%, P= 1), primary surgery (69% vs. 69.2%, P= 0.99), adjuvant chemotherapy (54.8% vs. 56.6%, P= 0.69), radiotherapy (23.8% and 10.3%, P=0.11) and intraperitoneal chemotherapy (31.6% vs. 6.2%; P=0.096). Median time to recurrence was 9 vs. 13 months (P vs. A; P=0.13). 2-years overall survival and recurrence-free were 46.4% vs. 60.13% and 14.3% vs. 16% (P vs. A; P=0.834 for OS, 0.156 for EFS).

Conclusion: Clinical, therapeutic, and features of DRSCT look comparable between paediatric and adult populations. This study suggests a similar management and evolution of paediatric and adult patients affected by DRSCT.

P-0705 | Skin Tumours in Equatorial Children Hospital

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Background/Objectives: Most of the paediatric skin neoplasms are benign naevi and benign vascular tumour. Malignant Melanoma is the most common skin tumour in adults, however, during childhood, is expected less of 2% cases per year and only 0.4% of cutaneous malignant melanoma. According to literature, most cases are female before 15 years old. The risk factors associated are UV radiation, nevus, xeroderma pigmentosum and familiar predisposition.

Design/Methods: A retrospective study was performed with pathology data of 660 samples, obtained from 2009 to 2013 at HBO Pediatric hospital in Quito, Ecuador. Using this data we obtain the incidence of malignant and benign skin tumour, and these results were compared with worldwide incidence.

Results: Of a total of 660 histopathology specimen of the histopathology area, we obtained 167 skin tumour (25%), corresponding 2.4% to malignant and 97.6% to benign tumour. Rate male/female was 1.2/1, mean age was 5 years old. Benign Cutaneous tumours distribution of this study was classified as follows: Haemangioma 31.68%, Lymphangiomas 12.6%, Pilonatrixoma 20.8%, Melanocytic naevi 7.8%, Neurofibroma 4%, Granuloma 7.79%, others 15.33%.

Malignant skin tumors such as NH Lymphoma, Cutaneous Lymphoma, Malignant Melanoma, and Neuroblastoma were found in a 0.6% of cases each one and all of them were found in children under 6 years, in non-exposed sun of skin areas.

Conclusion: As described in medical literature, most cases belonged to benign tumour, only 2.4% was a malignant tumour, being the lymphomas most frequent. Our results showed that Melanoma it is not a tumour of high incidence and a health problem in children of Ecuador even though of a higher exposition to UV radiation characteristic of this equatorial area. But education and prophylaxis will be done to prevent it, specially in the adolescence and adults.

P-0706 | Childhood Intra-bronchial Tumors

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Background/Objectives: Presentation of intra-bronchial tumors in the paediatric population can usually mimic non-specific lower airway diseases like asthma, recurrent pneumonia and atelectasis. In this case series, we aim to evaluate the symptoms and findings of this rare entity in the childhood period.

Design/Methods: Between 2015-2016, patients with intra-bronchial tumors, treated at Pediatric Pulmonology were retrospectively evaluated. All the patients underwent fiberoptic bronchoscopy.

Results: There were 3 girls and 2 boys with the median age of 4 years old. All presented to our outpatient clinics with the findings of asthma (n=2), atelectasis (n=2) and recurrent pneumonia in the same location (n=1). Investigation including chest tomographies were obtained. Fiberoptic bronchoscopy was performed to all and there were intra-bronchial lesions which were biopsied during the procedures. Two inflammatory pseudotumor and 3 carcinoid tumors (n=5) pathologies were diagnosed.

Conclusion: Intra-bronchial tumors are rare lesions in the childhood period. However, in persistent lower airway pathologies, the diagnosis should be kept in mind. Bronchoscopy should be performed in all these persistent cases in order to diagnose the intra-bronchial lesions.

P-0707 | Gorham-Stout Syndrome with Massive Pleural Effusion Responsive to Sirolimus

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Background/Objectives: Gorham-Stout Syndrome (GSS) is a benign proliferation of lymphangiomatic tissue resulting in massive progressive osteolysis. When it is complicated by chylothorax, the prognosis is poor. We report a patient with GSS having chylothorax who is responsive to sirolimus treatment.

Design/Methods: A 2-yrs old girl with cystic hygroma, was followed-up with unremarkable ultrasound examinations until an uneventful right sided pleural effusion. Since the effusion progressed to both sides of thoracic cavity, and led to an unresolving respiratory insufficiency, the baby was internalized to the intensive care unit after drainage via bilateral chest tubes. Thoracentesis revealed chylothorax. Thorax CT showed bilateral basal pleural effusion with multiple lytic lesions at ribs and thoracic and lumbar vertebrae. MRI showed dilated vascular ducts in the thoracic wall and there were hypodense nodular cystic lesions all over the spleen. These findings were compatible with the diagnosis of systemic lymphangiomatosis and based on the clinical and radiological findings, the patient was diagnosed as GSS.

Results: Since the disease was considered unresectable, feeding with middle-chain fatty acids, octeotide, and propranolol were initiated. As the patient lost albumin and sodium via chylothorax, intense electrolyte and protein supplementation were administered. However, the effusion did not resolve via these medications. Sirolimus was started while propranolol was stopped. After three weeks of sirolimus, the lesion shrank in size. After cessation of drainage, octeotide was ended. Sirolimus treatment lasted two months with no recurrence of effusion. Middle-chain fatty acid feeding gradually was changed to normal daily life feeding. The baby is in follow-up for 14 months now with no symptoms and signs.

Conclusion: GSS is a very rare disorder. No single treatment modality has proven effective. Sirolimus, an mTOR inhibitor, achieved resolution of pleural effusion in this patient. Further experience with sirolimus as a treatment option for resistant lymphangiomatosis and/or GSS is required.

P-0708 | Treatment of Paediatric Thyroid Cancers: A Consistent Institutional Approach

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Background/Objectives: Thyroid cancer is a rare paediatric malignancy with an incidence of 1.5-3%. Management controversies exist. Patients often present with large volume disease, high metastases and local recurrence rates, yet high survival rates. We report our institutional treatment and outcomes since 2002.

Design/Methods: Twenty seven paediatric thyroid cancer patients referred to our dedicated paediatric thyroid cancer clinic between 2002-2016 were treated and followed (Median follow-up of 4.4yrs [0.1-13.7yrs]). Patient demographics, pathology, investigations, treatment, outcomes and recommendations are presented.

Results: Median age at diagnosis was 15 years [5-17], 77.8% of patients were female, and 3 patients had risk factors (1 treated with previous RT, 1 with environmental radiation exposure, and 1 with genetic syndromes). Dominant histology was papillary (85.2%), then follicular (11.1%) and medullary (3.7%). At diagnosis 48.1% of patients had disease limited to the thyroid, 48.1% had lymph node metastases and 3.7% with distant metastases (lungs). Median largest dimension was 2.5cm [0.4-4.5cm]. Lymphovascular space invasion was seen in 22.2%, extracapsular extension in 33.3%, positive margins in 14.8% and multifocality in 51.9% of patients.

All patients received total thyroidectomy, 70.4% had a lymph node evaluation, and 55.5% had both thyroid lobes involved. Three patients did not receive radioactive iodine ablation with I-131 (RAI) (size under 1cm), while 70.4% of patients received 1 course and 18.5% of patients required multiple ablations. Median dose of RAI per patient was 50 mCi [30mCi-450mCi]. All patients were placed on thyroid suppressive therapy. Over the course of follow-up only 1 patient was treated for local recurrence. All patients were alive at follow-up.

Conclusion: Pediatric thyroid cancer patients tend to present with multifocal disease, lymph node metastases and large tumors (>1cm). Patients have excellent survival and low recurrence rates when treated with total thyroidectomy and adjuvant treatment with radioactive iodine ablation and long term thyroid stimulating hormone suppression.

P-0709 | Clinical Outcome of Melanoma and Atypical Melanocytic Lesions in Children

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Background/Objectives: Melanoma is rare in children. Histological distinction between atypical nevi, particularly Spitzoid lesions, and melanoma, is challenging, and there is often lack of consensus even among experts. Clinical outcome in children is better than in adults, even when nodal disease is present. Given their rarity, there is little published data on the long term outcome in children. The aim of the study was to add to this data.

Design/Methods: A retrospective review was undertaken of atypical melanocytic lesions and melanomas diagnosed at a tertiary institution in the preceding 12 years. The pathology report and expert dermatopathologist report (where available), was reviewed. The pathology data were tabulated with the latest available clinical status for each patient.

Results: Seventeen cases were evaluated. Age ranged from 1 to 15 years, with 10 males and 7 females. Anatomical site included 6 torso (4 on the back), 5 upper extremity, 4 lower extremity and 2 head and neck. Five were diagnosed as melanoma: 2 without nodal involvement, 2 with nodal involvement, and 1 with metastatic disease (a 12 year old boy who subsequently died of his disease); the other 4 are alive and disease free. Five were classified as melanocytic tumours of uncertain malignant potential. None had nodal involvement and all are alive and disease free. Three were classified as atypical Spitz naevi, 1 had nodal involvement and all are alive and disease free. There were 2 dysplastic compound naevi, 1 dysplastic junctional naevus and 1

pigmented epithelioid melanocytoma; none had nodal involvement and all are alive and disease free.

Conclusion: In our experience, the long-term outcome of atypical naevi and melanoma in children is good. Surgeons and pathologists should be aware that melanoma does occur in children, and such lesions should be adequately excised and carefully examined histologically.

P-0710 | Oncomir miR17, Tumour Suppressor miR146a, miR302d, and Oncogene miR19b Expressions in Hepatoblastoma Patients

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Background/Objectives: Hepatoblastoma (HB) is the most common primary liver malignancy in children, usually occurring in the first 3 years of life. The pure fetal-type hepatoblastoma has the best prognosis, whereas the small cell histology has been associated with unfavorable outcome. In the present study, we aimed to characterize the expression level of selected miRNAs in HB subtypes, and to consider the association with the prognosis.

Design/Methods: A total of 15 Formalin fixed paraffin embedded (FFPE) HB tumour samples were evaluated in this study. Total RNA was isolated from frozen tissue sections and areas of tumour. Expressions of miR17, miR146a, miR302d, and miR19b were analyzed in 15 HB cases by RT-qPCR. To make the relative quantitation of the results, Δ / Δ Ct method was used. miRNA Ct values were normalized by Snord 48 housekeeping gene with this method. Comparative 2- $\Delta\Delta$ Ct methods were used for the cycles above threshold values.

Results: The patient group included 15 children (mean age 17.6 months, range 3-108) diagnosed with HB. Higher miRNA146a, miRNA19b, and lower miRNA17, miRNA302d levels were detected in tumour samples in comparison with normal tissue samples. Overall survival was found correlated with histological subtypes (log rank, $p=0.048$). Mixed subtypes showed better survival than pure epithelial subtypes. The fetal subtype was found to be significantly better event-free and overall survival in comparison with embryonal subtypes (log rank, $p=0.034$; log rank, $p=0.011$). Expression of miRNA19b was found correlated with event-free and overall survival (log rank, $p=0.023$; log rank, $p=0.005$). A higher-level of miR19b was found in embryonal samples (ki square test, $p=0.044$).

Conclusion: In conclusion, higher or lower expression of miRNAs in hepatoblastoma, can provide important data for predicting clinical outcome in HB.

P-0711 | Cytopenias in Children and Adolescents with Kaposi Sarcoma: A Unique, Common and Potentially Severe Clinical Manifestation

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Background/Objectives: Kaposi sarcoma (KS) is caused by human herpesvirus-8 (HHV-8) and is currently the second most common childhood malignancy in Malawi. Pediatric KS is uniquely characterized by high rates of cytopenias and lymphadenopathy as presenting clinical features. We evaluated the nature of cytopenias in HIV-infected children and adolescents with KS.

Design/Methods: We analyzed data from two cohorts of patients with KS < 18 years of age with baseline full blood count analyses. These data included a retrospective observational cohort from 2010-2013 ($n=67$) and a prospective cohort from 2013-2015 ($n=25$) in Lilongwe, Malawi. Cytopenias were defined at time of KS presentation as having baseline anaemia (hemoglobin < 8 g/dL), thrombocytopenia (platelet count < $100 \times 10^9/L$), or neutropenia (absolute neutrophil count [ANC] < $1,000$ cells/mm³). Treatment was anti-retroviral therapy combined with chemotherapy.

Results: There were 92 patients total; the median age was 8.2 years (range 1.7-17.9) and there were 44 females (48%). Biopsy confirmation was established in 37 (40%). Overall, 45 patients (49%) presented with some form of cytopenia. Median hemoglobin was 9.4 g/dL (range 1.8-13.6), median platelets $211 \times 10^9/L$ (range 6-729), and median ANC $2,015$ cells/mm³ (range 300-8,600). Specifically, 31 (34%) presented with anaemia, with 16 (17%) having a hemoglobin < 6 g/dL. Thrombocytopenia was found in 24 (26%) patients; 19 (20%) presented with platelets < $50 \times 10^9/L$. Fifteen (16%) had neutropenia but only 3 (3%) had ANC < 500 cells/mm³. Of those patients presenting with platelet count < $100 \times 10^9/L$, 86% resolved without transfusion within 2 weeks of initiating chemotherapy and 100% had normalized without transfusion by 4 weeks post-chemotherapy initiation.

Conclusion: Cytopenias are a common presenting clinical feature in paediatric KS in Malawi, an HHV-8 endemic region. The severity of cytopenias can be life threatening. Severe thrombocytopenia resolves promptly after initiation of chemotherapy even in the absence of transfusion.

P-0712 | Increasing Incidence of Kaposi Sarcoma in Children and Adolescents in a Human Herpesvirus-8 Endemic Region of Sub-Saharan Africa Despite the Wide Availability of Anti-Retroviral Therapy

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Background/Objectives: Kaposi sarcoma (KS) is caused by human herpesvirus-8 (HHV-8) infection and accounts for the majority of human immunodeficiency virus (HIV)-associated malignancies in children and adolescents in eastern and central Africa—a region where HHV-8 is endemic. During the post-highly active anti-retroviral therapy (HAART) era in the United States and Europe, there has been a steep decline in the overall incidence of KS. However, recently published data from South Africa and Zambia demonstrate that in adults, KS risk and incidence rates remain high despite increased HAART coverage. We evaluated paediatric KS incidence rates in an HHV-8 endemic region with high HIV prevalence.

Design/Methods: We retrospectively evaluated the experience of our paediatric HIV-associated malignancy program at the Baylor Children's Foundation Malawi Clinical Centre of Excellence (MW-COE) in Lilongwe over the past decade. It includes all HIV-infected children and adolescents diagnosed with KS younger than 18 years of age.

Results: From 2006-2015, there were 3,716 children initiated on HAART at the MW-COE. During the same time period, there have been 215 incident KS diagnoses. From 2006-2010, the average annual paediatric KS incidence was 17.8 cases/year (range 13-24) compared to 25.2 cases/year between 2011-2015 (range 20-33). Using a denominator of number of new HAART initiations as a proxy for number of new paediatric HIV diagnoses, we compared percentages. From 2006-2010, incident cases of KS represented 4.1% (89/2,196) of HAART initiations. From 2011-2015, incident cases of KS represented 8.3% (126/1,520) of HAART initiations. The highest single-year number of incident KS diagnoses occurred in 2015 ($n=33$).

Conclusion: The number of incident diagnoses of KS in children and adolescents in Malawi appears to be increasing despite the scale-up of HAART. Although causative factors contributing to this phenomenon are multiple and complex, KS remains an important complication in HIV-infected children and adolescents living in HHV-8 endemic regions of Africa.

P-0713 | A Prospective Observational Analysis of the Clinical, Pathological, and Virological Characteristics of Kaposi Sarcoma in Children and Adolescents

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Background/Objectives: Kaposi sarcoma (KS) is the second most common childhood malignancy in Malawi. The clinical characteristics of paediatric KS are distinct. Little is known about the biological mechanisms that explain these unique clinical features.

Design/Methods: We performed a prospective observational pilot study of the clinical, pathological, and virological characteristics of KS diagnosed in HIV-infected children and adolescents in Lilongwe, Malawi. Diagnoses were confirmed via biopsy and baseline plasma samples were collected. Clinical features and treatment response were documented. Patients received treatment according to institutional standard of care combining chemotherapy and anti-retroviral therapy (ART).

Results: There were 25 patients enrolled between June 2013 and August 2015. Biopsy confirmation was obtained in 23 (92%). The median age was 6.4 years (range 1.7-17) with 10 females (40%). Based upon the Lilongwe Pediatric KS Staging Classification, there was one patient (4%) with stage 1 mild KS, 17 (68%) with stage 2 lymphadenopathic KS, 3 (12%) with stage 3 woody edema, and 4 (16%) with stage 4 visceral and/or disseminated skin/oral KS. Baseline median laboratory data included hemoglobin 9.9 g/dL (range 4.8-12.5), platelet count $317 \times 10^9/L$ (range 7-729), CD4 count 515 cells/mm³ (range 2-2,013), and HIV viral load 97,000 copies/mL (range suppressed-2,163,000). Twelve patients (48%) were on ART at KS diagnosis, 6/21 (29%) with baseline CD4 data were severely suppressed, 5/22 (23%) with baseline HIV viral load data were suppressed, and two (8%) presented with a concurrent opportunistic illness. Overall, 18 patients (72%) were alive with median follow-up of 19.5 months (range 6-26); 17 were in complete remission. Baseline histological characteristics, plasma HHV-8 viral load and circulating IL-6 and IL-10 levels (molecular markers associated with lytic phase HHV-8) will be analyzed and correlated with clinical characteristics and treatment outcomes.

Conclusion: A clinicopathological study of paediatric KS has been performed. Virological and biological mechanisms of disease will be explored.

P-0714 | Undifferentiated Nasopharyngeal Carcinoma in Children: Experience of Pierre & Marie Curie Center

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Background/Objectives: Evaluate the disease characteristics and outcome of the patients with nasopharyngeal carcinoma in paediatric age group treated with protocol included taxane in our institute.

Design/Methods: A retrospective study was undertaken on 50 patients in paediatric age group with diagnosis of nasopharyngeal carcinoma, treated from 2008 to 2013 at our oncologic center. For all the patients, the diagnosis was made after biopsy. They were treated with combined chemotherapy and radiotherapy. Patients with all received adjuvant chemotherapy including 3 courses of a regimen included taxotere; 5fluoracil; cisplatinum followed by concomitant radiochemiotherapie. The median dose of radiotherapy was 60 gray.

Results: The median age was 13 years (3 months to 16 years) -Male /female ratio was: 1.9.-the patient consult 3 to 8 months after onset. The revealing signs are otologica l(49%) cervical nodes(43%) neurological injury (8%).Histological type was und UCNT undifferentiated carcinoma of nasopharyngeal type).Patients with all were classified T3 or T4. Evaluation: clinical examination, nasofibrosocopy and CT Scan of nasopharynx. Partial response were 55% complete response 45%.-After median follow-up of 48 months, overall survival and disease free survival was 60% and 54%.

Conclusion: The combined modalities of chemotherapy and radiotherapy results are satisfactory for loco regional control and survival and acceptable for toxicity in patients with nasopharyngeal carcinoma in paediatric age group.

P-0715 | Childhood Adrenocortical Tumors in Southern Brazil - Report of 8 Cases

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Background/Objectives: Purpose: Adrenocortical cancer (ACC) is a rare tumour, but the incidence is remarkably high in southern Brazil. We report eight cases of children with ACC followed at a single institution in the south of Brazil.

Design/Methods: This is a retrospective study based on review of medical records of paediatric patients treated at oncological reference hospital from 2007 to 2015.

Results: The median age at diagnosis was 24.3 months and 5 (62.5%) were female. In 100% of cases, the tumors were functional and the most common clinical manifestations were: hypertrophy of the clitoris /penis (62.5%), palpable abdominal mass (62.5%), hypertrichosis (50%), Chushing's syndrome signals (25%), abdominal pain (25%), pimples (25%), deepening of the voice (12.5%) and increase in muscle mass (12.5%). The hormones measured were dehydroepiandrosterone sulfate (DHEA-S), testosterone, cortisol, androstenedione and 17-alpha hydroxyprogesterone. All patients underwent surgical resection with or without chemotherapy. Two patients with pulmonary metastases at diagnosis died, five remain in clinical remission and one continues to receive chemotherapy.

Conclusion: The most of our patients were female, developed the tumour before the age of five and the clinical manifestations were due to excess hormone production. The curative treatment is surgery and the chemotherapy should be used just in cases of relapse or metastases. The prognosis of ACC is still poor, mainly, in advanced stages of the disease, considering this, is necessary more attention for the clinical of this tumour, particularly in those under 5 years-old.

P-0716 | The Potential for Epigenetic Therapy of Rhabdoid Tumors – First in vitro Results for the Epigenetic Modulators Resminostat and 4SC-202

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Background/Objectives: The histone deacetylases 1 and 2 (HDAC1, 2) are overexpressed across all currently defined molecular subgroups of AT/RT (Johan *et al.* Cancer Cell 2016). Likely they play an important role for rhabdoid tumors regardless of anatomical origin. Resminostat is an orally available inhibitor of HDAC classes I and IIb; whereas 4SC-202 is a combined inhibitor of HDAC1/2/3 and the lysine specific demethylase LSD1. Moreover, 4SC-202 impedes the SMO-independent HH signaling often aberrantly activated in rhabdoid tumors. Both compounds have proven tolerability and efficacy in phase I or II trials in adult populations. Their toxicity profile appears to be favorable while still sustaining targeting efficiency.

Design/Methods: Proliferation and viability of cell lines G401 (RTK), A204 (MRT) and CHLA-02 (AT/RT) were assessed by crystal violet staining and MTT, spheroid and colony formation assays. Gene expression associated with the phenotype of rhabdoid tumors such as *SMARCB1*, *CDKN1C*, *MYC*, *CyclinD1* and *HHIP* was examined by qRT-PCR. The wellknown HDACi Vorinostat, Panobinostat, Entinostat, Mocetinostat and Ricolinostat served as comparative compounds.

Results: Resminostat as well as 4SC-202 exhibited dose dependent inhibition of proliferation and impeded the viability of RT cells. Inhibition of the capacity for clonogenic growth was demonstrated.

Conclusion: As paradigmatic epigenetic malignancies rhabdoid tumors appear to be the optimal aims for drugs targeting the epigenetic framework of cancer cells. The epigenetic modulators Resminostat and 4SC-202 warrant further testing in clinical trials in children affected by rhabdoid tumors. Likely combinatorial therapy will be needed to substantiate a significant effect on outcome for affected high-risk patients.

P-0717 | Though it is Very Rare But be Aware: Type 1 Pleuropulmonary Blastoma in a 3 Month Old Male Mimicking Complicated Congenital Pulmonary Airway Malformation

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Background/Objectives: There is no single, widely accepted definition for rare diseases. The definitions used in the medical literature and by national health plans state that it is the disease that affects population ranging from 1 in 1,000 to 1 in 200,000. Pleuropulmonary blastoma (PPB) is one of these rare diseases that physicians should be aware of. It is a rare aggressive malignant tumour of infancy and early childhood. The tumour arises in the lung and pleura and is regarded as a pulmonary dysontogenetic or embryonic neoplasm. Four types are defined in literature. Type I PPB is a rare, cystic lung neoplasm in infants characterized by subtle malignant changes and a good prognosis. Recurrences after type I PPB are usually advanced with a poor prognosis.

Design/Methods: Case Presentation.

Results: We present a 3 month old male who was referred from the Pediatric Pulmonologist with 2 week history of cough and shortness of breath. Both chest radiograph and a Computer-

ized Tomography (CT) were in favor of Congenital Pulmonary Airway Malformation. As the baby was in distress he underwent resection of the right lung cystic lesion. The Histopathology revealed a Type I PPB. He was kept under close surveillance by CT every 3 months. The 6 months post op CT showed a suspicious lesion that was further resected. The latter histopathology was benign. Due to the risk of recurrence the parents agreed to go for adjuvant chemotherapy. He is now disease free and under surveillance.

Conclusion: The rarity and subtle malignant features of type I PPB contribute to difficulty in making the correct diagnosis. Adjuvant chemotherapy appears to benefit patients with type I PPB. Salvage after types II and III recurrence is poor. A rigorous surveillance schedule after type I PPB diagnosis might detect early recurrence and be an acceptable alternative to adjuvant chemotherapy.

P-0718 | Surgical Aspects in the Treatment of Bronchial Tumors in Children and Adolescents

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Background/Objectives: Bronchial tumors are extremely rare in children and adolescents. Therefore no standardized treatment protocols are available and therapy is guided by personalized strategies. Here we present our experience of 5 patients with bronchial tumors.

Design/Methods: Retrospective analysis was performed of five patients (4y, 12y, 14y, 15y, and 16y) treated at our institution between 2010 and 2014. Preoperative work-up included laboratory tests, plain chest radiograph, CT-, MRI-scan, and bronchoscopic biopsy. Metastatic spread was excluded by additional PET-scans. The patients' follow-up ranged from 23 month to 6 years (median of 43 months).

Results: Complete resection was achieved in all patients by (bi-)lobectomies. In one patient, sleeve lobectomy of the medial lobe was performed with re-anastomosis of the remaining lower lobe. Histological diagnoses were bronchial carcinoid tumors (n = 2), hemangiopericytoma (n = 1), mucoepidermoid carcinoma (n = 1), and inflammatory myofibroblastic tumour (n = 1). Adjuvant chemotherapy was given to the patient with the hemangiopericytoma according to the CWS protocol. None of the patients relapsed during follow-up or show any respiratory impairment. One patient with bronchial carcinoid developed a fibromatosis of the right chest wall 31 month after initial resection.

Conclusion: Although there is a lack of standardized treatment protocols, good to excellent results can be achieved by complete tumour resection. According to recent literature and our experience, these tumors are unlikely for local or distant relapse; therefore lung sparing surgery should be targeted. The use of adjuvant chemotherapy has to be discussed for each individual case in an interdisciplinary setting.

P-0719 | Surgical Treatment of Pancreatic Tumors (One Centre Experience)

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Background/Objectives: Solid pancreatic tumors are the rare pathology at the young age. The surgical treatment for this group of patients is technically complicated. A surgical treatment experience is not sufficiently advanced in a modern literature.

Design/Methods: Ten patients (9 girls and 1 boy) were given the surgical treatment of pancreatic tumour for the last 15 years. The average age of patients was 10.7 years (children from 1 till 15 years old). The following operations were carried out: one patient received pancreatic tumour enucleation, two patients – splee-preserving distal pancreatectomy, four patients – radical antegrade modular pancreatosplenectomy, one patient – radical antegrade modular pancreatosplenectomy with left adrenalectomy, two patients – pancreaticoduodenectomy with duct-to-mucosa pancreatojejunostomy and author's method of totally isolated Roux-en-Y pancreaticobiliary tract reconstruction with microjejunostomy and microgastrostomy (patient age was 1,10 year old).

Results: Pathology conclusion of operation materials shown as follows: in four cases tumour was verified as a solid pseudopapilloma pancreas cancer (all female patients), three cases - a malignant neuroendocrinological tumors (G3), one case - a malignant paraganglioma (G3), next one - as an adenocarcinoma and another one - as a mature teratoma with involving to a head of pancreas. The average time of surgery is 250 min., the average hemorrhage was 156 ml (max was 300 ml). During the postoperative period one patient had an abscess which was success treated via US drainage. Three patients have been treated with adjuvant chemotherapy. One patient died because of metastatic recurrent, nine patients - still alive, without signs of disease.

Conclusion: Surgical treatment of solid pancreatic tumors is a complicated method that provides long term survival.

P-0720 | Racial and Ethnic Disparities in Survival of Paediatric Sarcoma

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Background/Objectives: Childhood sarcomas are rare diseases, and the interdisciplinary care these patients require is specialized and expensive. The goal of this study was to determine if racial or ethnic disparities exist for paediatric sarcoma patients in the United States.

Design/Methods: The United States' National Cancer Institute's Surveillance, Epidemiology, and End Results database (SEER) was used to identify patients aged 0-21 diagnosed with primary sarcomas from 1973-2012. Patients were considered by race and ethnicity. Survival curves were computed using the Kaplan-Meier method and the log-rank test. Cox proportional hazard regression was used for multivariate analysis.

Results: A total of 11,502 patients with histologically confirmed sarcoma were included in this study. A greater proportion of patients were male (57%), and the largest proportion of patients was between the ages of 11 and 17 at time of diagnosis. There were 6877 patients with soft tissue tumors (60%), and 4625 patients with bony tumors (40%). Among the soft tissue tumors, a majority were non-rhabdomyosarcoma (66%), with osteosarcomas the most common among bony tumors (58%). Overall 10-year survival for the study population was 63.4%. Overall 10-year survival improved during the study period from 52.5% in 1973-1979 to 65.3% in 2000-2012. The 10-year OS was 64.5% for non-Hispanic White patients, 62.3% for Hispanic patients, and 61.8% for non-Hispanic Black patients ($p=0.01$). Among those patients with soft tissue sarcomas, 46% of non-Hispanic White patients received radiation therapy, compared to 40% of non-Hispanic Black patients ($p=0.01$), while there was no significant difference between the proportion of patients receiving surgery ($p=0.21$).

Conclusion: While an improvement in paediatric sarcoma survival was seen over the past 4 decades, this survival improvement still lags far behind that of hematologic malignancies. Racial and ethnic disparities are seen in the treatment patterns and survival of these rare tumors in the United States.

P-0721 | Paediatric Inflammatory Myofibroblastic Tumour: Experience of Multicenter Cooperation

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Background/Objectives: Inflammatory myofibroblastic tumour (IMT) is a rare type of childhood malignancies with intermediate biologic behavior. The aim of the study was to analyze clinical data and treatment results in a cohort of patients with IMT treated in four Russian children's hospitals.

Design/Methods: 9 patients with IMT for the period of 01.2012 - 12.2015 (48 months) were included in the analyses. Central review of histology was obligatory. Anaplastic lymphoma kinase (ALK) immunohistochemistry and FISH for ALK gene rearrangements were performed in all cases. Surgery was the first treatment option.

Results: Male: female ratio was - 0.8:1. The median age at the diagnosis was 61.9 months (range 5.9-102.5). Tumour detection was an incidental finding in 3 (33.3%) patients. Most frequent symptom was fever - 4 (44.4%). Tumour located in lungs - 4 (44.4%), abdomen - 4 (44.4%) and the liver - 1 (11.2%). Regional lymph node involvement was observed in 1 (11.1%) case. Laboratory findings included leukocytosis (4/9), anemia (5/9) and thrombocytosis (7/9). ALK expression was revealed in 4/9 (44.4%) cases. ALK rearrangements were not detected in 4 studied cases. All patients were operated. Extent of the surgery included gross total excision in 8/9 (88.9%), biopsy - 1/9 (11.1%). Microscopic positive margins were confirmed in 2/8 (25%) cases. Surgery was the only therapy in 6/9 (66.7%), 2/9 (22.2%) patients with positive margins received celecoxib, 1/9 (11.1%) with unresectable tumour was treated with chemotherapy without response. All patients are alive. Median follow-up time was 10.5 months (range 1.3-27). 2/9 (22.2%) relapses were observed. Time to relapse was 5.9 and 9 months. Both patients received surgical procedure.

Conclusion: Our data confirm lungs and abdomen as the most frequent sites of the disease. Surgery is the mainstay of therapy. More data are needed regarding the role of adjuvant therapy in IMT.

P-0722 | Malignant Melanoma in Children

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Background/Objectives: Malignant Melanoma (MM) is very rare in childhood, comprising 1-3% of all malignancies. We aim to evaluate the clinical aspects, histopathologic features and treatment outcome of children with MM.

Design/Methods: Between 1999-2015, patients < 15 yrs old, treated in the Istanbul University Oncology Institute were retrospectively evaluated.

Results: Fourteen patients (10 female, 4 male) with a median age of 7 years (1-14 yrs) were evaluated. All had cutaneous melanoma except one with conjunctival melanoma. The localization was the lower extremities in five (35.7%); upper extremities in 4, head and neck in 4, and abdomen in one. Sentinel lymphoscintigraphy + sentinel node biopsy and PET/CT were performed for staging. Localized disease was present in four patients; 7 patients had regional lymph node metastasis; and 3 patients (%21.5) had distant metastasis (bone, lung, brain). The median Breslow width of the tumour was 3,5 mm (1.7-14 mm). The treatment was surgery in localized disease; surgery and interferon in patients with regional lymph node metastasis. All are with no evidence of disease with a median follow-up of 30 (1-140) months. One patient with brain metastasis (8 yrs) received surgery, radiotherapy and temozolomide, he had a history of resection of a benign hairy nevus as an infant. Another metastatic patient died in 5 months. The patient with conjunctival melanoma and distant metastasis had no response to temozolomide, BRAFV600E mutation was negative, immunotherapy with ipilimumab was initiated, palliative radiotherapy was administered to bone and brain metastasis. The median follow-up for all patients was 28 (1-140) months. The 5 year overall survival was %83.

Conclusion: MM is rare in children, prognosis is good if diagnosed at early stages. Metastatic disease has poor diagnosis. Clinicians should be aware of skin lesions and full layer biopsy should be obtained in suspicious skin lesions.

P-0723 | Triple Therapy of Vincristine, Bleomycin and Etoposide for Children with Kaposi Sarcoma - Results of a Study in Malawian Children

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Background/Objectives: Kaposi sarcoma (KS) is the most common paediatric cancer in HIV-endemic countries of sub-Saharan Africa but there is little research on management and outcomes.

Design/Methods: Children with KS at Queen Elizabeth Central Hospital, Blantyre, Malawi were treated with antiretroviral therapy if HIV infected and six courses of vincristine, bleomycin and etoposide combination chemotherapy, and followed up from August 2012 to March 2015. Outcomes were compared with previously reported results.

Results: Of 56 children: 38 (68%) were male; 48 (86%) were HIV positive, with 36 (75%) on antiretroviral therapy at diagnosis. Median age was 8 years (IQR 3-12) and follow-up was 5.8 months (IQR 2.3 - 16.1). Quality of life increased from a median Lansky Score of 80%, to 100% post-treatment; with increases for survivors and those who died of 71% and 88%, respectively. Overall survival was 76% at 6 months and 69% at 12 months. Survival in children completing 6 courses of treatment was higher than those not completing the full course: 96.0% v 37.8% at 6 months and 86% v 37.8% at 12 months. Retention (no death or loss to follow-up) after a full course was 83% at 6 months, and 71% at 12 months. Event-free survival was 73% at 6 months and 54% at 12 months. Increasing number of treatments was associated with reduced risk of death HR 0.45 (95% CI 0.30 - 0.69) and of any event HR 0.48 (95% CI 0.34 - 0.68). For children completing ≥ 6 treatments; previous TB treatment was associated with increased risk of attrition HR 3.47 (95% CI 0.94 - 12.7), and of any event, HR 2.68 (95% CI 0.86 - 8.33).

Conclusion: Survival, event-free survival, and quality of life were improved with three-agent combination chemotherapy compared to reports of individual agents. Larger, randomised studies are needed to determine optimal management.

P-0724 | Neoadjuvant Chemotherapy Providing Resection of the Locally Invasive Large Cell Anaplastic Carcinoma of the Pancreas

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Background/Objectives: Pancreatic carcinomas are extremely rare in children and adolescents, consisting only less than 5% of pancreatic tumors in this age group. Only one case with anaplastic carcinoma of the pancreas was reported in English speaking literature. Surgery is the mainstay of the treatment and the disease is always fatal in inoperable cases.

Design/Methods: Here we report a case of locally advanced anaplastic carcinoma of the pancreas which became resectable after neoadjuvant chemotherapy.

Results: A 17-year-old girl was admitted with an abdominal mass detected during investigation for dyspepsia of 3 months. Physical examination revealed conjunctival icterus and a large fixed hard mass of 6x7cm on the right abdomen extending to midline. Computerized tomography of the abdomen showed a mass of 9x10x11.5 cm originating from the head of the pancreas while invading stomach, duodenum, and main portal vein and surrounding mesenteric vein. An ultrasound-guided tru-cut biopsy was performed and a diagnosis of a high-grade anaplastic tumour was made. BRAF c.1799T>A (V600E) and KRAS codon 12, 13, 61, and 117 mutations from tumour sample were negative. Whole body 18F-FDG PET/CT imaging showed no metastases. Neoadjuvant FOLFIRINOX chemotherapy consisting of oxaliplatin, irinotecan and 5-fluorouracil was started as it was impossible to resect the tumour. The tumour shrank in size after 3 courses but additional 2 courses was administered because hepatic, portal and coeliac vessel invasion. After five courses, en bloc resection of the tumour with pancreas, left liver lobe, gallbladder, antrum, and duodenum was performed. Histopathological and immunohistochemical examination of the tumour revealed the diagnosis of large cell anaplastic carcinoma of the pancreas. After an uneventful postoperative period, adjuvant chemotherapy with gemcitabine and radiotherapy was started.

Conclusion: Pancreatic carcinoma is typically seen in advanced stage and chemoradiotherapy provide only palliation in elderly patients. Rare paediatric patients may benefit from chemotherapy and aggressive surgery.

P-0725 | Undifferentiated Embryonal Sarcoma of Liver: An Institutional Experience of Seven Cases

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Background/Objectives: Undifferentiated embryonal sarcoma of the liver (UESL) represents less than 5% of all malignant hepatic tumors in childhood. It is considered an aggressive neoplasm with an unfavorable prognosis. The aim of this review is to present a single center experience in the treatment of children with UESL.

Design/Methods: We conducted a retrospective review of patients referred to Hospital Infantil de Mexico Federico Gomez with a definitive pathologic diagnosis of USL between January

2000 to December 2014. There were 7 children, six were female. Age at diagnosis ranged from 2 to 12 years (median: 7.5 years). The main presenting complaints were abdominal mass (n=7), fever (n=3) and abdominal pain (n=2). All lesions were unique, nonmetastatic, and heterogeneous. Lesions involved the right lobe in 5 cases and the left lobe in 1. Surgery after neoadjuvant chemotherapy (CHT) was performed in 2 patients, and in 4 patients primary surgery was done. Final surgery consisted of five right extended hepatectomies; one left hepatectomy. All patients received adjuvant CHT with Vincristine, Actinomycin D, Doxorubicin and Cyclophosphamide, the number of courses was 1 to 13.

Results: The follow-up information of 6 cases was available. Follow up from diagnosis is ranged from 13 to 158 months. One patient with upfront surgery had local recurrence at 14 months after initial surgery. One of seven patients underwent radiotherapy for relapse after surgery. The overall survival was 71.4%. One patient died and 1 lost follow up.

Conclusion: Excellent results with long-term survival can be achieved in children with UESL with conventional therapy, including a combination of chemotherapy and surgery, even in large extensively growing tumors.

P-0726 | Germline DICER1 Mutations in Twelve Chinese Patients with Pleuropulmonary Blastoma

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Background/Objectives: Pleuropulmonary blastoma (PPB) is a rare and highly aggressive mesenchymal neoplasm in childhood and germline *DICER1* mutations were reported contributing to PPB development. Germline *DICER1* mutation frequency of PPB is about 75% via Next-Gen sequencing and targeted aCGH. Almost all mutations are reported to be heterozygous nonsense or frameshift mutations of germline origin.

Design/Methods: Medical history and family history of 12 children with PPB were collected. Blood samples from children with PPB and their first degree relative were tested for *DICER1* mutations by Next-Gen sequencing. The Institutional Review Board of Beijing Children's Hospital approved this study, and all participants' parents signed a consent form to genetic testing and medical history collection.

Results: Twelve patients with PPB (6 patients suffering from type II PPB and 6 patients suffering from type III PPB, respectively) were evaluated for germline *DICER1* mutations, and 7 had a deleterious *DICER1* mutation. Six mutations lead to premature protein truncation as a result of frameshift mutation (p.Q766fs, p.R342fs, p.P956fs) or nonsense mutations (p.Y1225X, p.R392X, p.Y976X). In addition, one case carried a germline *DICER1* mutation which was suspected to deleteriously affect splice site (c.2987+1G>A). One child had a remarkable family history of thyroid diseases. Thyroid goiter and thyroid nodules were common findings in mutation-positive family members of other cases and disproportionately affected female carriers.

Conclusion: These cases illustrate the genetic and clinical characteristics of Chinese patients with PPB. Further study will be imperative to understand the etiology of mutation negative patients with PPB.

P-0727 | Paediatric Nasopharyngeal Carcinoma: A Single Centre Experience from India

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Background/Objectives: Pediatric Nasopharyngeal Carcinomas (NPC) are rare tumors. There is paucity on data on outcomes in paediatric NPC from developing countries. The present study was conducted to ascertain the outcomes of children with NPC at our centre.

Design/Methods: We retrospectively analyzed the outcomes of 37 consecutive patients less than 18 years of age with paediatric NPC treated at our centre between 2000 and 2015.

Results: The median duration of follow-up after relapse was 36.6 months. The median age of the patients was 15 years (range 8-18years), 22/37 (%) patients were male. The most common presenting complaint was neck mass (70%) followed by nasal bleeding (16%). The median duration of symptoms was 4 months. The distribution of stage 1, 2, 3 and 4 patients was 1/37 (3%), 2/37 (6%), 14/37 (38%) and 20/37 (53%) respectively. Distant metastasis at presentation was seen in 4/37 patients. The 4 year Event Free Survival (EFS) was 56.7%. Concurrent Chemo-radiotherapy (CTRT) with cisplatin and 5-FU followed by adjuvant chemotherapy with cisplatin and 5-FU was given in 32/37 (87%) patients, 3/27 patients received RT followed by adjuvant chemotherapy and 2/37 patients received RT alone. Complete Response (CR) after definitive treatment was seen in 31/37 (84%) patients, 4/37 patients had partial response and 2/37 patients had progressive disease. There was no significant difference in EFS between stage 3 and 4 patients.

Conclusion: Majority of patients with paediatric NPC present with advanced stage disease at our centre. Even though a 84% of patients achieve CR, the 4 year EFS is only 56.7%.

P-0728 | Pleuropulmonary Blastoma: 25 Years of Experience at Texas Children's Cancer Center Rare Tumour Program

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Background/Objectives: Pleuropulmonary blastoma (PPB) is a rare primary lung cancer that occurs almost exclusively in young children. We describe the clinical features, treatment and outcome of patients treated at our institution.

Design/Methods: We retrospectively reviewed the medical records of all patients diagnosed with PPB at Texas Children's Hospital (TCH) from 1990 to 2014.

Results: Twenty-one patients were treated for PPB at TCH over a 25-year period. Thirteen of the patients (62%) were diagnosed with type I, 4 (19%) with type II and 4 (19%) with type III PPB. Median age at diagnosis was 26 months (range 0 -142 months), and two were diagnosed prenatally. The most common symptom at presentation was respiratory distress. Three patients (two type I and one type II PPB) presented with bilateral lung disease. Upfront complete surgical resection (CR) of the primary tumour was successful in 16 patients. Two patients had CR after neoadjuvant chemotherapy. One patient had positive surgical margins and two other patients had partial tumour resection (PR). All patients with type II or III PPB received chemotherapy that included vincristine, dactinomycin and cyclophosphamide (VAC) combined with doxorubicin, ifosfamide or cisplatin. Three patients (23%) with type I PPB received VAC chemotherapy. One patient with type III PPB and PR received radiotherapy. One patient with type II PPB recurred with type III, and one patient with type II PPB, who had positive surgical margins of the cystic component, recurred with type I. Eighteen patients were alive at last follow-up. All three patients who died (one type II and two type III PPB) had an incomplete surgical resection. The 5-year overall survival was 73% (95% CI: 46 - 100%).

Conclusion: All patients with type I PPB had an excellent outcome following complete surgical resection regardless of chemotherapy. Complete surgical resection was necessary for cure in type II and III patients.

P-0729 | Paediatric Salivary Glands Carcinomas: Diagnostic and Therapeutic Management

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Background/Objectives: Carcinomas of salivary glands are rare in children. Pediatric clinical specificities and optimal treatment remain unclear. Analyze clinical presentation, treatment modalities and evolution of paediatric cases of salivary gland carcinomas in order to discuss a standardized approach in these rare diseases.

Design/Methods: We included in this retrospective study all children and adolescents (≤ 18 years) treated from 1992 to 2014 in 6 paediatric centers in Paris area. Pathologic tumour specimens' review was planned.

Results: Forty-three children were selected (sex ratio M/F=19/24, median age=13years). Four (9%) patients had a previous history of another malignancy. Parotid glands were mainly concerned (37 cases). Histological subtypes were mucoepidermoid carcinomas (n=19), acinic cell carcinomas (n=15), and other subtypes (n=9). Initial fine needle aspiration was performed in 15 cases (33%), and was concordant to final diagnosis in only 3 cases (20%). Primary surgery was performed in 42 patients: 30 total parotidectomies, 3 superficial parotidectomies, 5 tumorectomies and 2 other gland exeresis (2 missing data), leading to a complete microscopic resection in 80%. Overall concordance of histologic diagnosis during frozen section analysis was only 56%. Associated lymph node dissection was performed in 29 patients (homolateral: 28; bilateral: 1) and showed lymph node metastases in 3 patients. One patient had distant metastases. Adjuvant irradiation was delivered to 10 patients (median: 60 Gy; Range: 50-65) and chemotherapy in 5 cases. After a median follow-up of 5 years, 6 tumors relapse but no death occurred.

Conclusion: Childhood salivary glands carcinomas have good prognosis despite possible recurrences. Fine needle aspiration (mainly to eliminate differential diagnosis) and extemporaneous histologic examination are helpful but not totally reliable. Treatment is mainly based on surgery, with simultaneous node dissection in case of clinical or radiologic node enlargement. Radiation therapy seems to be restricted to inoperable high grade tumors or after recurrence.

P-0730 | Paediatric Investigation Plan (PIP) - Triggered Trials in Adolescents with Metastasized Melanoma: Questionable Value and Unethical

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Background/Objectives: With few exceptions, EU paediatric legislation requires all drugs in development for adult malignancies to also be tested in minors according to a paediatric investigation plan (PIP) approved by the Paediatric Committee (PDCO) of the European Medicines Agency (EMA). In 2008 the EMA removed adolescent melanoma from the official list of diseases exempted from PIPs, claiming that enough adolescent patients exist for clinical trials. Published concerns about PIP-imposed melanoma trials are based on (1) the rarity of paediatric melanoma, (2) inclusion of adult patients in the EMA justification, that (3) 75% of adolescent melanoma patients need no systemic treatment (only surgical removal); and (4) that the physiology of adolescents >15 years old is indistinguishable from adults. We questioned whether these legitimate concerns influenced EMA decisions, and if PIP decisions translated into clinical trials.

Design/Methods: We examined PIP decisions on the EMA website (1) using the keyword 'melanoma' in the website search function, and (2) by screening the full text of all oncology PIP decisions. We also searched www.clinicaltrials.gov for worldwide melanoma trials that are also recruiting minors.

Results: We found 6 melanoma PIPs using the keyword 'melanoma' and 2 more through our text search that include melanoma in various paediatric malignancies studied. We identified worldwide 45 clinical melanoma trials also recruiting minors, performed predominantly

by research centers, and 4 obviously PIP-triggered global industry-sponsored trials recruiting exclusively adolescents aged 12-17 years with metastasized melanoma.

Conclusion: The EMA melanoma PIP policy remains unchanged. This has translated into actively recruiting, industry-sponsored clinical trials that will not recruit enough patients for meaningful results and that compete for subjects with important academic trials. This makes both the conduct of these trials and the EMA PIP decisions that triggered them of questionable value and unethical.

P-0731 | Kaposiform Hemangioendothelioma: A Benign Vascular Tumour with Multiple Treatment Options, A Systematic Literature Review

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Background/Objectives: A kaposiform hemangioendothelioma (KHE) is a rare vascular malformation of the infant and young child. Although this tumour is benign, it can be associated with severe morbidity and mortality especially with a Kasabach-Merritt Syndrome (KMS). Until now there are only case reports or small series published. We conducted a literature search to collect data and make recommendations for future treatment trials.

Design/Methods: Within 1993 and 2013 we found 75 publications with 157 patients <21 years. We added 12 patients from our department and 4 from the CWS-data base. We collected the following data: localisation and size of the tumour, presence of KMS, applied therapy, response and outcome.

Results: We found that KMS was present in infants in 77%, in patients 1-5y in 48%, 6-12y in 30% and 13-21y in 13% (99pts). All children with tumour located in the retroperitoneum, mediastinum and region exceeding tumours had a KMS (25pts). KHE without KMS had a median size of 12 cm², KHE with KMS 49 cm² (44pts). With complete resection all patients were cured (32pts). In case of inoperability response regarding KMS was seen in 62% with vincristine (28/45pts, 5 with monotherapy), in 43% with interferon-alpha (16/37pts, 9 monotherapy) and in 31% with steroids (19/62pts, 3 monotherapy). Regression of the tumour size was seen in 54% with vincristine (26/48pts, 6 monotherapy), in 39% with interferon-alpha (15/39pts, 7 monotherapy) and in 31% with steroids (22/70, 6 monotherapy). All patients with sirolimus had a response regarding KMS (4pts) and regression in tumour size (5pts).

Conclusion: Patients with resectable KHE should undergo complete resection. For patients with unresectable tumour we recommend sirolimus since it showed excellent response in the few patients reported. In case of non-response we would recommend vincristine. Sirolimus should be examined in a prospective study.

P-0732 | TP53 p.R337H Loses its Function of Inducing Dna Damage-Induced Apoptosis in Cell Lines Grown Under Alkaline Conditions

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Background/Objectives: The high incidence of adrenocortical tumors in children from Brazil is associated with p.R337H mutation. The tetramer mutation TP53 p.R337H activity may be affected by the alkalization of intracellular pH. We investigate the p.R337H function in cell-lines grown under alkaline conditions and compare its activity with another tetramer mutant p.R337C.

Design/Methods: Saos-2(TP53-null) and NCIH295(TP53-mutant) cell-lines were grown at 2% or 5% CO₂. p.R337H and p.R337C mutants were generated through site-directed mutagenesis. Luciferase assays were conducted using dual-luciferase kit. Western blot, clonogenic assay and apoptosis of cells treated or not with doxorubicin were carried out.

Results: Growing of cells at 2% CO₂ for 48h caused pHi to increase. Luciferase activity showed that p.R337H and p.R337C mutations displayed decreased activity versus WT in both cell-lines at 5% CO₂, however, at 2% there was a reduction in the WT that lead to a lack of activity difference between the p53 variants. Functionally, the two mutants retained significant levels of wild-type function to interfere with Saos-2 colony formation. Saos-2 cells transfected with the mutants underwent apoptosis at a similar level to that of WT at 5% CO₂. However, at 2% CO₂ there was a drop in the TP53^{p.R337C} capacity to induce apoptosis compared to TP53^{WT} and TP53^{p.R337H}. Moreover, TP53^{p.R337C} transfected cells treated with the DNA damage agent doxorubicin are not able to cause apoptosis either at 5 or 2% CO₂, while the TP53^{p.R337H} transfected cells(dox treated) keeps its apoptosis induction capacity at 5% but it loses this ability at 2% CO₂.

Conclusion: The underlying mechanisms of TP53 tetramer mutations p.R337H and p.R337C are distinct. While both mutants are able to affects cell growth in a similar way to TP53^{WT}, TP53^{p.R337C} apoptosis function is strongly affected by intracellular pH alkalization whereas TP53^{p.R337H} only loses its apoptosis function when it is triggered by DNA damage mechanisms at alkaline conditions.

P-0733 | Pleuropulmonary Blastoma: 20-Year Experience at the National Institute of Paediatrics, Mexico

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Background/Objectives: Pleuropulmonary blastoma (PPB) is an exceedingly rare malignant primary lung tumour of infancy. Three types are described: I: cystic, II: cystic/solid, and III: solid. Progression between types is well documented. It presents with non-specific respiratory symptoms. Treatment includes resection and chemotherapy for type I, radiotherapy added for types II and III lesions.

Design/Methods: Patients treated for PPB at the Surgical Oncology Department of the National Institute of Pediatrics (1995-2015) where retrospectively studied. Age, sex, clinical and radiological findings, surgical details, histology, adjuvant treatment, and follow-up were recorded. Survival was calculated through Kaplan-Meier.

Results: There were 10 cases with equal sex distribution and a median age of 4 years (2-8). Nine presented with respiratory distress, one had pleural effusion and another pneumothorax. Other symptoms included fever, chest pain and weight loss. One had history of cystic lung malformation. Nine had a solid mass on CT (Right sided in four, left in five and one bilateral). Most common Dehner type was III (60%), with type I only in one patient. One child was admitted on ventilator support and died before surgery. Posterolateral thoracotomy was performed in six cases, median sternotomy in two, and clamshell thoracotomy in one, achieving complete resection in 8 children. One had incomplete resection due to pulmonary vein involvement. Average blood loss during surgery was 650 ml (100-1200), ICU stay was 6.6 days (1-30), and chest tube was removed on postoperative day 4 (3-5).

All received chemotherapy and radiotherapy, except 3 patients (type III) when no RT was available. Five-year overall survival is 70% (95%CI 16.9%-100%).

Conclusion: PPB is a rare paediatric primary lung malignancy, presenting with non-specific respiratory symptoms. Study of choice is CT-scan. Multimodal therapy is used. Complete resection is paramount to avoid recurrence and achieve survival.

Our higher incidence of type III tumors may represent an effect of referral center.

P-0734 | Primary Lymphoma of the Ovary. Case Report and Literature Review

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Background/Objectives: Ovary is the most common primary site for lymphomas affecting female genitalia. Presentation is insidious and non-specific, but lower abdominal pain and a pelvic mass are common clinical findings. They are mostly detected incidentally. Surgery and chemotherapy are standard treatment.

Design/Methods: Case Report:

This 12-year-old girl was two years into routine follow-up after surviving ALL. She presented with a pelvic mass and a CT identified an ovarian tumour.

Results: Neoadjuvant chemotherapy achieved a 50% volume reduction and she underwent surgical paediatric ovarian protocol. Pathology reported primary ovarian non-Hodgkin lymphoma with leukemic infiltration to Douglas pouch and pelvic peritoneum, with free fluid positive for blast cells.

She is currently stable (three months after surgery), undergoing intensified chemotherapy, restaged to protocol BFM 90 for very high-risk.

Conclusion: Although primary ovarian lymphoma is rare, incidence has increased over the past decades. A high index of suspicion is needed to detect these lesions. Even though lymphoma is a systemic disease, surgery confirms the diagnosis and prevents complications such as torsion, bleeding, and mass effect on pelvic organs.

P-0735 | A Single Institutional Experience of Hypofractionated Intensity Modulated Chemoradiotherapy in the Treatment of Nasopharyngeal Cancer in Children and Adolescents

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Background/Objectives: Paediatric nasopharyngeal carcinoma (NPC) is very uncommon, with an incidence of around 1 per 1 million per year in children and adolescents (Casanova et al). Over 90% of cases present with advanced disease, with a survival rate of >70%. Combined modality treatment with chemoradiation is the standard of care, however, this is associated with significant treatment related toxicities (Merten et al).

The aim of this review was to evaluate the toxicities experienced and the outcome of patients whom had received hypofractionated intensity modulated radiotherapy (IMRT) with simultaneous integrated boost (SIB) at the Royal Marsden Hospital.

Design/Methods: A retrospective data collection of patients, aged ≤ 18 years with histologically proven NPC, treated at The Royal Marsden Hospital since 2005. All eligible patients were treated according to the paediatric NPC protocol: IMRT dose-fractionation regimen of 57Gy/25# to primary tumour and involved lymph nodes; and 45Gy/25# to uninvolved elective nodal group, with at least 2 cycles of neoadjuvant Cisplatin and 5Fluorouracil. Demographics, diagnostic information, toxicities (CTCAE 4.0) and outcomes were collected.

Results: Twenty-five patients were selected from the database and six patients were eligible for data collection, aged 10-16 at diagnosis. The median follow-up period was 45 months. Two patients had stage III disease and the rest had stage IV disease.

Apart from a single patient experiencing out-of-field disease progression, all the other patients in the cohort are alive and disease free.

Grade 3 acute toxicities (CTCAE 4.0) were observed in all the patients, most notably pharyngeal mucositis and the requirement for feeding tubes. No cardiac or ototoxicity was seen. Significant Grade 3 (G3) late toxicity is seen in only 1 patient treated for hypothyroidism and hypopituitarism, other long term side effects include trismus (G2) and xerostomia(G1).

Conclusion: IMRT with SIB is feasible and effective in paediatric NPC, which offers excellent locoregional control and comparable toxicity profiles.

P-0736 | Thymus Tumors in Paediatric Patients. A Report from the European Cooperative Study Group for Paediatric Rare Tumors (EXPERT)

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Background/Objectives: Thymoma and thymic carcinoma are exceptional tumors in paediatric population. Histologically they are categorized according to the WHO classification. Thymic carcinoma is highly aggressive, may arise from malignant transformation of a pre-existing thymoma and have poor prognosis due to the local invasiveness and the risk of metastasis. The commonest staging system is the Masaoka classification. Most thymomas are associated with autoimmune disease. The prognosis of patients with invasive thymoma and thymic carcinoma remains poor despite multidisciplinary approach. There are no standardized therapeutic guidelines in children.

Design/Methods: Retrospective analysis of clinical data and therapeutic characteristics of paediatric patients less than 18 year with thymic tumors treated between 2000 and 2012 registered in the EXPERT database of the cooperating national rare paediatric tumors working groups from France, Italy, Germany, United Kingdom and Poland.

Results: Sixteen children with thymoma, median age 11 years and 20 patients with thymic carcinoma, median age 14 years were enrolled into study. At diagnosis complete primary resection was possible in 11 patients with thymoma and one with thymic carcinoma; R1 resection was performed in 3 cases and R2 in 4p. Chemotherapy with various regimens was administered to 22 children; 17 of them as neoadjuvant chemotherapy. Eight patients with thymic carcinoma received additional radiotherapy. Seventeen children died (15 thymic carcinoma, 2 thymoma). Five-year overall survival for patients with thymic carcinoma is 21.0±10.0%.

Conclusion: Prognosis in patients with thymic ca is poor, so multidisciplinary team discussion is mandatory at diagnosis and during therapy.

P-0737 | Paediatric Inflammatory Myofibroblastic Tumours - A Single Centre Experience

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Background/Objectives: Inflammatory myofibroblastic tumours (IMT) are unusual tumours that occur in soft tissues and visceral organs of children and young adults. The tumours consist of myofibroblastic spindle cells and inflammatory cells and are believed to be of intermediate malignant potential since they can be locally aggressive, recur or rarely metastasize. There are no clear consensus guidelines on treatment for patients with such tumours. We describe our experience with a case series from our tertiary academic paediatric institute in Singapore.

Design/Methods: All paper and electronic records, and histology slides of patients diagnosed with IMT between 1997-2012 were reviewed retrospectively.

Results: Three patients diagnosed with IMT were identified. All patients had intra-abdominal tumours (omentum, spleen, supra-renal) with one patient also having a concurrent IMT located in the left hemi-thorax. Histopathological findings reported positivity for ALK -1 stain in 2 patients. Primary complete surgical resection of the tumours was attempted without achieving complete remission and hence adjuvant chemotherapy was administered in all cases. A variety of chemotherapeutic agents in combinations were used as adjuvant therapy as per physician preference. Two patients also received monotherapy with non-steroidal anti-inflammatory drug (NSAID) when the tumours did not respond to chemotherapy. Both the patients on NSAID therapy showed partial response initially and then progressed. One patient with aggressive IMT died due to neutropenic sepsis. The mTOR inhibitor sirolimus was started on one patient who now remains with stable disease for the past three years. Another patient subsequently developed further intra-abdominal masses and remains in remission after further surgery. These two patients remain on active follow up.

Conclusion: Sirolimus appears to offer disease control in children with inoperable or resistant inflammatory myofibroblastic tumours. Further studies need to be done to understand these tumours better.

P-0738 | Long-Term Health Related-Quality of Life, Fatigue, and Anxiety and Depression in Adult Survivors of Paediatric Differentiated Thyroid Carcinoma

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Background/Objectives: Pediatric differentiated thyroid carcinoma (DTC) is an uncommon malignancy with an excellent survival. Little is known about long-term quality of life (QoL) of survivors. The aim of this study was to evaluate self-reported levels of health-related quality of life (HRQoL), fatigue, anxiety and depression in adult survivors of paediatric DTC, compared with controls.

Design/Methods: Adult survivors of paediatric DTC, diagnosed between 1970 and 2013 at age <18 years and treated in The Netherlands were included. Exclusion criteria were a follow-up <5 years, diagnosis of a secondary malignancy or lack of command of the Dutch language. Controls were matched by age, gender and socio-economic status. All survivors and controls were asked to complete 3 questionnaires (SF-36 (HRQoL), MFI-20 (fatigue) and HADS (anxiety/depression)).

Results: Sixty-seven survivors and 56 controls were included. Median age of survivors at evaluation was 34.0 years (range 19-60). Most survivors (all Dutch) were female (86.6%), were married/in a relationship (64.2%), and were employed/active students (91.0%). Median follow-up after diagnosis was 17.6 years (range 5-45). On most subscales of the three QoL questionnaires, scores of survivors and controls did not differ significantly. Survivors suffered more than controls from physical problems ($P = .031$), role limitations due to physical problems ($P = .021$), and mental fatigue ($P = .016$). For 13/16 subscales, scores were more dispersed towards worse well being in survivors. Longer follow-up was correlated with higher vitality ($P = .044$). Other tumour-, treatment-, and follow-up characteristics were not associated with well being in survivors.

Conclusion: This is the first study to evaluate long-term QoL in adult survivors of paediatric DTC. Overall, survivors of paediatric DTC do well with regard to HRQoL, fatigue, and anxiety and depression. However, a small subset of the survivors is more prone to develop worse QoL. Longer follow-up after diagnosis is associated with better QoL.

P-0739 | Diastolic Dysfunction is Common in Long-Term Survivors of Paediatric Differentiated Thyroid Carcinoma

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Background/Objectives: Long-term exogenous subclinical hyperthyroidism has been associated with diastolic dysfunction in survivors of adult-onset differentiated thyroid carcinoma (DTC). The presence of cardiac abnormalities in survivors of paediatric DTC is unknown. Our objectives were to study the prevalence of systolic and diastolic dysfunction in survivors of paediatric DTC in relation to the level of TSH suppression during follow-up, and to assess the association between diastolic dysfunction and plasma biomarkers.

Design/Methods: In this prospective multicenter study, cardiac assessments were performed in 66 more than 5-year survivors of paediatric DTC (age at diagnosis ≤18 years) treated in the Netherlands between 1970 and 2009. Evaluation included echocardiography with measurements of systolic and diastolic functions, and assessment of plasma biomarkers (N-Terminal-pro brain natriuretic peptide, high-sensitive Troponin-T, galectin-3). Echocardiographic measurements were compared with retrospective data of 66 sex- and age matched unaffected Dutch controls. Multivariate linear regression analysis was performed to explore the association between diastolic function and TSH level.

Results: The survivors (86.4% women) had a median age at diagnosis of 15.9 (7.9-18.9) years. Median follow-up time was 16.7 (range 4.8 to 42.9) years. Left ventricular ejection fraction <50% was found in 1 survivor, and median longitudinal strain was -19.6% (range -24.2 to -17.6%). However, diastolic dysfunction was present in 14 asymptomatic survivors (21.2%). Overall, diastolic function of survivors was decreased compared to controls (e' mean 14.8 versus 16.0 cm/s, $p = 0.013$). TSH level during follow-up was not associated with diastolic function in survivors. Biomarkers were not associated with diastolic dysfunction.

Conclusion: While systolic function is unaffected, diastolic dysfunction is frequently observed in asymptomatic long-term survivors of paediatric DTC compared to unaffected age- and sex matched controls. TSH levels during follow-up are not associated with diastolic function. More research is needed to reveal the cause and clinical implications of our findings.

P-0740 | From Common to Rare: Paediatric Head and Neck Tumors with Radiopathologic Correlation

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Background/Objectives: Approximately 12% of paediatric tumors occur in the head and neck. Radiologists play a critical role in determining an initial diagnosis, preparing for surgical intervention, and guiding treatment. The goal of this exhibit is to assist learners in developing an approach to both common and rare paediatric head and neck tumors.

Design/Methods: The information will be presented in a case based format to display key imaging findings on CT and MRI of both benign and malignant paediatric head and neck masses. The pictorial review will showcase both common and rarer tumors to allow viewers to establish a comprehensive differential diagnosis. It will also include pertinent epidemiological, radiographic, and pathological findings to allow viewers to gain a thorough understanding of each malignancy. The exhibit will begin with more prevalent tumors such as non-hodgkin lymphoma, rhabdomyosarcoma, and neurofibromatosis type 1 and will then move on to less commonly encountered tumors such as esthesioneuroblastoma, juvenile nasopharyngeal angiofibroma, and sinonasal hemangiopericytoma. It will end with a table summarizing key imaging findings of paediatric head and neck masses as well as a table categorizing head and neck masses based on several distinguishing characteristics.

Results: There are key imaging findings on CT and MRI that point to certain paediatric head and neck tumors. These findings, as well as pertinent information regarding epidemiology, clinical history, and radiopathologic correlation allow a thorough understanding and establishment of a differential diagnosis.

Conclusion: The incidence of paediatric head and neck tumors has increased by 45% over the years. With cancer being the second leading cause of death in the paediatric population, having a fundamental knowledge of paediatric head and neck tumors is vital to a practicing radiologist. This case based presentation will allow learners to integrate clinical information with key radiologic features to arrive at a limited, and in many cases, a specific diagnosis.

P-0741 | Serum Levels of Vascular Endothelial Growth Factor and Basic Fibroblast Growth Factor in Infantile Hemangiomas Treated with Propranolol

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Background/Objectives: Vascular Endothelial Growth Factor (VEGF) and basic Fibroblast Growth Factor (bFGF) are the two angiogenic factors that play central role in the pathogenesis of infantile hemangiomas (IH). In this study, we aimed to investigate the relationship between serum VEGF and bFGF levels and clinical characteristics in infants diagnosed with IH.

Design/Methods: Blood samples were taken from 34 IH patients and 10 healthy babies as the control group. Serum VEGF and bFGF levels of patients and controls at the time of diagnosis, studied by ELISA, were compared. The relationship between serum VEGF and bFGF levels and clinical characteristics and their courses in the follow up were analyzed in 18 infants treated with propranolol and followed regularly.

Results: At the time of diagnosis, median serum levels of bFGF were: IH patients (n=34) 11.1 pg/mL (4.8-16.6), controls 2.6 pg/mL (1.7-4.7) [p<0.001]; median serum levels of VEGF were: IH patients 58.5 pg/mL (25.3-190.2), controls 11.4 pg/mL (8.2-19.8) [p<0.001], respectively. Serum VEGF and bFGF levels were not correlated. In 18 infants treated with propranolol and followed regularly, at initial diagnosis, the first and third months, median serum levels of bFGF were 10.8, 9.8 and 10.5 pg/mL (p=0.8); median serum levels of VEGF were 68.6, 63.5 and 45.1 pg/mL (p<0.001), respectively. Median percent regression rates of the hemangiomas by size and appearance at the first and third months were -%47.3 and -%58.3 (p<0.001), respectively.

Conclusion: Serum VEGF and bFGF levels were significantly elevated in IHs. Decline in the serum VEGF levels seem to follow the natural course of IHs; while the contribution of propranolol treatment should also be considered, possibly by downregulation of VEGF expression. Serum VEGF levels might be a marker for IH follow-up. Despite decline in VEGF levels, bFGF levels remained high which might indicate different effects in the pathogenesis and course of IHs.

RENAL TUMOURS

P-0742 | Five Year Experience of Wilms Tumour at a Tertiary Care Centre, Where We Stand, A Developing Country Perspective

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Background/Objectives: The main objective of the study is to discuss presentation and outcome of children with Wilms tumour (WT).

Design/Methods: We present a retrospective study, looking at demographics and outcome of children with WT presented to the haematology and oncology department of the Children's hospital Lahore between January 2009 and December 2013.

All Children diagnosed as WT on radiological findings and proven on histopathology after needle biopsy were included. Data regarding age, gender, initial staging and outcome were recorded and analyzed. CT scan abdomen, chest and needle biopsy were done in almost all patients. According to SIOP WT 2001 (UKCCSG) Protocol all patients were treated with Pre-operative chemotherapy, surgery followed by post-operative chemotherapy and radiotherapy in some cases. Results were analysed by using SPSS version 16.

Results: A total of 175 patients were included. Males and females were equal in number 51.4% and 48.6% respectively. Majority 88(50%) were between 2-5 years of age, 44(25%) patients were above 5 years and 43(24.6%) below 2 years. Majority 150 (86%) presented on initial diagnosis without getting any treatment. Sixty two (36%) presented in stage III, 37 (21%) stage

IV metastatic disease, 26 (15%) stage II and only 5% in stage I and V each. Seventy four (42.2%) patients had completed treatment advice, 20(11.4%) died and 10(5%) had relapse while 65(22.2%) were lost to follow up with missing record.

Conclusion: Most of patients presented at less than five year of age with advance disease stage III and IV. Treatment outcome is fair 42.2% with abandonment and 67% without abandonment with overall mortality 11.4%. Abandonment is major factor affecting the overall survival rate.

P-0743 | Hook-Wired Tomography-Guided Pulmonary Metastasis Resection in Paediatric Wilms Tumour

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Background/Objectives: This study aims to evaluate the usefulness of pulmonary metastasis resection in children with Wilms tumour.

Design/Methods: We retrospectively reviewed medical records of children diagnosed of Wilms tumour in our hospital between January 2000 and 2016. All patients received treatment according to SIOP-2001 protocol. The patients were evaluated based on age, gender, stage at diagnosis and after induction treatment, surgical procedures performed on pulmonary metastasis, and histology.

Results: Among 37 children diagnosed of Wilms Tumour (20 boys; 17 girls). There were 14 patients Stage I (38%), 6 stage II (16%), 6 Stage III (16%), 2 stage V (5%) and 9 stage IV at diagnosis (25%; 8 due to pulmonary metastasis and 1 hepatic metastasis). One stage III patient developed pulmonary metastasis during a complication (sinusoid obstruction syndrome); and one stage I patient relapsed with local and pulmonary metastatic disease.

So, out of 10 patients with pulmonary metastasis (8 at diagnosis, 1 relapse and 1 progression disease), indication for pulmonary metastasis resection was made in 6 cases with persistent metastatic nodules. A total of 5 hook-wire tomography-guided thoracoscopies and 1 thoracotomy were performed. Histology of resections made after induction chemotherapy (due to doubtful nodule images) was negative for tumour in all 3 cases, avoiding pulmonary radiotherapy in all of them and anthracyclines in 2 cases (the other one was stage III so anthracyclines were still indicated). Resections made after treatment were performed in 3 patients, one of them as a local treatment (thoracotomy) and 2 in patients who had already received pulmonary radiotherapy, and avoided further treatments due to negative result.

Conclusion: Multidisciplinary treatment involving paediatric oncologists, surgeons, radiologists and radiotherapists is key for patients with Stage IV Wilms tumour. Hook-wire tomography-guided thoracoscopy for pulmonary metastasis resection may be worthwhile to avoid anthracyclines or pulmonary radiotherapy in some cases with low grade of complications.

P-0744 | Renal Tumors in Children: A Report from a Single Institution in Algeria

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Background/Objectives: Renal tumors are relatively frequent in young children. Imaging plays a key role both at diagnosis that during follow-up. Etiology is dominated by Wilms tumors (WT).

Purpose: Describe patients' characteristics, and to evaluate their outcome

Design/Methods: We retrospectively reviewed a series of 78 children diagnosed in the Pediatric Oncology Unit of CHU de Beni Messous, from 1st January 2003 to 31th December 2015 as having a renal tumour.

Patients were classified and treated according to the SIOP protocol regimens, with a follow up time varying from 6 to 132 months.

Results: Of 78 patients, 74 were identified, as having a Wilms tumour, including 15 with bilateral presentation. There were 4 patients with renal sarcoma (2 cases), adenocarcinoma (1 case) and Bolande tumour (1 case). Age ranged from 2 months to 11 years. Majority was aged less than 5 years and 25% of patients were younger than one year at diagnosis. Tumors were initially documented by ultrasound in most cases, chest X-ray was routinely performed, and has demonstrated pulmonary locations in 7 cases. However, referred patients presented more often, with abdominal CT.

Management consisted on preoperative chemotherapy followed by nephrectomy, and / or tumorectomy in bilateral forms. Radiotherapy was performed in less than 10%. The overall survival was 84%.

Conclusion: Outcome of patients with Wilms tumour has considerably improved in Algeria thanks to advances in imaging process and chemotherapy.

P-0745 | Hemolytic Uremic Syndrome in Paediatric Patients with Wilms Tumour

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Background/Objectives: Wilms tumour (WT) is the most common paediatric renal malignancy in the United States. Survivors with unilateral nephrectomy are at higher risk for subsequent renal injury. Hemolytic uremic syndrome (HUS), consisting of microangiopathic hemolytic anemia, thrombocytopenia and acute kidney failure, is a common cause of paediatric kidney injury. HUS in WT patients has not been reported.

Design/Methods: Retrospective review of the National Wilms Tumour Study (NWTs) database and a single institution database (St. Jude Children's Research Hospital, SJCRH) for patients diagnosed with WT and HUS. Pertinent clinical data were identified.

Results: Three patients (2 male) were identified from NWTs3 (n=2496), NWTs4 (n=3335) and NWTs5 (n=3031). One patient was diagnosed at SJCRH. No prior case of HUS was identified in an institutional database (n=438). Patients were Caucasian (n=2), Hispanic (n=1), and African American (n=1). Two patients had stage I, favorable histology, one patient had stage II FH with local spill during surgery, and one patient (stage III, diffuse anaplasia) presented with pre-operative rupture. All patients received chemotherapy (as per EE4A, n=3; as per Regimen I, n=1). Two patients received whole abdomen radiation; both patients were diagnosed with HUS four months following radiation. Supportive care for HUS included transfusions (n=4), peritoneal dialysis (n=1) and ecuzimab (n=1). One patient was diagnosed with HUS prior to WT with subsequent end stage renal disease requiring dialysis. This patient received 12 weeks of chemotherapy and remained in remission, but died 23 years after WT diagnosis due to medical complications related to renal failure.

Conclusion: Patients with WT and unilateral nephrectomy may be at increased risk for further renal injury. HUS cases reported among WT patients may be higher than the incidence of HUS in the general paediatric population (2 per million). These patients present a therapeutic challenge and require intensive management to preserve adequate function of the remaining kidney.

P-0746 | Management of Bilateral Wilms Tumour (BWT) in One Center

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Background/Objectives: Management of BWT is challenging, focused on the eradication of tumour and preservation of renal function. We present our experience with such cases.

Design/Methods: Analysis of 30 patients (out of 212 patients with BWT: 27 synchronous, 3 metachronous-, 11m, 1y3m, 2yrs8m from 1-st diagnosis), 20 girls and 10 boys, median age 1yr8m treated between 1997-2014 was performed. Twenty nine patients were treated with pre-operative chemotherapy. 1 patient had a nephrectomy in the neonatal period. Type of preoperative chemotherapy: 2 drug ACTD, VCR or 3 drug ACTD, VCR, DOXO and its duration depended on tumour response. Post surgical treatment was carried out according to disease stage and histology. Treatment, tumour histology and outcomes were analyzed.

Results: Pre-resection chemotherapy with ACTD, VCR was administered to 4 patients, 26 required 3 drug chemotherapy (ACTD, VCR, DOXO) to decrease tumour volume. The median duration of preoperative chemotherapy was 3 months. 41 kidneys in 27 patients were managed with delayed resection: 16 complete unilateral nephrectomies, 6 partial nephrectomies and 7 tumour enucleations in 21 patients were performed; 6 pts had unresponsive to chemotherapy, progressive tumors and underwent bilateral nephrectomies. Two patients required irradiation – 1 to the one remaining kidney due to relapse, the other to one kidney with unresponsive to chemotherapy tumour. Tumour histology was as follows: standard risk 19 pts, high risk 8 pts (3 diffuse anaplasia, 5 blastemal type). Twenty five patients are alive with a median follow up of 7.5 years, 2 of them after bilateral nephrectomies with transplanted kidney. Five patients died, 3 of disseminated disease – all with unfavorable histology, 2 of dialysis complications.

Conclusion: Preoperative chemotherapy is crucial in the management of patients with BWT allowing to perform nephron sparing surgery. Type of chemotherapy and its duration must be adjusted to tumour response. Unresponsive tumors not amendable for resection require radical bilateral nephrectomies.

P-0747 | Renal Tumour Clinical Stage III: Are All Wilms? Debut Biopsy to Optimize Treatment and Increase Survival

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Background/Objectives: An accurate diagnosis etiological by histopathology in all renal tumour leads to a specific and timely treatment, increasing their survival.

To determine the importance of biopsy in Renal tumour clinical stage (EC) III.

Design/Methods: Epidemiological, descriptive-retrospective longitudinal case series study period from January 2000 to December 2015, aged 0-14 years in 51 cases of renal tumour of a population of 2033 cases of childhood cancer Rebagliati Hospital.

Results: Of the 51 patients with renal tumour EC III, 40 (78.43%) Wilms and 11 (21.57%) did not Wilms. Female / male 1.12. the age group was 6 (12%) under 1 year, 39 (76%) 1 to 5 years, 6 (12) over 5 years.

The 11 patients not Wilms: 4 sarcomas (36.36%), renal cyst 3 (27.27%), neuroblastoma 2 (18.18%). Neuroectodermic primitive (PNET) one (9%) and one lymphoma (9%).

Debut biopsy, 33 cases: Wilms 26 (78.78%) and 7 (21.22%) did not Wilms.

Eighteen patients were not biopsied, received neoadjuvant- chemotherapy standard risk, after that were nephrectomized 50%, and 50% after two courses more of chemotherapy high risk, where four cases were not Wilms (2 renal cyst, one neuroblastoma and one lymphoma) and 14 was Wilms: blastemals 50%, epithelial with poor necrosis 7.15% and mixed 42.85%.

In 26 Wilms confirmed by biopsy, 61.5% blastemal and 38.46% mixed; six cases anaplasia.

Forty Wilms received adjuvant chemotherapy high risk and radiotherapy and died 4 (10%), one intraoperative bleeding and three blastemals with anaplasia for relapse; of 11 cases not Wilms 5 died (45.45%): one febrile neutropenia and sepsis and 4 relapse. Renal cancer EC III in remission 81.63%. Overall survival 84.07 + - 2.3 months.

Conclusion: Biopsy in Renal tumour EC III contributes to an accurate diagnosis and specific treatment, avoiding mistakes in the etiology and inadequate or insufficient treatment for tumour histology Wilms blastemal or other kidney pathology.

P-0748 | Our Knowledge about Renal Cell Carcinoma in Children and Youth

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Background/Objectives: Scientific evidence about renal cell carcinoma (RCC) in children is missing. Sporadic case reports has been stated. The aim of our study are to assess the medical presentation and result in children with RCC.

Design/Methods: Evidence of 15 children and teenagers, from 2007 to 2011, who were treated for RCC were retrospectively investigated in oncologic paediatric unit of the Hospital "Mother Theresa" in Tirana, Albania. Age, scientific appearance, any tumour sign, hematological, biochemical examinations, pathological reports and treatment details were used from hospital proceedings and results were examined. The patients were recorded with total haemogram, biochemical examinations and ultra-sonography. They were followed-up for 5 years.

Results: All had undertaken open major nephrectomy with six hilar lymph node dissections and four formal lymph-adenectomy. None had obtained adjuvant therapy. Five patients with phase I were well at 5, 3.5, and 2 years. One patient with step I was lost to be recorded. Three patients with stage 2 were well at 5, 4 and 2 years of follow-up while two with stage 3 were well at 4 and 3 years of follow-up.

Conclusion: Lymph node dissection not only advances the survival, but it shows one the correct pathological performance and one can assume the more destructive follow-up in complex pathological staging and severe follow-up is obligatory.

P-0749 | Bilateral Wilms Tumour. Fifteen years-Experience following Siop Strategy in a Paediatric Tertiary Center of Argentina

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Background/Objectives: To analyze the clinical and pathological features and the outcome of patients with Bilateral Wilms tumour (BWT) and Wilms tumour (WT) in solitary kidney, diagnosed and treated in our hospital following SIOP 93-01 and 2001 protocols.

Design/Methods: Between December 1997 and July 2012, 144 patients with WT were diagnosed. A retrospective analysis of 23 patients with BWT (15.9%) (19 patients with bilateral synchronous tumors, include one with WT in a horseshoe kidney, and 4 with metachronic tumour) was performed.

Results: Median age at diagnosis was 18 months (range: 8-84), 16 females and 7 males. Eight patients had associated genetic abnormalities. All patients with synchronous tumors (n=19) received pre-operative chemotherapy with two (Vincristine plus Dactinomycin) or three drugs (plus Doxorubicine) according to protocol. One patient received high-risk protocol due to the possibility of bilateral nephrectomy. Only one patient had metastatic disease at diagnosis. Median time of neoadjuvant therapy was 4 weeks (4-21). A Nephron-sparing surgery in one kidney could be done in all patients however, eleven nephrectomies were performed. Among 37 pathological specimens reviewed: stage I=20, stage II=2, stage III=15. Only 2/37 had high-risk histology. Radiotherapy was adapted according to stage and histology. The median follow-up was 65.5 months (13.7-205.7). The 5y-EFS=0.78 and the 5y-OS=0.89.

Among 4 patients with metachronic tumors, 2 had metastatic disease. Nephrectomy was performed in two patients after intensified chemotherapy. One patients required renal graft and is still alive. The other patient died of disease progression. The 5y-EFS and 5y-OS were 0.75.

Nineteen out of 20 alive patients had normal renal function, one patient after renal graft.

Conclusion: In our series the strategy of preoperative chemotherapy and partial nephrectomies with the aim of preserving as much normal renal parenchyma as possible, has demonstrated safety and excellent results in terms of survival and renal function.

P-0750 | Results of Treatment of Bilateral Wilms Tumour: A Report from the Instituto Nacional De Pediatría, Mexico City, Mexico

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Background/Objectives: Treatment of bilateral Wilms tumour (BWT) presents the challenge of resecting the malignancy while preserving nephrons to avoid renal failure. In the NWTSG experience, 14.5% patients with BWT developed endstage renal disease (ESRD) at 20 years, most commonly associated with progressive disease, genetic predisposition, nephrotic effects of treatment, and hyperfiltration injury. The 8-year EFS was 74%.

Design/Methods: Retrospective, longitudinal and clinical study performed from January/1995-December/2011 in children younger 18 years old with BWT included in a multimodal approach based in NWTSG that included preoperative chemotherapy and nephron-sparing surgery for all patients, and radiation-therapy for select patients. Regimen DD-4A (Dactinomycin/Vincristine/Doxorubicin) was given. An initial biopsy was performed mainly to assess anaplastic histology.

Results: 8 (16.3%) of 49 Wilms tumors were BWT. At diagnosis, all had synchronous disease, median age was 18months (6-90months), 5 (62.5%) were male, all patients had an abdominal mass, 87.5% abdominal pain, 62.5% microscopic hematuria (no macroscopic hematuria was reported), 25% hypertension, 25% fever, 50% had metastatic disease (lung 50%, liver 25%, and distant lymph nodes 12.5%), and 50% had some known syndromic association (Denys-Drash and overgrowth-syndromes) or congenital anomalies (clubfoot-equinovarus, double renal pelvis and bilateral cystic renal dysplasia). Initial biopsy identified favorable histology in 7 patients and anaplastic histology in 1 patient. Nephrogenic rest was presented in 50%. Preservation of renal tissue with clear margins was obtained in nephron-sparing surgery. Unilateral nephrectomy was also required in 3 patients by extensive tumour, radiation-therapy to the involved flank was given. 5-year EFS was 86%. No ESRD, no important toxicity and no second malignancies were observed at 15-year follow-up.

Conclusion: Substantial differences were observed in our results. It is possible that addition of doxorubicin could have contributed to improve EFS and enhance nephron-sparing surgery. Identifying anaplastic histology at initial biopsy allowed the assignment of appropriate treatment.

P-0751 | Wilms Tumour Treatment in Dar Es Salaam, Tanzania

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Background/Objectives: Wilms tumour accounts for 5-7% of childhood cancers worldwide. The 2 year survival rate in developed countries is reported to be 85-90%. There is limited data in resource poor settings, but reported survival rates are much lower. The aim of this study was to evaluate the patient characteristics, extent of disease, survival outcomes and complication rates of children treated for Wilms tumour in Dar es Salaam, Tanzania using a modified chemotherapeutic protocol.

Design/Methods: All patients admitted to Ocean Road Cancer Institute (ORCI) from January 2008 to December 2009 with Wilms tumour (presumed and subsequently confirmed where possible) were included. Patients received pre-operative and post-operative chemotherapy according to an adapted version of the SIOP WT2001 protocol. Outcomes were analysed at 8 months, 1, 2 and 5 years from their date of presentation.

Results: Twenty-eight patients met the inclusion criteria for this study. Presenting symptoms included abdominal distension (100%), abdominal pain (50%), fever (25%) and gross haematuria (21%). 50% (n=14) had metastases at presentation, and mean tumour volume at diagnosis (where available) was 1.48 litres. 86% (n=24) received pre-operative chemotherapy and underwent nephrectomy at a neighboring hospital. Of the remaining 14% (n=4), 3 had an up-front nephrectomy prior to presentation at ORCI and 1 died before initiating treatment. A further 7% (n=2) defaulted after surgery and 1 more patient was lost to follow up. Overall survival was 72%, 61%, 50% and 46% at 8 months, 1 year, 2 years and 5 years respectively.

Conclusion: The results of this study compare favorably to other similar African centres, possibly due to the free comprehensive treatment and the modified chemotherapeutic protocol. Despite this, outcomes continue to fall short of those in developed countries for a number of factors including delays in presentation and lack of resources. Ongoing work is required to further bridge this gap.

P-0752 | "Zero-Ischemia" Laparoscopic-Assisted Partial Nephrectomy for the Management of Selected Children with Wilms Tumors Following Neoadjuvant Chemotherapy

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Background/Objectives: To describe the experience and technique of zero-ischemia laparoscopic-assisted partial nephrectomy at The Hospital for Sick Children, as an alternative to the traditional open approach for nephron sparing surgery in selected children with Wilms tumors (WT).

Design/Methods: Patients with diagnosis of WT, treated with neoadjuvant chemotherapy and who underwent laparoscopic-assisted nephron-sparing surgery at the Hospital for Sick Children from 2012-2016 were identified and charts were reviewed retrospectively.

Results: Five patients were identified; all patients underwent successful resection. One patient required radical nephrectomy due to inability to safely define negative margins.

Mean operating time was 296.25 ± 57.35 minutes, with an average duration of pneumoperitoneum of 217.5 ± 30.95 minutes. No intra-operative tumour spillages occurred. Pathology revealed negative margins in all specimens. Tumors ranged in size from 1.8 to 5.6 cm in diameter. All tumors were confirmed to be WT.

Two cases of urinary leak occurred postoperatively, with spontaneous resolution. No other complications were observed. Normal renal function was preserved in all children.

At a mean follow up of 12.7 months, all patients have no evidence of recurrent disease in the area of resection. One child with metastatic disease at presentation has developed lung and liver recurrences.

Technique: Patients underwent laparoscopic exploration, laparoscopic lymph node sampling, kidney mobilization, vascular control and adrenal sparing. This was followed by open nephron-sparing surgery through a small flank incision; no clamping of the hilum or major renal branches was performed.

Conclusion: The herein presented laparoscopic-assisted partial nephrectomy strategy allows for safe nephron-sparing resection of selected WT with, few complications, good short-term disease free survival, and potentially better cosmesis and recovery than traditional open surgery.

P-0753 | A Multiscale Hypermodel to Predict the Nephroblastoma Response to Preoperative Chemotherapy

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Background/Objectives: According to the SIOP approach, treatment of nephroblastoma patients starts with preoperative chemotherapy. In around 10% of patients the tumour is not responding. If we would know this response, a stratification of patients according to such a prediction could be done already at the time of diagnosis.

Design/Methods: In a collaborative effort of basic scientists, clinicians, IT-specialists and lawyers, a multiscale hypermodel predicting the nephroblastoma response to preoperative chemotherapy at the time of diagnosis has been developed. This hypermodel is composed of different hypomodels including the Oncosimulator and metabolic, vasculature, biomechanical, molecular and gross phenomenological hypomodels.

Results: Clinical, imaging and molecular data (mainly miRNA) of single patients are used to fit the different hypomodels together with data from basic science simulating the cell kill ratio of actinomycin and vincristin in nephroblastoma. The different hypomodels composing the hypermodel will be explained. Clinicians have access to the hypermodel via the clinical research application framework (CRAF) of the CHIC project (<http://chic-vph.eu/>). It will be demonstrated how a clinician can run the nephroblastoma hypermodel using CRAF. First results are presented and compared with the real response to preoperative chemotherapy in individual patients.

Conclusion: After further validation and optimization of the hypermodel, the latter may serve as a decision support service in the future, if it precisely predicts the response to preoperative chemotherapy in single nephroblastoma patients.

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P-0754 | Renal Tumors in Infants

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Background/Objectives: Renal tumors are rare in children under 12 months of age. To better define the characteristic of renal tumors in infants authors reviewed their 12-year institutional experience.

Design/Methods: We retrospectively reviewed the medical database of 104 children with primary renal tumors, resected during the period 2003-2015. There were 9 (8.7%) infants in this group (6 boys and 3 girls). Age of diagnosis ranged from 1 day to 8 months (median 5.25 months). Two boys were diagnosed with Denys-Drash syndrome. Seven patients presented with abdominal mass at physical examination, 1 tumour was detected prenatally, in 1 case USG was performed because of fever and abdominal disorders. Four patients older than 6 months received pre- and postoperative chemotherapy in modified doses. All children underwent unilateral nephrectomy, in 1 case partial nephrectomy of the second kidney due to metachronic bilateral tumour was performed 1 month after first operation.

Results: Histopathologic examination showed Wilms tumour in 6/9 patients (5 were stage I, 1 stage II, all of intermediate risk histology), renal cell carcinoma with clear cell and papillary features in 1 patient, congenital mesoblastic nephroma (CMN) in 1 patient and multilocular cystic nephroma in 1 case. All children alive from 2 months to 12 years from diagnosis (median 37.5 months).

Conclusion: Normal 0 21 false false false PL X-NONE X-NONE

1. In our material the most common renal tumour in infants was Wilms tumour.
2. Renal tumors in infants generally present at an early stage and have an excellent prognosis overall, however in children older than 6 months chemotherapy in modified doses may be considered.

P-0755 | Outcome of Renal Tumours among Children at Single Center in a Developing Country

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Background/Objectives: Wilms tumour (WT) is the most common malignant renal tumour in children. Since the introduction of multi modal chemo-radiotherapy, 90% survival rates are now achievable. However paediatric onco-surgeons, in developing countries are still uncertain regarding different treatment practices, protocol of National Wilms Tumour study Group (NWST) follow immediate nephrectomy while Societe internationale D'oncologie Pediatrique (SIOP) follows pre-nephrectomy chemotherapy in patients. Our objective was to report the outcomes of both the therapies in a developing world tertiary center.

Design/Methods: Data representing children diagnosed as WT, between 1988- 2015 was retrospectively reviewed and analyzed via SPSS version 19.

Results: 52 patients were diagnosed with WT, 57% were male and most common age group was 1-5years (68%). 28 patient received SIOP whereas 21 received NWST protocol. In SIOP group 2/3rd underwent biopsy and all patients received pre chemotherapy followed by surgery. Post op 16 patients received radiotherapy and 10 chemotherapy. Recurrence was noted in 4 patients at 6 months and two patients expired. In NWST group all patients underwent complete excision and received post-surgery chemotherapy while 2 received additional radiotherapy. Recurrence was noted in 2 patients at 2 months and 1 year, one patient expired. No significant difference was found in terms of recurrence and mortality in both the groups. Surgical complications were 21% in SIOP as compared to 9% in NWST. A higher, Stage 3 tumour presentation was seen in SIOP compared to stage 1 in NWST group at initial presentation. 5 years survival rate was >80% with a mean of 119 and 114 months in SIOP and NWST respectively. A trend of increased use of SIOP and a decline in use of NWST protocol was documented from 1990 onwards.

Conclusion: A preset treatment protocol based on staging of tumors should be recommended in Guidelines.

P-0756 | Wilms Tumour: Single Center Experience

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Background/Objectives: To evaluate the clinical and pathological characteristics and treatment outcome of Wilms tumour (WT) cases treated in our institution.

Design/Methods: Between 1988-2016, patients with WT were reviewed retrospectively. Twenty-six patients were treated according to the TPOG-WT protocol, remaining patients were treated according to the NWST protocol. TPOG-WT treatments were stage-I favorable (FH) and unfavorable histology (UH) patients, VCR + Act-D; stage-2A FH, VCR + Act-D; stage-2B FH, VCR + Act-D + radiotherapy (RT); stages-3-4 FH, VCR + Act-D + adriamycin (ADR) + RT; stages-2-4 UH tumors, VCR + Act-D + ADR + etoposide + RT.

Results: Thirty-six patients were eligible out of 46. The median age was 45 months, M/F:1.6. Median duration of complaints was 1 month. There was one familial-WT. Genetic abnormalities were genitourinary abnormalities (n:6), hemihyperplasia (n:3), aniridia (n:1), Denys-Drash (n:1). Tumour was unilateral in 92% of cases. There were two patients with extrarenal-WT. Complete tumour resection was performed in all cases except of one case. There were intraoperative tumour rupture (n:3) and partial resection (n:1) in patients without neoadjuvant chemotherapy (n:17). Stage distribution was stage-1 31%, stage-2 19%, stage-3 17%, stage-4 31%, stage-5 3%. There were 11 metastatic patients (pulmonary:10, liver:3, bone:1). Histopathology revealed 81% FH, 19% UH. Radiotherapy was performed to the primary tumour site in 16 cases, to whole abdomen in two cases. Median follow-up-time was 45 months for all cases, and 5-years OS was 87%, 10, 15-years OS were 81%. Median relapse time:10 months. Pulmonary relapse occurred in 5 patients, one of them also had primary tumour relapse. Additional three patients had refractory disease. Five patients died with disease progression. 5, 10, 15-years EFS were 72%.

Conclusion: Surgical complications occurred in patients who didn't received neoadjuvant chemotherapy. Obtained survival rates were similar with original protocols. No prognostic factor could be determined owing to the limited patient number.

P-0757 | A Rare Entity: Bone Marrow Metastasis in a Patient with Wilms Tumour

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Background/Objectives: Wilms tumour (WT) is the most common primary malignant renal tumour of the childhood. The most frequent sites of metastases are the regional lymph nodes and the lungs. WT tumour metastases in the bone marrow is not expected and not included as part of the staging procedure. Here we present a 2- years old girl with WT and bone marrow metastasis.

Design/Methods: A 2-years old patient was referred to our department due to abdominal distention, ascites and dyspnea. The laparotomy was planned due to the abdominal mass in the previous center, but only a tru-cut biopsy could be taken since the tumour was too big to be grossly resected. Abdominal examination revealed a 5x5 cm hard, mobile and non-tender mass in the right lumbar region and ascites. Laboratory tests revealed normocytic, normochromic anemia (hemoglobin, 9.1 g/dL), high lactate dehydrogenase level (654 U/L) and elevated NSE level (84ng/ml). Contrast-enhanced MRI of the abdomen showed a heterogeneously enhancing lobulated solid-cystic mass measuring 8x5x7 cm in the upper pole of the right kidney. Since the NSE levels was too high, neuroblastoma (NBL) was taken into consideration in differential diagnosis. As the staging procedure of NBL, bone marrow biopsy was performed.

Results: Micrometastasis to bone marrow that was consistent with WT was determined in the bone marrow aspiration. After the 6th week of chemotherapy, the patient underwent nephroureterectomy and control bone marrow aspiration showed no metastatic cells.

Conclusion: WT presents with distant metastases in 12% of the patients during initial diagnosis; almost never metastasize to the BM and seldom require bone marrow evaluation. There are only limited number of case reports in the literature. In our patient, since NBL was in the differential diagnosis, bone marrow aspiration was performed and incidentally micrometastasis was found. Thus it is not worthy to do bone marrow aspiration in WT.

P-0758 | The Second Wilms Tumour (WT) Study (GFA NEPHRO II) of the French African Group of Paediatric Oncology (GFAOP) : Results from 3 North African Centers

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Background/Objectives: Following the first Nephroblastoma feasibility study of GFAOP (Moreira PBC 2011), this second trial was run from 2005-2011. The objectives were to evaluate improvements with respect to procedure, data collection and outcome.

Design/Methods: This prospective single arm study registered all children suspected of having renal tumour, but included in the trial only patients with diagnosis of unilateral standard risk WT. The protocol is identical to the initial GFAOPNEPHRO I study, based on the SIOP2001 protocol. Data was collected locally and sent for analyses to Gustave ROUSSY. Here we report results of 3 North-African centers (Morocco:2, Tunisia:1).

Results: Two hundred sixty seven children were registered, 42 of whom did not fulfill study criteria, 85 were excluded secondarily (6 preoperative deaths, 8 abandoned treatment, 47 unfavorable histology, 16 not WT, 8 poor response to initial treatment) leaving a trial study group of 140 (Casablanca: 53, Rabat: 63, Tunis: 24); 118 localized and 22 metastatic WT with metastases in lungs (21), liver (2) and brain (1). During the preoperative period, 86% children were treated according to protocol. After surgery and pathological findings, 53 (38%) were stage I, 31 (22%), stage II, 34 (24%) stage III. Seventy-nine percent of patients received post-operative chemotherapy according to protocol. Shortage of Dactinomycin was the main obstacle. Thirty-five patients (25/28 stage III, 10 stage IV) were irradiated. Twelve patients (8.5%) relapsed and 11 (7.8%) died, 7 following relapse. Eighteen patients (12.8%) were lost to follow up. At 3 years, EFS and OS after surgery were respectively 82.4% and 91.4% for all stages and 90% and 93% for localized stages.

Conclusion: Although caution must be taken given the high number of pre-operative exclusions, improvements are evident when compared to the previous study with excellent survival of operated patients. Further improvement will include better access to drugs and better follow-up.

P-0759 | What is Important for Congenital Mesoblastic Nephroma?

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Background/Objectives: Congenital mesoblastic nephroma (CMN) is most common renal tumour in neonatal period. Some of CMN could be diagnosed by prenatal ultrasound as renal or abdominal mass. In postnatal period, palpable abdominal mass, hematuria, hypertension, hypercalcemia, vomiting could appear. Treatment is nephroureterectomy and chemotherapy in selected cases.

Design/Methods: Cukurova University Medical Faculty Hospital records, between 2003 to 2016, were investigated and 8 CMN patients have been found. Diagnosis of CMN was re-evaluated and approved by the same researcher in Department of Pathology. Surgical details of 3 patients were not found as the operation had been undertaken at different medical centers.

Results: Five patients¹, operated and followed up at our hospital, mean age at the time of operation was 57 days. Two patients were male and 3 were female. Three patients had cellular, 1 patient had classic and 1 patient had mixed histological type. Renal hilar soft tissue tumour infiltration was found in 1 patient which had negative surgical border. One patient's surgical border was found tumour positive which has been treated with post operative chemotherapy. These patients followed up by Pediatric Oncology department. Each of 3 patients which did not treated at our hospital, had different histological type. One of them had perinephritic tissue tumour infiltration and it's surgical board was tumour negative. Partial nephrectomy has been done to 1 patient and ureter was not found in pathology specimens. Other 1 patient had both perinephritic tissue tumour infiltration and positive surgical border.

Conclusion: As CMN could reason to intra paranchimal and extra renal tumour infiltration, to attain total cure and to avoid from recurrence and metastasis of CMN, nephroureterectomy should be done with large margin. To reach successful treatment, patients should be operated and followed-up by experienced centers.

P-0760 | Clinical and Histological Correlation of Hepatic Venous-Occlusive Disease in Children Treated for Wilms Tumour

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Background/Objectives: The hepatic veno-occlusive disease (VOD) is a rare but potentially severe complication of chemotherapy (CT), well described in paediatric patients undergoing stem cell transplantation but also reported in patients treated for solid tumors, mostly for Wilms Tumour (WT).

Design/Methods: To assess the incidence and outcome of VOD, we conducted a retrospective study of 120 children treated for WT in our Institution according to SIOP93-01 or 2001 protocols over the past 20 years. We analyzed the clinical and laboratory features of hepatotoxicity (VOD was defined according to the McDonald criteria) and the histopathological abnormalities detected in the liver biopsy performed during nephrectomy following the preoperative CT. We also evaluated the long term liver function.

Results: A hepatotoxicity episode occurred in 16 patients (13%), compatible with VOD in 12 (10%); 8 were classified as moderate and 4 as severe with a child dying from multiorgan failure. Hepatotoxicity was more frequent in younger children, despite appropriate dose adaptation, and during preoperative CT (60%).

Sixtyseven liver biopsies were performed: in 5 cases the clinical diagnosis of VOD (occurring during preoperative CT) was confirmed; in 1 case biopsy diagnosed a VOD even if not all the clinical criteria were satisfied. Liver biopsies were not predictive for the development of VOD during postoperative chemotherapy. Hepatotoxicity did not affect survival and long term liver function resulted normal 0.5 to 18 years after the conclusion of treatment (median follow up 6.5 years).

Conclusion: VOD occurred in 10% of children with WT. Performing a liver biopsy at the time of nephrectomy appears to have a diagnostic but not prognostic value. The development of VOD during treatment does not reduce the chances of survival and does not damage the long term liver function.

P-0761 | Frequency and Outcome of Bilateral Wilms Tumour; Experience at Children's Cancer Hospital - Egypt 57357

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Background/Objectives: Bilateral Wilms tumour (BWT) is rare, accounting for 4 to 7% of all Wilms tumour patients. It poses the special challenge of establishing local tumour control while preserving renal function. This study aimed to assess frequency, clinical characteristics and treatment outcome in BWT patients.

Design/Methods: A retrospective study including all patients with BWT treated at Children's Cancer Hospital- Egypt 57357 from July 2007 to March 2012 were included and treated according to COG treatment guidelines.

Results: Twenty-five patients (9% of all Wilms tumour patients) presented during the study period, with a median age of 2.7 years (range 0.3 to 8.6 years). Four cases had associated congenital anomalies. Using the COG staging system, 20%, 12% and 68% of patients had stages I – III respectively. Metastatic BWT was present at diagnosis in 8 (32%) cases. Preoperative vincristine, actinomycin D, and doxorubicin chemotherapy was given in all cases for an average duration of 12 weeks. For the whole cohort, bilateral partial nephrectomy was performed in 5 cases, while 18 patients had radical nephrectomy in one kidney & partial nephrectomy in the other. Two patients died before surgery. Postoperative local radiotherapy was given in 13 cases (stage III local disease). Median follow up duration is 49 months; the 5 year overall survival (OS) and relapse free survival (RFS) are 71.2% and 55.7% respectively. Presence of metastatic disease was the only factor having statistically significant effect on OS and RFS. Treatment related complications were minimal, and end stage renal disease (ESRD) was reported in only 2 patients that required dialysis.

Conclusion: Multimodality therapy in BWT resulted in reasonable survival although 45% of patients had recurrent disease. ESRD remains a rare but significant long-term complication for these patients. Renal sparing surgery is technically feasible and should be offered to almost all children with BWT.

P-0762 | Outcomes of Children with Unilateral Wilms Tumour in Southern Vietnam

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Background/Objectives: The aim of this study was to evaluate the efficacy of SIOP 2001 protocol and to identify challenges that could be addressed in further adaption of treatment protocols in Vietnam.

Design/Methods: A retrospective analysis included 44 patients under the age of 15 years old who were diagnosed with unilateral Wilms tumour and treated according to SIOP 2001 protocol at the Children's Hospital No.2 from June 2011 to December 2014. The patients who were between 6 months and 5 years of age and had imaging characteristics compatible with Wilms tumour received pre-operative chemotherapy. Other patients who were either outside of the above age range, presenting with rupture at admission, or with unusual imaging findings underwent surgical excision first. Event free survival was defined as the time since initial surgery to recurrence, metastases, complications or intolerance of treatment. Survival rates were analyzed by Kaplan-Meier estimates using SPSS.

Results: Two-year overall survival (OS) and event free survival (EFS) rates were 89.5% and 88.7%, respectively. There was higher percentage of stage I disease in patients with pre-operative chemotherapy as compared to other patients (34.8% vs 19.0%, $p = 0.21$). There was lower rate of tumour spillage during surgery among patients who had pre-operative chemotherapy (4.3% vs 23.8%, $p = 0.09$). Pre-operative chemotherapy resulted in significant decrease in tumour volume (389.04 mL vs 227.72 mL, $p < 0.001$). Grade 3 and grade 4 therapy-related adverse events occurred in 11.2% and 5.1% patients, respectively. Four cases were treated

with chemotherapy first but the pathological findings of these cases were not Wilms tumour at surgery, representing a misdiagnosis rate of 14.8%.

Conclusion: Treating Wilms tumour according to SIOP 2001 protocol resulted in relatively high survival outcomes with acceptable rate of complications. We identified limitations in imaging and pathological studies as major challenges in applying SIOP 2001 protocol in Vietnam.

P-0763 | Characteristics of the Anaplastic Histology Wilms Tumors Registered to the Japan Wilms Tumour Study Group

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Background/Objectives: o evaluate the clinical features and treatment results of patients with anaplastic histology (AH) Wilms tumors (WT) in the Japan Wilms Tumour Study (JWiTS) group and compared the results with those from the fifth National Wilms Study (NWTS-5) group to describe elucidate the characteristics of AH WT between Japanese and American populations.

Design/Methods: Of 344 patients enrolled in JWiTS between 1995 and 2013, 17 had AH. JWiTS participants included nine boys and eight girls; mean age was 40.9 months. Chemotherapy and/or radiotherapy were performed according a protocol similar to that from NWTS-5. Records (clinical data, treatments, outcome, and TP53 mutation status) were collected, evaluated, and compared with those from NWTS-5.

Results: The incidence of AH in JWiTS was 4.9%, which was lower than that in NWTS-5. Seven tumors had focal AH and 10 had diffuse AH. The clinical stage was I in seven cases, II in three, III in five, and IV in one. There were no bilateral cases. The estimated rates of 4-year event-free survival and overall survival for assessable patients with AH were 90.9% and 86.7%, respectively. Genetic analysis revealed that two patients with diffuse AH had TP53 mutation.

Conclusion: Patients with AH enrolled in JWiTS had earlier stage tumors and better outcomes than those enrolled in NWTS-5, indicating a possible biological heterogeneity among AH tumors and a higher incidence of AH tumors with low grade malignancy and a lower incidence of tumors with high grade malignancy in Japanese children than in Caucasian children. Further analysis of tumour biology, including TP53 mutation status, is required to elucidate the genetic basis of characteristic differences of AH WT between the Japanese and Western populations.

P-0764 | Image-Based Surgical Risk Factors for Wilms Tumour

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Background/Objectives: In the USA and Japan, the standard treatment for Wilms tumour (WT) is primary resection followed by chemotherapy. However, in cases of unresectable tumors, chemotherapy is administered prior to tumour resection, and abdominal radiation therapy with more intensive chemotherapy should be reserved for cases of tumour spillage. Such cases are considered to have "surgical risks (SRs)." In the present study, we analyzed pre-operative image analyses in order to identify factors associated with the SRs.

Design/Methods: Twenty-nine patients with WT treated between 2000 and 2015 were enrolled in this study. Seven patients had SRs (SR(+) group); three had unresectable tumors, and four had tumour spillage due to rupture of the tumour or its extension beyond the tumour capsule. Patients' clinical records and image results, including CT scans, were collected and retrospectively analyzed. Several factors, such as tumour size, volume, relationship between the large vessels, and contralateral extension of the tumour were evaluated and compared between the SR(+) and SR(-) groups.

Results: The horizontal tumour diameter/body height ratio was greater than 10% in the SR(+) group. Although the estimated tumour weight/body weight ratio was larger in the SR(+) group than in the SR(-) group, it was not statistically significant. Displacements of the abdominal aorta and/or vena cava by the tumour compression were more frequently observed in the SR(+) group than in the SR(-) group. Extensions of the tumour beyond the center of the vertebral body were significantly more frequent in the SR(+) group than in the SR(-) group.

Conclusion: The tumour size, its compression of large vessels, and its extension to the contralateral side were significantly correlated with the SRs. These factors are useful in predicting the unresectability of tumors and deciding whether to use preoperative chemotherapy as a primary treatment strategy for large localized WT.

P-0765 | Clinical Behaviour of Patients with Wilms Tumour Treated in the Oncology Department of the Costa Rican National Children's Hospital

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Background/Objectives: In Costa Rica, a different protocol from the one being used in Central America has been implemented for low risk patients suffering from Wilms Tumour (WT). This study documents the outcomes of treatment and characterises their clinical behaviour.

Design/Methods: 20 year retrospective chart review study (1/1/1991-1/12/2011). The study comprises a total of 71 cases, from which epidemiological and clinical characteristics were obtained. Protocol treatment separated in five different groups to analyse relationship between failure and protocol, histology or disease stage. We created a statistical disease severity indicator based on risk factors found at diagnosis or disease progression that allowed us to identify which ones would impact patient's outcome. The failure probability was statistically analysed to identify correlation with treatments.

Results: Mean age 2.97 years (CI95%). Most frequent clinical presentation abdominal mass (60%). No predominance for kidney side involved. Most cases had a favorable histology (78%). 28% with metastatic disease, mostly lung complications. 66% presented with disease recurrence or progression, 22% relapsed and 23% failed treatment. Our severity indicator found a statistical significance in patients who presented with unfavourable histology (UH) ($p=0.042$) or metastatic disease (MD) ($p=0.000$). According to the failure probability tool, it occurred regardless of the treatment used. ($p=0.642$).

Conclusion: We found that our patients clinical and epidemiological characteristics were similar to the ones reported internationally. The severity indicator confirms that, in our population, UH and MD represent risk factors in children with WT outcome. Interestingly failure does not depend on treatment used.

P-0766 | The SIOP Africa Wilms Tumour Collaboration: How do the Children Present?

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Background/Objectives: The SIOP Africa Wilms Tumour collaboration started in January 2014 with participating centres in Malawi, Cameroon, Ghana, Ethiopia and Uganda. We aim to improve outcomes for children with Wilms Tumour, using a SIOP approved protocol. This is modified from the International SIOP protocol and takes into consideration the unique challenges faced by centres in African low-middle income countries. Establishing an active regional childhood cancer network is important for future success.

Design/Methods: Participating centres obtained local ethical approval to join this collaboration. With guardian consent, all children suspected of having Wilms Tumour have their demographic, clinical, laboratory and treatment information entered into each unit's data base and subsequently copied to a central data base in Amsterdam for analysis. The presenting clinical features for the first cohort are presented here.

Results: A total of 128 children, median age 3.4 years (range 0.5 – 12 years) with a male: female ratio of 1:1.43, were registered up until January 1st 2016. Eighty two percent had symptoms prior to presentation for over a month with nearly a quarter for more than four months. Most tumours were large with 69/105 (65.7%) over 15cm in diameter using a tape measure and 76/88 (86.4%) over 10cm as assessed by ultrasound scan. Twenty-nine percent presented with metastases, 24/27 (88.9%) in the chest and 7/27 (25.9%) in chest and liver. Gross haematuria was evident in 27%. Weight loss was noted in 86%. Co-morbidities identified were, 3/99 (3%) with HIV infection, 4/100 (4%) with malarial parasitaemia and 9/40 (22%) tested sickle cell positive.

Conclusion: Children with Wilms tumour in these settings commonly present with metastases and weight loss and should be tested for co-morbidities including sickle cell disease. These may affect response and outcome.

P-0767 | Prognostic Factors in Unilateral Wilms Tumour; Two Centers Experience from Turkey

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Background/Objectives: Management of Wilms tumour (WT) in children depends on a multidisciplinary approach to treatment, and outcomes have significantly improved as reported by cooperative group clinical trials. Therapy consists of nephrectomy, chemotherapy, and in some cases radiotherapy. Clinical trials in Wilms tumour (WT) have resulted in overall survival rates of greater than 90%. Tumour histology is perhaps the most powerful prognostic factor for WT. Blastemal-type WT (BT-WT) has been identified as a high risk histological subgroup in WT assessed in trials of the SIOP-RTSG.

Design/Methods: Seventy-four cases were diagnosed as unilateral Wilms tumour between January 1999 and January 2016, and followed up in Ege University, Dept. of Pediatric Oncology, and in Dr. Behcet Uz Pediatric Hospital, Dept. of Pediatric Haematology-Oncology.

Results: The median age of 74 patients was 34.5 (1- 153) months. Twenty-two of them were under 2 years old. Male to female ratio was 1/1. Fifty six (75.67%) patients had favorable histology (trifazic, no anaplasia), 18 (24.32%) patients had unfavorable histology (bifazic- blastemal

predominance, diffuse anaplasia). There were 18 (24.3%) patients in stage IV (with pulmonary metastasis), 14 (18.9%) patients stage III, 17 (23%) patients stage II, 27 (36.5%) patients stage I.

COG (NWTS) protocols were applied to all patients.

Follow-up median time was 77.5 (5-131). Relapse was occurred 7 (9.5%) patients. Age (> 2 years old), stage (III, IV) and histology (diffuse anaplasia, bifazic blastemal predominance) were affected to relapse but not significantly. Two patients died with progressive disease. In all patients 10-year RFS was 90.5%, and OS was 97.5%.

Conclusion: Therapy for WT has been advanced in part by an increasingly complex risk-stratification system based on patient age; tumour stage, histology, and volume; response to chemotherapy; and molecular findings.

P-0768 | Prognostic Impact of Her/2 Expression on Survival of Preoperatively Treated Children with Wilms Tumour at South Egypt

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Background/Objectives: Wilms tumour (WT) is the most common paediatric renal tumors. Her/2 is an onco-protein, its over-expression shown to play an important role in the development and progression of certain tumors. This study evaluates the potential role of Her/2 as prognostic indicators in with previously treated WT.

Design/Methods: Immunohistochemical expression of Her/2 was studied in paraffin material of 40 patients with WT treated according to SIOP 9 protocol. Patients' medical records reviewed for clinical, pathological and outcome data and correlated with HER/2 expression. Additional 15 samples of normal surrounding renal tissue specimens were included.

Results: Her/2 was expressed in normal kidney tissue (renal tubules but not glomeruli) and at variable levels in the three elements of WT. At a median of 84 months 70% of patients are living and under follow-up, surgical stage and pathologic subtypes were the only two factors significantly affect outcome of our patients ($p=0.000$, $p=0.007$ & $p=0.004$, $p=0.005$ for Overall survival (OS) and Disease Free survival (DFS) respectively). Her/2 expression was associated with epithelial differentiation ($p<0.001$). Her/2 expression had no statistically significant effect on OS or DFS of our patients.

Conclusion: Although the major progress in studying biology of WT, stage and pathological subtype remain the only predictive factors of significant value affecting the outcome of patients with WT. Significant association was found between Her/2 expression and histological differentiation in previously treated Wilms tumour. Non-conclusive results regarding influence of Her/2 expression on the outcome of WT patients was found.

P-0769 | Vincristine, Irinotecan and Bevacizumab in Relapsed Anaplastic Wilms Tumour

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Background/Objectives: The prognosis of relapsed anaplastic Wilms tumour (WT) is dismal and novel therapeutic strategies are needed.

Design/Methods: Combining antiangiogenic therapy with cytotoxic chemotherapy may be synergistic. We describe two consecutive relapsed anaplastic WT cases who received a combination of irinotecan, vincristine and bevacizumab (IVB).

Results: Case 1: a 5 year-old female with stage III anaplastic WT early relapsed at both local and metastatic sites (abdomen, liver and lungs). IVB regimen was administered. The schedule was: vincristine 1.5/ sqm iv on day 1 and 8, bevacizumab 15 mg/Kg iv on day 1, irinotecan 20 mg/sqm iv on day 1-5 and 8-12, every 3 weeks. After 2 courses, the radiological assessment showed a partial response on abdomen and lung metastases and a complete response on liver metastases. The response lasted two months. Hematological toxicity and diarrhea were the main side effects. The girl died of disease four months after relapse.

Case 2: a 10 year-old male with stage III anaplastic WT presented lung metastases and mediastinal nodes one month after the end of high risk SIOP 2001 protocol. He received subtotal surgery/radiotherapy, but new lung nodules were early detected at CT scan. IVB regimen was administered (VCR 1.5mg/ sqm iv on day 1 and 8, bevacizumab 15 mg/Kg iv on day 1, irinotecan 20 mg/sqm iv on day 1-5, every 3 weeks). A partial response on mediastinal nodes and a complete disappearance of new lung metastases were obtained after 2 courses without toxicity. The patient is under IVB chemotherapy yet.

Conclusion: This regimen may have a role in the treatment of patients with anaplastic advanced WT.

P-0770 | Outcome of Relapsed Wilms Tumour: A Single Center Experience

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Background/Objectives: To review event free (EFS) and overall survival (OS) for children with relapsed Wilms tumour (WT) treated according to the SIOP 93-01 and SIOP 2001, over 22 years in a single center.

Design/Methods: Information were retrospectively extracted from the file of patients treated at Pediatric Oncology Unit of "Sapienza" University of Rome. Relapsed disease is defined as reappearance of tumour in local and/or in distant sites. We excluded the cases that presented with early progressive disease. Relapsed patients were divided into 3 groups according to the initial treatment received: standard risk (no RT and 2-drug CHT), high risk (RT and/or 3-drug CHT) and very high risk (unfavorable histology and/or more than 3-drug CHT).

Results: Out of 65 cases with WT, 9 (13.8%) relapsed at a median age of 70 mos, range 18-368 months. Male-to-female ratio was 2:7. Four cases at standard risk [2 treated with nephrectomy and 2 with nephron-sparing surgery (NSS)] were successfully re-treated with conventional therapy (surgery/radiotherapy and carboplatin based regimen chemotherapy). They are alive without disease at 20 yrs, 19 yrs, 1 yr and 0.1 yr of follow-up (FU) calculated from the end of relapse-therapy. The other 5 cases were at high (n=2) and at very high (n=3) risk. Out of these, 4 died of tumour: 3 treated with conventional therapy and 1 with high dose chemotherapy. One case at very high risk is alive in very good response under treatment with vincristine, irinotecan and bevacizumab. OS and EFS was 55.5% and 44.4%, respectively.

Conclusion: Relapsed cases with WT at standard risk, initially treated both with nephrectomy and with NSS are salvageable with conventional therapy, although, in our series, cases treated with NSS have a short FU. In high and very high risk relapses novel therapeutic strategies are needed.

P-0771 | Exigent Clinicopathological Facets of Paediatric Renal Tumors Sans Wilms

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Background/Objectives: The aim was to study the clinicopathological characteristics of non-Wilms renal tumors in children.

Design/Methods: Case files of patients registered in the Pediatric Surgery Tumour Clinic who visited the clinic for follow up from Jan 2015 to March 2016 were studied. Out of 25 cases subjected to work up for renal tumours, 17; 8 had Wilms; non-Wilms Tumours.

Results: Eight children had non-Wilms Tumours. Their ages ranged from new born to 11 years. Two cases had antenatal diagnosis of renal tumours. Both these tumours were subjected to upfront nephroureterectomy in newborn period. One baby had an invasive tumour being adherent to the liver, retroperitoneum and inferior vena cava. The histopathology was Congenital mesoblastic nephroma. Another case of Congenital mesoblastic nephroma presented with hydronephrosis and the diagnosis was established on table. All patients underwent nephroureterectomy with lymph node sampling. One patient had intra renal neuroblastoma. Two patients had clear cell sarcoma of kidney (CCSK). One patient had a peripheral neuroectodermal tumour of the kidney. One patient initially diagnosed as a tubercular kidney elsewhere was subjected to nephrectomy on suspicion of malignancy. The histopathological diagnosis was Xp 11 translocation renal cell carcinoma. Four patients were treated with nephrectomy alone, chemotherapy was added for 4. Two patients underwent neoadjuvant chemotherapy (CCSK, NB). At a follow up of 2 to 61 months, six patients are healthy. Two patients (PNET and CCSK) are still undergoing chemotherapy. Two patients died; one CCSK and one intrarenal neuroblastoma (NB). The causes of death were advanced malignancy with ruptured tumour (NB) and chemotoxicity after week 18 chemotherapy (CCSK).

Conclusion: Though Wilms tumour is the most common renal tumour in children, we encountered non-Wilms tumours in one third of our cases. A high index of suspicion and clinicopathological team work alleviates inappropriate chemotherapy and accomplishes accurate diagnosis.

P-0772 | Bilateral Wilms Tumour: A Ten Year Experience in Two Academic Centers

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Background/Objectives: Nephroblastoma is the most common genitourinary malignancy, affecting 1 in 10 000 children worldwide. Five to 10% present bilaterally. The aim of this study was to describe the experience of Bilateral Wilms tumours (BWT) and patient outcomes at Wits University.

Design/Methods: Retrospective record review of all Bilateral Nephroblastomas treated at Wits University after institutional approval by ethics committee (HREC No. M140629) was obtained.

Results: Nephroblastoma was diagnosed in 222 patients during the study period, of which 17 (7.6%) presented with bilateral disease. Patients with BWT presented at a younger age than those with unilateral disease. Three of the 17 patients presented with metachronous disease at a mean age of 71 months, the remaining 14 with synchronous disease at a mean age of 30.4 months. One patient had a syndromic predisposition to Nephroblastoma, hypermyelination at H19 DMR on chromosome 11P15. Treatment was according to SIOP 9 protocols. Of 17 patients treated 2, both with synchronous disease, died before any surgical intervention could be undertaken and 1 patient died before renal sparing surgery on the residual kidney. Thirteen kidneys were completely removed, and nephron sparing surgery performed in 12. Of the kidneys that had nephron sparing surgery, 6 had positive margins. 1 patient developed metastatic disease in the liver. Only 3 kidneys showed unfavourable histology. Eight patients are alive and disease free, with well preserved renal function between 1 to 84 months post diagnosis. Six patients are dead (1 from CCF secondary to Adriamycin induced CMO, 1 with IVC involvement, 1 from sepsis and 3 with metastatic disease).

Conclusion: BWT is a complex disease to manage. Appropriate bimodal therapy, including appropriate nephron sparing surgery, achieves good long-term survival and good renal function can be expected. Presentation with metastases or recurrence outside the kidney has poor outcomes.

P-0773 | Wilms Tumour Associated with Genetic Syndromes and Congenital Malformations

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Background/Objectives: To evaluate the presence of genetic anomaly, clinical malformation and syndromes with a tendency to develop Wilms tumour (WT).

Design/Methods: 683 patients with Wilms tumour who were treated between 1972 and 2016 were retrospectively analyzed. Clinical details, treatment and survival analysis were done. Associated congenital anomalies, genetic syndromes were noted.

Results: We found 54 patients with genetic anomaly, clinical malformation and syndromes with a tendency to develop tumors out of 683 patients with WT (7%). Male/female ratio was 3.1. Mean age of diagnosis for WT was 3.3 years (0.18 years- 4 years). Syndromes with a tendency to develop tumors were Denys Drash (n=10), Beckwith Wiedemann (n=1), WAGR (n=2), Fanconi (n=1), Bloom (n=1) and familial WT (n=1). Genitourinary anomalies were horse shoe kidney (n=6), hydrocele (n=5), undescended testis (n=11), hypospadias (n=3), bilateral vesicoureteral reflux (n=1), duplex ureter or collecting system (n=1), renal hypoplasia (n=1) and inguinal hernia (n= 4). Clinical malformations were hemihypertrophy (n=8), isolated aniridia (n=1) and other malformations (n=2). We found 9 patients with bilateral WT. Thirty (55.6%) patients received radiotherapy, 53 patients received chemotherapy (98.1%) and 4 patients underwent partial nephrectomy. Three and five year overall survival rates were 74 and 63%. Event-free survival rate was lower in female patients (p= 0.04).

Three out of 10 patients with Denys Drash syndrome are alive and 3 of them did not survive after 10 years due to secondary problems; the patient with Fanconi anemia died at the early period; the patients with Bloom and WAGR syndrome died in 11 and 18 years, respectively and the patient with vertebra anomaly died after 4.5 years due to syndrome related complications.

Conclusion: The most common associated anomalies were genitourinary anomalies and in long term follow up tumour unrelated deaths were more in syndromic patients.

P-0774 | Outcome of Patients of Wilms Tumour Over Four Consecutive Years - Questions Specific to Low Middle Income Countries

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Background/Objectives: Wilms Tumour(WT) outcomes may be affected by problems specific to low middle income countries(LMIC). In this study we document the stage wise outcome, check the correlation with socio-economic status and parental education and attempt to find the direct costs of treatment.

Design/Methods: Retrospective audit of a prospectively maintained data was done for patients of Wilms Tumour(WT) over four years - January 2012 to December 2015. Outcomes were documented as on 31st March 2016. Direct costs of treatment were analysed from hospital records.

Results: In the defined period 137 consecutive patients of WT were registered in a tertiary cancer care centre in LMIC. Median age of presentation-30 months. Stage I,II,III,IV,V were 13(9.5%),26(19%),53(38.7%),27(19.7%),10(7.3%) and 8(5.8%) presented with relapse after treatment elsewhere. After a median follow up of 22.9 months, the respective stage wise survival were 11/13(84%),18/26(70%),35/53(66%),19/27(70%),5/10(50%). Of the patients presenting after relapse only 1/8(12.5%) is disease free. Sixteen/137(11.7%) patients relapsed, 2(1.5%) died, 11(8%) are lost to follow up and 19(13.9%) are on chemotherapy. Of the patients who received complete treatment at this centre (96/137-70%), 81/96(84.4%) are alive without disease.

Of these 96 patients, 51(53.1%),26(27.1%) and 19(19.8%) belonged to lower, middle and upper socio-economic groups respectively. Paternal education status was basic education (21/96-21.9%), higher education (44/96-45.8%) and graduate/postgraduate(31/96-32.3%). We could not find correlation of outcome with socio-economic status or paternal education.

The average direct cost of treatment for stage I,II,III,IV,V patients was INR 15676, 30900, 41874, 45211, 34037 or approximately USD 260, 515, 700, 750 and 570. This does not include any indirect costs to the patients or to the institute.

Conclusion: Outcomes of patients of WT are affected by various factors, stage being the most important. Complete treatment in single centre may portend favourable outcome. Socio-economic status or parental education may not affect outcomes. The direct cost for treatment of WT are documented.

P-0775 | Wilms Tumour (WT): Twenty-One Year Experience at the Instituto Nacional De Enfermedades Neoplasicas (INEN)

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Background/Objectives: Introduction: WT is the most frequent renal tumour in children representing 5.1% of paediatric neoplasms at INEN.

Objective: Evaluate results of treatment between January 1992-December 2013.

Design/Methods: A total of 395 children with renal masses were evaluated, with 68 being excluded because of surgery performed elsewhere and other types of renal tumors, as well as 18 stage V cases.

Results: A total of 310 patients were treated according to the SIOP protocol. The median age was 36 months (3-157 months), 180 were girls (F/M 1.2) After an open biopsy a six-week course of weekly Vincristine and Actinomycin and Doxorubicin on weeks 0 and 3 were administered. Since June 2012 no biopsy was required and treatment begun with clinical and radiological findings. Group A: primary nephrectomy 152 cases (48%), Group B: Pretreatment biopsy 134 cases (43%), Group C: No biopsy 24 cases (8%). In Group A: Stage I 45 cases, Stage II 46 cases, Stage III 42 cases, Stage IV 19 cases. In Group B: Stage III 97 cases, Stage IV 37 cases. In Group C: Stage III 11 cases, Stage IV 13 cases. Median tumour weight: Group A 555 gm; Groups B/C 480 gm. Post chemotherapy staging in groups B and C showed downstaging

in 50.6%, 43% remained the same and 2% were upstaged. Those downstaged after June 2012 only received Vincristine and Actinomycin postop. Radiation was given to those with ruptured tumors and with involved nodes. Evaluable patients in continuous remission, disease free for a median of 8.5 years (26 months – 20 years); 227 (73%). Patients lost to follow up disease free: 23. Eleven patients died during surgery or induction therapy.

Conclusion: Three-drug induction in developing countries can downstage in 50% of cases thus eliminating Doxorubicin from therapy and decreasing future late effects.

P-0776 | A Retrospective Analysis of Paediatric Patients with Wilms Tumour from a Tertiary Care Center in Pakistan

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Background/Objectives: Wilms Tumour (WT) is the most prevalent renal malignancy in Paediatrics and requires a multidisciplinary team comprised of oncologists, surgeons and radiotherapists. Although outcomes for patients with WT have dramatically improved as a result of this collaboration, in resource poor countries limited treatment centers and delayed treatment initiation cause disparities in overall survival. Our analysis reports time to oncologist among other factors impacting outcomes.

Design/Methods: A retrospective analysis was done of paediatrics patients with WT presenting to Hospital from 1/1/2009 to 19/2/2014 after IRB approval.

Results: A total of 109 patients with WT were reported (64 male, 45 female). Seventy-seven percent of patients were <5 years and 23% ≥5 years. Time to referring physician after onset of presenting complaint was ≤4 weeks in 83% of patients. Time to oncologist was ≤4 weeks (20%), 4-12 weeks (38%) or ≥12 weeks (42%). Diagnosis was made by Trucut biopsy in 40 patients with a 95% yield and no complications. Sixty-seven patients (64%) had an upfront nephrectomy, of these, 40 patients (38%) had recurrent/residual disease. Radiation and pre and post-operative chemotherapy was per SIOB WT-2001. Local stage post-nephrectomy was Stage I (31%), Stage II (18%), Stage III (51%). Eighty-eight percent of patients had favourable-histology WT. On last follow up 42% were in complete remission, 9% had progressive disease, 25% succumbed to disease, 1% abandoned treatment and 17% were lost to follow-up.

Conclusion: High rates of metastases and disease recurrence post-nephrectomy are significant contributors to poor survival of children with WT. Our institution accepts patients regardless of ability to pay after diagnoses have been confirmed histopathologically which can be burdensome on families owing to socio-economic constraints, causing delays in treatment initiation. We propose the need for initiatives to broaden awareness within the community, for earlier referral and to prevent inappropriate surgery.

P-0777 | Inhibition of Autophagy in Nephroblastoma and the Potential Therapeutic Significance

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Background/Objectives: Nephroblastoma (NB) has overall good prognosis, however, patients still suffer from the side effects of traditional therapies. Autophagy is a self-digestion physiological event to maintain cellular homeostasis. Investigations of the autophagic activity in NB have not been reported in the literature. However, abnormal expressions of Bcl-2, b-catenin and p53, which directly regulate the autophagy activity, are manifested in NB. Hence we hypothesize a potential link between autophagy deregulation and the onset of NB. Furthermore, regulation of autophagy can be a potential strategy as adjuvant therapy to increase the efficacy and to decrease the side effects of traditional therapeutics.

Design/Methods: Our study attempts to explore the relationship between autophagy and NB with the purpose to find optimized protocol by autophagy regulation. The following experiments were performed. Expression of several autophagy-related genes (ATGs) were analyzed in the mRNA and the protein levels in NB tissues. In NB cell lines, novel therapeutic strategies were tested by combinational use of autophagy-targeting drugs and conventional chemotherapeutics to increase the efficacy and to decrease the side effects. In nude mice NB tumour model, the synergistic antitumor effect of chloroquine, a typical autophagy-suppressant, with the antimetabolite vindesine was tested.

Results: ① There was suppression of autophagy in NB tissues prior to chemotherapy compared with the surrounding normal kidney tissues; autophagy was activated after chemotherapy and might participate in chemoresistance development. ② The microtubule-targeting antimetabolites vincristine and vindesine had synergistic antitumor effect with both chloroquine (autophagy-suppressing drug) and rapamycin (autophagy-promoting drug). The anti-proliferative effect of rapamycin on NB was at least partly through activation of autophagy. ③ The synergistic antitumor effect of chloroquine with vindesine was confirmed by in vivo experiments in nude mice.

Conclusion: Autophagy level was suppressed and could be re-activated by chemotherapy in nephroblastoma. Inhibition of autophagy (by chloroquine) was shown to decrease tumour growth synergistically with microtubule-targeting chemotherapeutics.

P-0778 | Neoadjuvant Transcatheter Arterial Chemoembolization Combined with Systemic Chemotherapy for Treatment of Clear Cell Sarcoma of the Kidney(CCSK)

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Background/Objectives: Clear cell sarcoma of the kidney (CCSK) is a rare type of paediatric malignant renal tumour. It is known as an aggressive tumour with poor prognosis. The aim of the study was to evaluate the efficacy of neoadjuvant transcatheter arterial chemoembolization (TACE) combined with systematic chemotherapy for the treatment of CCSK.

Design/Methods: Five patients (2 boys and 3 girls, range 0.9-7.1 years) with unilateral CCSK were treated with preoperative TACE combined with systemic chemotherapy. At diagnosis, the mean maximal tumour diameter was 11.7 cm. Two patients presented with lung metastasis, 1 with bone metastasis, and 1 with inferior vena cava (IVC) thrombus. Patients subjected to TACE by Seldinger's method. Chemoembolization emulsion consisted of cisplatin, pirarubicin, vindesine, normal saline and iodized oil were infused. Preoperative systemic chemotherapy with vindesine, ifosfamide and etoposide was administered 3 weeks after TACE. Surgical resection carried out 3 weeks after intravenous chemotherapy. Postoperative received radiotherapy and chemotherapy for 24 weeks.

Results: No cardiotoxicity, renal insufficiency, or hepatic dysfunction were found in all patients. Grade III myelosuppression developed in 2 patients. In terms of RECIST criteria, 3 patients had PR, 1 had SD and 1 showed PD after neoadjuvant therapy. Four patients underwent radical nephrectomy after neoadjuvant therapy. Complete surgical removal of the tumour achieved in 3 patients and 1 had intraoperative tumour rupture. Surgical stages of this 4 patients were stage II in 1, stage III in 2, and stage IV in 1 patients. Pathologic examination of surgical specimens found tumour necrosis > 90% in all 4 patients. This 4 patients were recurrence free survival up to now with a median follow-up of 44 months (25-62 months). Another patient died of lung metastasis.

Conclusion: Neoadjuvant transcatheter arterial chemoembolization combined with systematic chemotherapy for the treatment of clear cell sarcoma of the kidney in children is safe and effective.

RETINOBLASTOMA

P-0779 | Challenges in Treating Retinoblastoma in Developing Countries: Children's Hospital Lahore Pakistan Experience

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Background/Objectives: While Retinoblastoma is highly curable in developed countries, the outcome is still dismal in Pakistan. The Children's Hospital Lahore is a public tertiary center receiving over 700 new cancer patients per year from all over the country. The purpose of this study was to analyze outcome of retinoblastoma in resource limited settings.

Design/Methods: Retrospective review of 68 patients enrolled between June 2013 - December 2015 was done. Data regarding their age, sex, stage, laterality, treatment course, outcome. Patients were treated according to UKCCSG RB 2005 11 protocol.

Results: Total 68 patients with age ranging from < 1 to 7 years (95% <5 yrs) were included. M: F Ratio was 1:1. 25/68 (37%) presented with bilateral Retinoblastoma and 38/68 (56%) with optic nerve involvement and brain metastasis 12/68 (18%) (P-value=0.001). 30/68(44%) defaulter treatment and 33/68 (49%) p-value=0.000, refused Enucleation at diagnosis, (p-value=0.002). Only 3/68(5%) had bilateral Enucleation and 50/68(73%) unilateral Enucleation with laser therapy in 7/68(10%). Total 38/68 (56%) have completed treatment, 1/68 (2%) are on treatment, 18/68 (27%) left against medical advice (LAMA) and 6/68 (9%) expired due to metastatic and progressive disease and sepsis. 5 patients (7%) relapsed. Neoadjuvant chemotherapy was given in 40/68 (59%) with 61% of total abandonment and 50 of deaths in this group. When compared with the previous study presented in SIOB 2014 mortality decreased from 18 to 9% and defaulter trend decreased from 66% to 44% (30/68) and Neoadjuvant chemotherapy used in 59% cases as compared to 54%. The number of bilateral RB was increased to 25/68(37%) as compared to 10/56(18%).the number of LAMA increased from 13% to 18/68(27%).

Conclusion: Mortality of 9% can be reduced by early diagnosis and early treatment. Management of RB needs efficient Multidisciplinary team and long term sustainable international collaborative programs to improve survival. The Neoadjuvant group needs extensive follow up and counseling to decrease abandonment.

P-0780 | 13Q Deletion and Pituitary Stalk Interruption in Bilateral Retinoblastoma

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Background/Objectives: Pituitary stalk interruption syndrome (PSIS) has been described in association with various midline brain structure abnormalities. We describe a new association with retinoblastoma.

Design/Methods: Case report of a 13 months old boy with bilateral retinoblastoma, 13q deletion and panhypopituitarism caused by PSIS.

Results: An Italian male infant was referred to our hospital for treatment of progressive bilateral retinoblastoma. At birth he presented hypoglycemia, respiratory distress and septicemia.

Physical examination showed dysmorphic signs with microphthalmia, large neck, low hair and ear implantation and bilateral cryptorchidism. He was diagnosed with panhypopituitarism, substitution was started and a cerebral CT scan performed which was normal. Soon after a unilateral retinoblastoma was diagnosed treated with systemic chemotherapy. A karyotype analysis revealed 46,XY, del13 (q12.3-q14.3) confirmed by FISH. At 6 months of age the child presented a bilateralisation of the retinoblastoma treated with further chemotherapy, and dysmorphism became more evident comprising severe microcephaly with frontal bossing, micro penis and delay of psychomotor development. Progression of retinoblastoma while on treatment resulted in referral to our hospital. We performed a brain MRI because of the endocrinological abnormalities which revealed a hypoplastic anterior pituitary gland with an interrupted stalk and ectopic neurohypophysial. A delayed myelinisation of the white matter as well as partial atrophy of the posterior part of the corpus callosum was also noted.

Conclusion: According to our knowledge, we are first to describe the association between 13qdel in a child with retinoblastoma and PSIS. The genetic link between these overlapping entities remains to be determined.

P-0781 | Retinoblastoma in Children Older Than 6 Years: A Single Centre Study of 58 Patients from India

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Background/Objectives: Retinoblastoma is the most common intraocular tumour of childhood. More than 95% of cases are diagnosed before the age of 5 years. Data on patients in patients with retinoblastoma diagnosed at age of more than 5 years are limited.

Design/Methods: Medical records were reviewed for data including age at diagnosis, gender, laterality, family history, first symptom, misdiagnosis; clinical findings, grade and stage of disease at diagnosis, treatment and outcome. Histopathology slides were reviewed and assessed for presence of histopathological high-risk features (HRF) for metastasis.

Results: Six hundred and sixteen retinoblastoma patients were registered from June 2003 to December 2013. Of these, 58 patients (9.4%) were more than 6 years at diagnosis. The median age was 7 years (range, 6-16 years) and 33/58 (57%) were males. Retinoblastoma was bilateral in 9 cases (16%). Most common presenting symptoms were leucocoria (50%) followed by impaired vision (19%). Median lag time from symptoms to presentation was 12 months. Thirteen cases (22%) were misdiagnosed at initial presentation; endophthalmitis being the most common (46%) misdiagnosis. Thirty-three patients had intraocular disease, 20 had locally advanced disease and 5 had metastatic disease at presentation. Thirteen of 23 (48%) enucleated eyes with intraocular disease had HRF. Of the 49 patients who completed treatment, 84% (41/49) patients are alive and healthy at last follow-up, while 16% (8/49) patients died of disease progression.

Conclusion: This is the largest study of older age retinoblastoma and shows that it forms a significant percentage of retinoblastoma, is misdiagnosed in one-fourth of the cases and may present in an advanced stage.

P-0782 | Prognostic Factors in Metastatic Retinoblastoma: A Study of 70 Metastatic Retinoblastoma Patients Treated at a Single Centre in India

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Background/Objectives: The prognosis of retinoblastoma has improved markedly with 5-year survival rates of more than 95% from Western world. Early detection accounts for most of improved outcome. However, presentation with advanced disease in less developed countries is not uncommon and outcome in these patients is guarded. Data on metastatic retinoblastoma suggest dismal outcomes.

Design/Methods: We conducted a retrospective analysis of patients with metastatic retinoblastoma treated at our centre from June 2003 to December 2013. Baseline demographic, disease-related and treatment data were collected from the records and analyzed by time to event analysis. Factors affecting the overall survival and progression free survival were identified using univariate and multivariate analysis.

Results: Seventy patients with metastatic retinoblastoma were identified. The median age at diagnosis was 36 (range, 3-192) months, with a male: female ratio of 2:1. The sites of metastasis included brain (48%), leptomeningeal (44%), bone marrow (24%) and bone (15%). More than one site of metastasis was observed in 30% of patients. Seventy-one percent (51/70) patients received VEC protocol (Vincristine, Etoposide, and Carboplatin). The median overall survival (OS) was 9.6 months. More than one site of metastasis (p=0.01), leptomeningeal spread (p=0.05) and duration of symptoms more than 6 months (p=0.05) predicted worse OS in univariate survival. On multivariate analysis, more than single site of metastasis emerged significant factor predicting OS (p=0.03) on Cox-regression model. Only 2 patients are long-term survivors, who were offered autologous stem cell transplant (ASCT) after good response to initial chemotherapy in bone-limited metastatic disease.

Conclusion: Despite improvements in retinoblastoma cure rates, patients with metastatic retinoblastoma have dismal outcome with 5-year OS of less than 5%. Early diagnosis remains particularly important to improve outcomes. In bone-limited metastatic disease, ASCT may offer a chance of cure if there is good response to chemotherapy. Thus, in resource-challenged situations, early diagnosis and treatment need further emphasis.

P-0783 | Cyst of the Pineal Gland in Patients with Retinoblastoma: Is there a Link with Disease and Treatments?

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Background/Objectives: Patients with retinoblastoma (Rb) present often midline abnormalities. In 2006 we were first to report on pineal cysts that appeared to be more common in children with hereditary bilateral Rb. We reviewed in a larger patient cohort the occurrence of pineal cysts and analyzed a possible link with disease characteristics and treatments received.

Design/Methods: Retrospective study of clinical and radiological data of 103 patients treated for Rb who had undergone a systematic cerebral magnetic resonance imaging (MRI) between 2006 and 2013 and had a follow-up. Clinical records were reviewed for sex, age at diagnosis, disease stage and heredity, tumour laterality, age at first MRI, treatments received, response to treatment, follow-up, long-term outcome, time interval from diagnosis of Rb to the diagnosis of a pineal cyst, and genetic data if available. Radiological reports and brain images were reviewed for each patient with pineal cyst to record its size and change over time.

Results: Of 103 patients with Rb 56 had unilateral and 47 bilateral disease. Ninety-five were sporadic and 8 familial. Forty-nine MRIs out of 103 (47.6%) presented a pineal cyst and were reviewed by a neuroradiologist to verify aspect and size of the pineal gland. Occurrence of cysts was more frequent in bilateral disease, in presence of a documented genetic mutation and in group D or E disease, but without statistically significance. Treatment had no impact on the occurrence of cysts. At 1 year of follow-up, cysts in bilateral Rb and those with documented genetic mutation showed no significant increase in size. Only one atypical cyst transformed into pinealoblastoma.

Conclusion: We found a high incidence of pineal cysts in Rb patients, but without significant relationship to the hereditary subgroup or genetic mutation. Its lower incidence in healthy children clearly indicates that pineal cysts are part of the disease-related midline brain abnormalities.

P-0784 | Treatment of Retinoblastoma in Serbia from January 2006 to December 2015

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Background/Objectives: Retinoblastoma (RB) is the most common intraocular malignancy in childhood. Clinical outcomes are excellent with early detection and multidisciplinary management. This study investigates the treatment and outcome of RB in Serbia.

Design/Methods: In 10 years period 21 children with RB and histopathology characteristic who needs additional oncology treatment received chemotherapy, adjuvant or neo-adjuvant with/ without orbital radiotherapy at Institute for Oncology and Radiology of Serbia. Patients were operated and histopathology diagnosed in Clinic for Eye Disease/ University Eye Hospital while conservative treatments are made abroad in European Union.

Results: Median age of total 21 patients was 14 months (range 14-27), 67% were female. Unilateral and bilateral disease was 57% (12 patients) and 43% (9 patients). Only one child had CNS disease. Enucleation of one eye was performed for the majority of children (71%) and 3 children were enucleated both eyes. Conservative treatment was performed for 3 children. Most cases are diagnosed at the intraocular stage (17 patients, 81%). Histopathology examination of the enucleated eye is used to evaluate microscopic invasion of the choroid, the optic nerve and the sclera, and postoperative therapy is decided upon this information. All patients received chemotherapy, neo-adjuvant 19% and adjuvant 86%. Conformal orbital radiotherapy was performed in 12 children, 57%. Total dose was 40Gy. The follow up period ranged from 4 to 118 months, median 55 months. Overall survival was 95% and disease free survival 86%. Two patients relapsed, both after conservative treatment.

Conclusion: Multidisciplinary approach resulted with very good outcomes. Early diagnosis, conservative treatment and preservation of affected eye and vision will be our next step.

P-0785 | Hydroxyapatite Orbital Implant (HAOI) Migration: A Longitudinal Study in Retinoblastoma Patients

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Background/Objectives: Integrated orbital implants such as hydroxyapatite are believed to have a lower risk of long-term migration due to fibrovascular ingrowth limiting need for later socket revisions. Herein, we quantify longitudinal HAOI migration in a cohort of retinoblastoma patients.

Design/Methods: Charts of 93 patients (47 males, 69 unilateral, median age at diagnosis 18 months) enucleated between 2003 and 2011 using HAOIs (median size 20mm) were reviewed. Pre-operative, initial post-operative and 5-year post-operative MRIs were analyzed. Vertical and horizontal migration were measured around an orbital center reference point, which we defined as the midpoint between the nasal and temporal orbital rims on the line created by the intersection of axial plane bisecting optic nerve entering muscle cone with coronal plane bisecting globe or implant. Impact of chemotherapy and radiation was studied.

Results: Average migration relative to intact eye (ΔD) at 5 years post-operatively was 4.50 mm (SD=2.9 mm). Average implant migration between 1 year post- and 5 years post-operative was 4.56 mm (SD=3.6 mm). Neither chemotherapy (N= 36) nor radiation (N=8) significantly affected ΔD at 5 years.

Conclusion: Hydroxyapatite orbital implants have minimal long-term migration in retinoblastoma patients providing a template for lifelong optimal cosmetic outcomes. Adjuvant chemotherapy and radiation have no adverse effects.

P-0786 | Eye Rescue in Patients with Retinoblastoma using Intravitreal Chemotherapy Injection in a Tertiary Institution at Mexico. Preliminary Report

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Background/Objectives: Retinoblastoma is the most common primary intraocular malignancy of infancy. Intravitreal chemotherapy is an effective modality for treating intravitreal disease. The purpose of this paper is to evaluate the efficacy and safety of intravitreal injection of melphalan for relapsed and refractory retinoblastoma in a period of two years (2014–2016).

Design/Methods: This is a prospective cohort of patients with viable vitreous seeds of relapsed and refractory retinoblastoma. The patients received injections of melphalan 30 µg (range: 7–8 injections).

Results: All patients were at stage C (International Classification of Retinoblastoma). The follow up was at the interval of 9–23 months (median: 16 months) and ocular status response was classified in 3 groups: ocular rescue with active disease (n=1), ocular rescue with complete response (n=8), and failure with enucleation (n=1). Successful control of vitreous seeds was achieved in 8 of 10 patients. No one presented complications related to the procedure. There was no local tumour spread.

Conclusion: Intravitreal chemotherapy with melphalan is an effective treatment in patients with vitreous seeds for eye rescue, actually standardized in developed and developing countries. This treatment also avoids the use of radiotherapy with the known consequences.

P-0787 | Pharmacokinetics of Intra-Arterial Melphalan in Patients with Recurrent or Progressive Retinoblastoma Treated on Spog-Rb-2011, A National Phase II Study of the Swiss Paediatric Oncology Group

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Background/Objectives: Since the 1990s, intravenous (iv) chemotherapy has been the systematic first-line treatment used in the management of retinoblastoma, to reduce tumour volume and render it accessible to focal treatments as well as to avoid enucleation and/or radiotherapy. This approach has allowed globe preservation in the majority of group A-C tumors and in 19–60% of group D cases. Relapse or tumour progression in this group D patients constitute a major concern for globe salvage. Techniques of local administration of chemotherapy, such as Selective Ophthalmic Artery Chemotherapy (SOAC) administration offers an interesting alternative. We report here pharmacokinetic analysis of melphalan administered by SOAC in eight patients, their clinical response to SOAC and observed toxicities.

Design/Methods: Monocentric single arm, phase II prospective non-randomized study. Among included patients, plasma levels of Melphalan were determined by high-performance liquid chromatography/tandem mass spectrometry (LC-MS/MS) at 0, 0.5, 1.5, 3, 4 and 24 hours after unilateral SOAC administration of melphalan. Full blood counts were collected weekly.

Results: A total of 47 melphalan plasma concentrations from 8 consecutive patients were collected. Each patient received between 1 to 3 SOAC. Mean administered dose was 0.33mg/kg (SD: 0.05). Mean maximal concentration (Cmax) was 743 ng/ml (SD: 235) at 0.5 hour. Clearance was calculated at 0.24 L/h/kg (SD: 0.05) and mono-compartmental volume of distribution (Vd) was estimated at 0.27 L/kg (SD: 0.07). Six patient needed additional treatment. Seven patients had a favourable (no enucleation, no radiotherapy) final outcome whereas 1 had an enucleation. Two patients developed mild neutropenia (ANC 500–1000 G/L) 2 weeks after the administration, without fever or infection.

Conclusion: We report pharmacokinetic parameters of melphalan administered by unilateral SOAC in 8 patients. Whereas 6/8 patient needed additional treatment, final outcome was favourable in the majority (7/8) of patients. Two patients developed a mild neutropenia which did not seem to correlate with pharmacokinetic parameters.

P-0788 | Intra-Arterial Chemotherapy (IAC) in Children with Retinoblastoma: An Alternative to Avoid Enucleation and Radiotherapy

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Background/Objectives: To outline eye salvage rates, patient survival and adverse events of IAC for newly and relapsed retinoblastoma patients.

Design/Methods: Single institution retrospective review of all retinoblastoma patients treated with IAC from 01/2012 to 03/2016. One to 5 cycles every 3 weeks of IAC with melphalan for newly diagnosed patients or melphalan and topotecan for salvage treatment; with carboplatin to all patients with no response or progression after 2 drugs. 20% were group C, 51% group D and 13% group E. Local therapy as indicated between IAC, intravitreal was performed for all patients with vitreous seeds. Primary outcome was eye retention without need for radiotherapy. Toxicity was evaluated.

Results: Seventy one eyes (59 patients) that underwent IAC were included (average follow-up was 4.3 months, range 1–18 months). 29 were newly diagnosed and 42 eyes received prior treatment elsewhere. Median number of IAC cycles/eye as 3 (range 1–9). 71 eyes received intra-arterial melphalan, alone in 7 eyes. 35 eyes received carboplatin and 64 received topotecan. 12 eyes received intravitreal carboplatin due to vitreous seeds. 12 eyes (8 pretreated and 4 newly diagnosed) failed treatment and required enucleation. Radiotherapy was avoided in all cases. Toxicity Grade 3–4 (4 grade III and 8 grade IV) was more common in patients receiving treatment bilaterally. No child died of metastatic disease.

Conclusion: IAC is effective for treating retinoblastoma, achieving rates of eye salvage higher than systemic chemotherapy even in eyes previously treated and with international classification

of retinoblastoma group D and E in most cases. It can be performed many times with multiple agents on one or both eyes. IAC with or without intravitreal chemotherapy can avoid external beam radiotherapy, reduced the use of systemic chemotherapy, and diminished enucleations without evidence of compromising patient survival. Toxicity is very mild.

P-0789 | Treatment of Retinoblastoma in Low Income Country Setting According to SIOP-PODC Guidelines – Interim Analysis

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Background/Objectives: Retinoblastoma is incurable in low income countries due to delayed diagnosis and poor access to health care.

Aim: To determine the outcome of children treated with low cost chemotherapy according to SIOP-PODC guidelines for low income countries.

Design/Methods: This is an interim analysis of 51 children recruited at Mbingo Baptist hospital, North-West Cameroon and treated with a modified treatment protocol for low income countries; surgery as indicated; Vincristine, Cyclophosphamide and Adriamycin on day 1 every 3–4 weeks if indicated. Ultrasound studies of the involved eye was done as other imaging studies were not available.

Results: Three patients were excluded due to toxoplasmosis retinitis. The male to female ratio was 1:1 and mean age 29 months (range 9 weeks–7 years). The majority (34%) had advanced disease (stages 3 and 4), followed by 29% with stage 1, stage 2 and 5 respectively 8 and 6%, stage 0 was 4%, and unknown stage in 19%. The left eye was most commonly involved (48%), while 16% were bilateral. Ultrasound was done in 46% of patients to determine the extent of disease prior to surgery and 73% had an enucleation done. The majority completed 6 cycles of chemotherapy (48%), while 10% received only pre-operative chemotherapy for tumour shrinkage before surgery and 10% were still on chemotherapy. A third are still alive, a third had died, while the rest were either still on treatment or being traced for final outcome.

Conclusion: Not all intraocular disease is retinoblastoma and in tropical regions toxoplasmosis must be excluded. Ultrasound may assist in determining extent of disease due to lacking of other imaging modalities. Chemotherapy is feasible for more extensive disease, especially for shrinking of large tumours prior to surgery. Final analysis will provide evidence for the efficacy of a modified treatment protocol.

P-0790 | Intra-Arterial and Intravitreal Chemotherapy for Advanced Intraocular Retinoblastoma: A Winning Combination

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Background/Objectives: To describe the efficacy of intravitreal chemotherapy (IVIc) combined with intra-arterial chemotherapy (IAC) for the treatment of advanced stage retinoblastoma.

Design/Methods: This non comparative interventional case series retrospectively reviewed the medical records of ten patients who presented within months of each other with unilateral advanced intraocular retinoblastoma, Reese-Ellsworth (R-E) stage Vb/D of ABC Classification in the affected eye. After clinical and ophthalmoscopic evaluation, they underwent MRI to exclude local and CNS dissemination. The IAC was given to treat retinal masses and intravitreal injections to treat vitreous seeding. Patients had received 2 cycles (six infusions) of IAC (melphalan and topotecan), and from 6 up to 10 melphalan injections (20 µg) into the vitreous. No permanent complications of procedures have been reported. All patients underwent fundus examination every three weeks and bimonthly MRI examination during treatment and every 3 months for 1 year after last injection, to exclude orbital dissemination.

Results: Successful control (100%) of tumour masses and vitreous seeds was achieved in all cases at 12 months follow-up. Complications were posterior lens opacity, acute ischemic papillitis, partial CVR thrombosis, hypotonia (case 1), partial vitreous hemorrhage (case 4). No complications appeared in cases 2, 3, 5 and 6,7,8,9,10. No intraocular or orbital tumour recurrence or retinoblastoma metastases (follow-up range, 12–36 months) were observed.

Conclusion: Combined and alternated intra-arterial chemotherapy and intravitreal melphalan for advanced retinoblastoma allowed to treat retinal and vitreous seed control.

P-0791 | A National Retinoblastoma Patient Engagement Strategy for Research

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Background/Objectives: Retinoblastoma is an aggressive childhood cancer of the eye. Approximately 8,000 children globally are newly diagnosed with retinoblastoma each year. Approximately half of retinoblastoma patients carry a mutation in the *RB1* gene in their constitutional cells. Patients with heritable retinoblastoma have heightened risk of second malignancies later in life, and a 50% chance of passing on the disease-causing allele to their offspring. Given the lifelong impact of retinoblastoma on patients, it is important to understand more deeply the experience of retinoblastoma survivors and their families, and incorporate this information into the research process to improve retinoblastoma care. However, there are relatively few opportunities through which those affected by retinoblastoma can contribute. We aimed to better engage Canadian retinoblastoma patients, survivors and their families in research.

Design/Methods: We invited retinoblastoma patients, survivors and their families to engage in focus groups to uncover personal stories, new research directions and communication preferences. We established a prospective research registry of people affected by retinoblastoma. Finally, we developed the Canadian Retinoblastoma Research Advisory Board (CRRAB) comprised of retinoblastoma patients, survivors, families, researchers, clinician-scientists and advocates.

Results: Focus groups results are pending. The research registry and CRRAB are ongoing tools to generate new knowledge from the patient perspective, foster integrated knowledge translation and enable the Canadian retinoblastoma community to become informed partners in research and healthcare.

Conclusion: Research registries and advisory boards are effective vehicles for creating meaningful, co-directed research. In the long-term, the research registry and CRAB will foster novel retinoblastoma research that is relevant and meets the needs of those affected.

P-0792 | Utility of the Magnetic Resonance for Noninvasive Detection and Imaging of the Retinoblastoma

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Background/Objectives: Retinoblastoma (Rb) is the most common intraocular malignancy in children caused by inactivation of both copies of the tumour suppressor gene *Rb1*, located on long arm of chromosome 13 (13q14) containing 27 exons & 26 introns. Rb may be sporadic or inherited, unifocal or multifocal, and unilateral, bilateral or trilateral. The diagnosis of Rb is based on examination by an ophthalmologist and imaging studies.

We present the analysis of magnetic resonance (MR) examinations performed in the group of patients with retinoblastoma and we review the role of different sequences for precise detection tumour extension.

Design/Methods: We retrospectively assessed contrast-enhanced brain MR of 69 patients, diagnosed between 2007 and 2016. 31 of them were females and 38 were males. The age of the patients ranged from 1 to 52 months (median age 11 months).

FSE T_2 -, T_1 -, diffusion-weighted images (DWI), SWI and CISS sequences were performed to study tumour characteristics and extent of invasion. Contrast-enhanced fat suppression T_1 -weighted MRI was done in axial as well as in the parasagittal plane parallel to the long axis of the optic nerve. Finally, axial post-contrast 3D T_1 weighted imaging of the brain was obtained.

Results: The lesion was unilateral in 34 patients, bilateral in 32 patients and trilateral in three patients. Retinal detachment was diagnosed in 18 eyes, vitreous hemorrhage was diagnosed in 7, optic nerve involvement was seen in 5 eyes. Brain metastases were found in 5 patients. DWI, CISS, and contrast enhanced T_1 - images are sensitive to the detection of the tumour extension as well as SWI has been shown to be a more effective sequence to detect calcified structures.

Conclusion: The different sequences and imaging planes of MR exams were important diagnostic tool for the detection of local and distant spread of the retinoblastoma.

P-0793 | Expression of BH3-Only Proapoptotic Bcl-2 Family Members Protein in Human Retinoblastoma

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Background/Objectives: Bcl-2 protein family play a key role in the control of apoptosis and in the initiation of the apoptotic pathways. Noxa and Puma are transcriptional targets of p53 which play an active role in p53-induced apoptosis. The aim of our study was to evaluate the expression of PUMA, p53 and NOXA and its prognostic significance in human retinoblastoma (Rb).

Design/Methods: Prospective analyses of 60 primary enucleated retinoblastoma specimens were immunohistochemically assessed for PUMA and NOXA expression and then confirmed by western blotting. Cytoplasmic staining was considered as positive and the expression was correlated with clinical parameters, tumour differentiation and histopathological high risk factors like massive choroidal invasion, scleral invasion, optic nerve invasions etc.

Results: There were total of 45 (75%) cases with poorly differentiated retinoblastoma. Necrosis and calcification was found to be present in 37 and 17 cases respectively. Of the 60 eyes, 20 (33.3%) had massive choroidal invasion, 17 (28.3%) had retrolaminar and cut end optic nerve invasion, 9 (15%) had iris & ciliary body invasion and 5 (8.33%) had anterior chamber invasion. Expression of PUMA was observed in 26/60 (43.33%) cases and NOXA was positive in 28/60 (46.66%) cases. On statistical correlation, PUMA and NOXA correlated well with tumour differentiation and various histopathological high risk factors.

Conclusion: Expression of PUMA and NOXA may be regulated by p53 tumour suppressor protein. Therefore, these proteins may be used as a future therapeutic target in combating retinoblastoma.

P-0794 | Retinoblastoma Disease Pattern Seen in a Large Regional Cancer Center in Pakistan

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Background/Objectives: Retinoblastoma (RB) is the most common paediatric intra-ocular tumour globally. There are about 250 to 300 new cases each year in the United States (U.S.) It is a very curable tumour when diagnosed early and treated promptly. In the developed world retinoblastoma accounts for <5% of all paediatric cancers. In the developing world retinoblastoma may comprise up to about 10-15% of all diagnosed paediatric cancers according to hospital-based studies in India (Sachdeva et al. Indian J Cancer 2010).

Design/Methods: Medical records at a large regional cancer center were retrospectively reviewed from January 2005 to September 2015 after IRB approval. Data was collected for patients less than 10 years of age at the time of diagnosis with RB.

Results: A total of 255 patients were identified for chart review. There were 160 males and 95 female patients. Out of which 89% (n=242) were diagnosed before the age of 5 years. Positive family history was documented for 7.8% (n=20) of patients. A majority of male patients (n=160) were seen as compared to females (n=95). Total number of bilateral disease was seen in 76 patients as compared 179 unilateral diagnoses. The median age at presentation was 24 months for bilateral disease and 36 months for unilateral disease. Thirty-nine patients abandoned treatment (15.2%).

Conclusion: The median age at presentation shows that there is a significant delay in the establishment of the diagnosis for both unilateral and bilateral RB. Compared to data from the U.S. and Europe there was higher number of male patients seen at a tertiary care center. Financial stability, access to health care and cultural practices are likely factors leading to delayed presentation and advanced disease state.

P-0795 | Ocular Implant Outcomes in Patients with Retinoblastoma

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Background/Objectives: Enucleation of the eye is often the best treatment option for patients with advanced retinoblastoma. Following enucleation, orbital implants made of various materials, including porous (e.g. porous polyethylene (Medpor®)), non-porous (e.g. silicone), and autologous (e.g. dermis fat graft) help augment the volume of the orbit and allow proper fitting of an ocular prosthesis. Benefits of using each type vary, but the ultimate goal is to minimize complications, such as exposure, extrusion, inflammation, and/or infection. Previous studies have found variable rates of exposure and complication risk factors for the different types of ocular implants used in retinoblastoma patients. The purpose of this study is to compare complication rates between porous (porous polyethylene) ocular implants and nonporous (silicone) implants in Retinoblastoma patients undergoing enucleation and to identify risk factors associated with complications in order to aid in implant choice.

Design/Methods: Retrospective review of medical records from patients between the ages of 0 to 17 years of age who have had an orbital implant placed at Children's Hospital Los Angeles between January 1, 2010 through July 1, 2015. Outcome measures were exposure, extrusion, and migration.

Results: 114 eyes were included: 103 with porous polyethylene and 11 with silicone orbital implants. 19 patients (16.96%) had a complication. In the porous polyethylene group (9.90%) had exposure. Younger age at enucleation (p=0.038) and shorter interval between chemotherapy and enucleation (p=0.025), were risk factors for complications, while history of external beam radiation therapy (p=0.097) was not.

Conclusion: Complication rates were comparable between porous (porous polyethylene) and non-porous (silicone) implants, although types of complications varied. Risk factors for complications included age at enucleation (less than 18 months) and recent chemotherapy. Porous and non-porous implants are safe ocular implants for retinoblastoma.

P-0796 | Cut End Optic Nerve Retinoblastoma Evolution and Treatment During A 10 Years Follow Up at a Tertiary Institution at Mexico

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Background/Objectives: Retinoblastoma with orbital and optic nerve involvement is frequently diagnosed in developing countries. This paper reports patients affected by retinoblastoma with intraocular affection and cut end optic nerve involvement.

Design/Methods: Retrospective review of 10 years research in age, pathological diagnosis, type of treatment and overall survival in a group of patients with specific characteristics.

Results: Results. From 288 patients, 36 cases were registered for the period of type researched. From the 36 cases, 28 patients had unilateral involvement, eight were bilateral and the media for age at diagnosis was 31 months. All 36 patients received chemotherapy; 16 with iphosphamide, carboplatin and etoposido, 7 received carboplatin, etoposido and vincristina and 4 patients received carboplatin and etoposido. Orbit radiotherapy was given to 23 cases.

The results obtained for overall survival were 17 patients (47.2%) alive with no tumour activity, 10 alive with tumour activity (27.8%) and 9 dead due tumour activity. Overall survival of 75.9%.

The 70% of patients who did not receive radiotherapy were alive in a 150 months follow up, whereas 30% of who receive radiotherapy survive in the same follow up time.

Conclusion: This category of special patients is not frequently found in developing countries due advance stage retinoblastoma is diagnosed in orbital stage with optic nerve involvement.

Biologically is established that cut-end optic nerve involvement should have nervous system involvement, however we establish that if treated with intense chemotherapy without radiotherapy patient can have a positive survival.

Conclusion: Cut end optic nerve retinoblastoma should be treated with intense chemotherapy without radiotherapy.

P-0797 | Analysis of the Result and the Clinical Significance of 91 Retinoblastoma's Bone Marrow Inspection

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Background/Objectives: To explore the early diagnosis value of the bone marrow inspection for detecting distant metastasis of children Retinoblastoma (RB), and to provide the basis for the occasion of RB performing bone marrow inspection.

Design/Methods: Retrospective analysis of the 206 RB patients' medical records who came to Beijing Children's Hospital (BCH) Affiliated to Capital Medical University from Nov.2009 to May.2014. According to the International Intraocular Retinoblastoma Classification (IIRC), the result of bone marrow aspirate and biopsy of group D and group E at first diagnosis was recorded emphatically.

Results: Among the 206 cases, there were 91 cases undergone bone marrow inspection, 70 cases was performed bone marrow biopsy at the same time. There were 48 male (52.7%) and 43 female (47.3%), with a mean age of 25.1 months (bilateral 16.3 months, unilateral 29.0 months). Among 91 patients who had undergone bone marrow aspiration, 16 cases were simple site while 75 two site (sternum and posterior iliac crest). As for the result, juvenile lymphocytes of bone marrow smear more than 5% in only eight cases.

Conclusion: On the basis of our analysis, the rate of early bone marrow involvement in group D and group E of intraocular RB is extremely low, so bone marrow examination could not do routinely. But when there is one as follows, bone marrow cytology recommended, bone marrow biopsy performing if necessary to identify: 1. extraocular RB; 2. radiology suggests across lamina cribrosa, or finding tumour cells at resection margin of optic nerve; or involving choroid extensively; or anterior chamber, ciliary body, or a serrate involving; 3. older than five years old; 4. clinical symptoms and signs distinctly, metastasis suspected. For the patient of positive in bone marrow cytology, we recommend conducting bone marrow biopsy to identify the properties of immatures, in consideration of the young age, the active proliferation of bone marrow cells and other influencing factors.

P-0798 | Clinical and MRI Features of Retinoblastoma in Children

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Background/Objectives: To investigate clinical presentations and MRI features of retinoblastoma (RB) in children.

Design/Methods: The clinical and MRI data of 148 cases of retinoblastoma in children, confirmed by clinic or pathology in our hospital in recent 5 years, were analyzed retrospectively, which to analyze patient's gender, age, location of masses, and MRI features.

Results: In total 148 cases, the male to female ratio was 1.5:1, the average age was 20.1 ± 16.7 months. 36 cases (24.3%) were bilateral in the research and the average age of bilaterales was 11.9 months and unilaterales was 22.8 months. MRI of tumors show slightly hypointense-or isointense on T1WI (92.9%), isointense on T2WI (52.7%), mild or moderate enhancement on contrast material-enhanced T1WI (97.8%), and obvious hyperintense on DWI. The apparent diffusion coefficient (ADC) value was $(0.939 \pm 0.225) \times 10^{-3} \text{ mm}^2/\text{s}$.

Conclusion: Retinoblastoma mostly occur in infants, and the age of bilateral eyes is even smaller than the unilateral eye. MRI performance of retinoblastoma has certain characteristics and DWI also play a significant role in diagnosis.

P-0799 | Clinical Characteristic and Treatment of Retinoblastoma: A Single Institute Experience in Japan

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Background/Objectives: Retinoblastoma is a rare tumour which is the most common primary intraocular malignancy in childhood. Recently, systemic chemotherapy became standard primary treatment for intraocular retinoblastoma for eye salvage. We investigated clinical features of retinoblastoma patients retrospectively in a single institute in Japan.

Design/Methods: The evaluation period was from October 2009 to June 2015. Twenty-one retinoblastoma patients (9 male, 12 female) were diagnosed by funduscopy.

Results: The median age at diagnosis was 15 months (range, 0-56 months). The median follow-up period was 50 months (range, 8-78 months). Seven patients had bilateral retinoblastoma, including one trilateral retinoblastoma. Three patients had familial history. We judged the tumour response by tumour size, number of seeds, and tumour vascularity. Eighteen patients (86%) were alive in remission; while 3 patients died of primary disease progression. Thirteen patients received systemic chemotherapy combined vincristine, carboplatin, and etoposide (VEC); cycles are given every 3 weeks for 6-8 cycles. Consolidation focal therapy is started after 3-4 cycles of chemotherapy and 5 patients received intra-arterial chemotherapy. We used topotecan for 4 patients (5 eyes) who did not be well controlled by VEC regimen. All eyes showed favorable response, but it was temporarily. Severe treatment related toxicity had not occurred. We had not experienced second malignancy. Among the 28 eyes (7 of 21 patients had bilateral retinoblastoma), seven eyes (25%) were able to be controlled without eye enucleation.

Conclusion: Systemic chemotherapy has been becoming more popularly to reduce tumour bulk, however, the treatment efficacy is not sufficient. We have performed conventional chemotherapy as indicated in our institute and some eyes had controlled without enucleation. Four patients received second-line chemotherapy including topotecan, and all of them had effective. It was necessary to establish appropriate treatment strategy including of new agents, and to consider the timing of focal therapy.

P-0800 | Spectrum of Somatic RB1 Mutations in Retinoblastoma- A First Study in Lebanese and Syrian Children

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Background/Objectives: The recent establishment of a multidisciplinary retinoblastoma program in Lebanon has allowed genetic screening for retinoblastoma mutations in patients treated within the program. We present the results of molecular genetic testing of the RB1 gene in this patient population.

Design/Methods: A total of 36 patients with retinoblastoma were included. Nationalities included Syrian (n=22), Lebanese (n=14), and Iraqi (n=1). Twelve (33%) had unilateral disease. Genetic testing was financially covered for all children with bilateral disease, and for children with unilateral retinoblastoma diagnosed before 2 years of age. Families of older children with unilateral retinoblastoma were advised gene testing. DNA and RNA extraction was done on peripheral blood of probands by a certified clinical laboratory; PCR and direct sequencing were performed, then multiplex ligation-dependent probe amplification (MLPA) analysis if the sequencing results were normal. Cytogenetic testing was performed for one patient with syndromic features.

Results: All patients with bilateral retinoblastoma (n=20) or unilateral disease diagnosed before 2 years of age (n=7) had the test performed. Six (22%) had normal testing (4 had unilateral retinoblastoma), 7 (26%) had benign polymorphism identified (2 had unilateral retinoblastoma), and 14 (52%) had pathogenic mutations (1 had unilateral retinoblastoma). Identified mutations in the 14 patients included one chromosomal deletion, 2 large deletions, 1 small deletion, 2 frameshift mutations, 4 nonsense mutations, 1 insertion (in 2 siblings), and 2 intronic alterations expected to affect exon acceptor splice sites. Thus, the detection rates in the bilateral and unilateral cases were 65% (13/20) and 14% (1/7), respectively. Eight of the 13 identified pathogenic alterations were not previously described.

Conclusion: This is the first description of RB1 genetic mutations in children with retinoblastoma treated in Lebanon. We observed a large heterogeneity of identified pathogenic mutations. Incorporation of affordable testing in national health care plans for such patients is needed.

P-0801 | Outcomes of Mexican Retinoblastoma Protocol at Tertiary Referral Hospital in Mexico - Instituto Nacional de Pediatría

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Background/Objectives: In Mexico, Retinoblastoma (RB) is the second most frequent solid malignancy after Central nervous system (CNS). The survival rate for retinoblastoma patients has improved dramatically over the last century. The popular insurance have had an impact over outcomes prognostic of paediatric patients with lower incomes and improved in 95 percent the adherence to treatment. The purpose of this paper is to present the 7 years clinical experience of ocular rescue program in patient with RB that were treated at single Mexican Pediatric referral center.

Design/Methods: A transversal study, observational, retrolective. The information analyzed included medical treatment (chemotherapy and radiotherapy), event-free survival, and overall survival at 7 years of patients treated between 2007 and 2014.

Results: One hundred and ninety-nine of two hundred and fifty-nine patient with diagnosis of Retinoblastoma were included; age range was from 1.7 to 90.3 months, with a median of 23.5 months. At diagnosis, the 85% of patients with RB had advanced ocular stage, reason for few favorable results about salvage of ocular globe (8.5%). All patients received as first line of chemotherapy with either carboplatin/etoposide/vincristine and second line with either ifosfamide/carboplatin/etoposide in relapse or progressive diseases. The use of radiotherapy is important for orbital stage with overall survival at 7 years of 100%, this decrease to 65% in patients who did not receive it.

Conclusion: In our experience, patients with retinoblastoma have delayed diagnostic perhaps lack of timely referral with personal and equipment necessary to offer opportunity treatment and preservation of vision. At Instituto Nacional de Pediatría, the most patient had advanced stage, reason for 8.5% salvage of ocular globe.

P-0802 | Long Term Follow Up of Retinoblastoma Survivors: Experience from a Tertiary Center in India

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Background/Objectives: Retinoblastoma (Rb) is the most common primary intraocular tumour of infancy and childhood. Survivors' ocular and visual problems and increased risk for subsequent malignancy are well documented but data on long term health status of Rb survivors are limited: this being particularly true for India.

Design/Methods: Children who had completed treatment for retinoblastoma at least 2 years before and were under follow up at the after cancer treatment clinic were evaluated.

Results: In our series of 213 patients, the median age was 29 months, there was a male preponderance, and majority had unilateral disease. Majority of the patients received chemotherapy, and few received radiation. Enucleation was done in almost three fourth. Growth was affected in about one third and majority were those who had received radiation. Diminished vision was there in about one-sixth and 3% underwent bilateral enucleation. Hypoplasia and contracted socket was seen in 14.1% cases. 2.7% were hearing impaired. About one-sixth had a global intelligence delay. Second neoplasms were seen in 0.01%. No other abnormalities seen.

Conclusion: Common late effects in our Rb survivors include diminished vision, Intellectual disability and contracted socket; there is a need for timely institution of prosthesis to avoid late effects like hypoplasia, contracted sockets and better cosmesis and enhanced self esteem. Second neoplasm is a concern. Lifelong follow up and counseling of a healthy lifestyle is needed for Rb survivors.

P-0803 | NADPH Oxidase-4 Dependent Reactive Oxygen Species Stress: An Expression Study in Human Retinoblastoma Tumour Cells

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Background/Objectives: Reactive Oxygen Species (ROS) have been shown to enhance proliferation of cancer cells. NADPH Oxidases (NOX4) are major intracellular source of reactive oxygen species and elevated ROS levels are often found associated with cancer, apoptosis resistance, tumour cell invasion etc. Under oxidative stress conditions, excessive ROS can damage cellular proteins, lipids and DNA, leading to fatal lesions/mutations in cell that contribute to carcinogenesis. Therefore, the purpose of this study is to examine ROS stress by evaluating the expression of NOX4 protein in human retinoblastoma.

Design/Methods: Immunohistochemical (IHC) expression of NOX4 protein was analyzed in 109 prospective cases of primary enucleated retinoblastoma specimens and then validated by western blotting and RT-PCR. Cytoplasmic staining was considered as positive and graded as weak/negative, moderate and strong. Expression of this protein was correlated with clinical parameters, tumour differentiation, and various histopathological high risk factors (HRFs).

Results: There was a slight male preponderance (55.9%) & 25/109 (22.9%) were bilateral. The tumour was poorly differentiated in 82/109 (75.2%) with extensive necrosis in 65 (49.6%) cases. Calcification was found in 34/109 (31.2%) cases. Massive choroidal invasion was the most frequently observed histopathological high risk factor in 33.3% cases. In addition, optic nerve cut end and retrolaminar invasion was seen in 26.6% cases, iris & ciliary body in 9.2% whereas scleral invasion was found in 8.25%. One or more than one HRFs were identified in 46/109 cases. NOX4 protein was expressed in 71.5% (78/109) primary retinoblastoma cases by immunohistochemistry which was confirmed by RT-PCR. NOX4 was statistically significant with massive choroidal invasion and poor differentiation.

Conclusion: This is the first study to show the expression of NOX4 protein in retinoblastoma tumour. Our results revealed that NOX4 was highly expressed in human retinoblastoma. Investigating NOX4 might be helpful for developing therapy with combination of ROS-eliminating strategies in the management of retinoblastoma patients.

P-0804 | Clinicopathological Significance of HMG Proteins in Retinoblastoma

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Background/Objectives: High Mobility Group proteins (HMG) are more abundant in rapidly dividing and transformed cells. HMGB1 is considered to be DNA chaperone as it binds without any specificity. It is the structural protein which alters nuclear homeostasis and genomic stability in chromatin. These are a group of proteins regulating tumorigenesis and tumour invasion. Increased expression of HMGA1, HMGA2 and HMGB1 has been reported in various benign and malignant tumors. The aim of present study was to analyze expression of HMGA1, HMGA2 and HMGB1 proteins in retinoblastoma.

Design/Methods: Protein expression of HMGA1, HMGA2 and HMGB1 in formalin fixed 60 retinoblastoma tissues was performed by immunohistochemistry and their mRNA expressions were analyzed on 30 fresh primary enucleated retinoblastoma samples by semi quantitative Reverse Transcription-polymerase chain reaction (RT-PCR). Results were then correlated with clinicopathological parameters. Western blotting performed on 10 fresh primary enucleated retinoblastoma samples to confirm the immunohistochemical expression.

Results: Immunohistochemical analysis of HMGA1, HMGA2 and HMGB1 was seen in 55%, 52.25% and 60% retinoblastoma cases respectively. mRNA expressions of HMGA1, HMGA2 was found to be 56.6%, 63.3% and 80% respectively. The mRNA results correlated well with Immunostaining results. Expression of HMGA1, HMGA2 and HMGB1 was significantly associated with poor tumour differentiation whereas HMGA1, HMGA2 are significantly associated with choroidal invasion and HMGB1 was significantly associated with optic nerve invasion.

Conclusion: HMG proteins may contribute to tumorigenesis of Rb. Our results show expression of HMGB1 is a marker of poor prognosis and could serve as a therapeutic target in the management of RB

P-0805 | Visual Acuity after Complex Retinoblastoma Treatment

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Background/Objectives: Retinoblastoma (Rb) is the most common intraocular tumour in childhood. Many children with affected eyes have to be enucleated for tumour persistence or relapse. Impaired vision can persist even if a bulb with Rb is successfully salvaged. We focused on visual acuity of patients with affected eyes after a complex retinoblastoma treatment.

Design/Methods: Since 1999 to the end of 2013, 74 children (5.2/year), 96 eyes (6.8/year) with retinoblastoma were treated at our Institution (22 patients had bilateral Rb, 1 trilateral Rb). Median age at diagnosis was 16 months (0 – 104.8 months). According to the International Classification of Rb (ICRb): A- were 7, B-19, C-15, D-24, E-31. Vision was measured using Snellen eye charts, best corrected visual acuity, displayed in decimal system.

Results: Initial enucleation was performed according to ICRb to A-0, B-0, C-0, D-1, E-22. Chemotherapy (CTX) and local therapy (laser-, cryo- and brachy- therapy) were used in 71 eyes, ICRb: A were 7, B-19, C-15, D-23, E-9. Three patients were treated with selective intra-arterial CTX to arteria ophthalmica in addition (1 C and 2 D). Thirty four eyes from 17 (47.9%) had to be enucleated, ICRb: A-0%, B-0%, C-35.8%, D-90.1%, E-100%; the visual acuity is therefore zero. In salvaged eyes, the median visual acuity is: A-1.0 (standard deviation (SD) – 0.28), B-0.23 (SD ±0.36), C-0.33 (SD ±0.41), D-0.2 (SD ±0.15), E-zero (all eyes were enucleated).

Conclusion: The visual acuity is generally low after Rb treatment. When we consider that a relatively good vision is the best corrected visual acuity greater than 0.35, the suitable vision after complex Rb treatment have A-100%, B-43%, C-27%, D-5% and E-0% eyes.

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P-0806 | Nonmetastatic Orbital Retinoblastoma in a Tertiary Referral Hospital in Mexico: A Retrospective Review of 145 Patients

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Background/Objectives: Retinoblastoma (RB) is the most frequent malignant eye tumour in childhood. In developing countries advanced stages are common, although there are many non-metastatic cases. The purpose of this paper is to present the 25-year clinical experience of patients with nonmetastatic orbital RB that were treated at a single Mexican Pediatric referral center.

Design/Methods: A retrospective analysis was carried out reviewing the clinical characteristics and treatment of patients with nonmetastatic orbital RB. The information analyzed included medical and surgical treatment, event-free survival and overall survival of patients treated between 1990 and 2015.

Results: One hundred and forty five patients were included; age range was from 0 to 108 months, with a median of 78 months. All patients received chemotherapy with either carboplatin/etoposide or ifosfamide/carboplatin/etoposide. One hundred and eight patients received radiotherapy, which had a better prognosis than those who did not receive it. Of the patients included, there was an event-free survival of 60.1% and a 38-month overall survival of 71.2%, with a 16-year follow-up.

Conclusion: In our experience, nonmetastatic orbital RB has a very high survival rate in spite of the use of different treatment regimens.

P-0807 | The Role of Local Chemotherapy in Case of Insufficient Tumour Response to Organ-Saving Treatment of Retinoblastoma (RB) in Children

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Background/Objectives: To evaluate the outcome of 27 eyes, with recurrent or refractory Rb after intravenous chemotherapy in combination with other techniques of focal tumour destruction and without, in a few cases after external beam radiotherapy (RT), using selective intra-arterial chemotherapy (SIAC) and/or intravitreal chemotherapy (IViC).

Design/Methods: A retrospective study was conducted after local chemotherapy in 27 eyes of 25 patients in our clinic. SIAC was used as first option in cases with retinal or subretinal disease with or without vitreous seeding. IViC was used for isolated vitreous disease or for complementary treatment in eyes with partial vitreous seeding response to SIAC. Focal therapy was used as needed to consolidate treatment and in 2 cases was used RT. 27 eyes of 25 patients were treated. 2 (7.4%) eyes were treated with SIAC, 14 (51.9%) eyes with IViC and 11 (40.7%) eyes with both therapies. SIAC was used melphalan 2-7.5 mg + topotecan 1 mg. The median infusions per eye were 2 (range 1-4). IViC was used melphalan 16-20 µg + topotecan 20 µg. The median injections were 3 (range 2-5).

Results: At a median follow up of 23 months (range 9-57 months) all patients with unilateral Rb (n=10) and of 39 months (range 12-77 months) all patients with bilateral Rb (n=15) are alive with no metastatic disease. 25 of 27 eyes (85%) were preserved.

Conclusion: The use of both therapies SIAC and IViC as isolated modality or in combination to treat recurrent or refractory retinoblastoma showed successfully results in globe preservation.

P-0808 | Is a Diagnostic Cerebrospinal Fluid (CSF) for Evidence of Metastasis Justified in Intraocular Group E Retinoblastoma?

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Background/Objectives: The necessity of performing a lumbar puncture for obtaining CSF for diagnosis of CNS metastasis in intraocular retinoblastoma is debated. There are very few studies that have analyzed results of metastatic workup in various stages of retinoblastoma.

Design/Methods: This is a retrospective, single-institution study. A compilation of results of CSF cytology performed in patients with retinoblastoma over a 13-year-period (2003-2015) is presented. The grouping was performed by 'international classification of retinoblastoma'. The staging was based on 'international retinoblastoma staging system'. As per the units' policy, a diagnostic CSF was performed in patients with Group E or in those with evidence of extra-ocular disease. In patients with bilateral retinoblastoma, the indication for lumbar puncture was based on the eye with the higher stage. A CSF was often not performed in patients with overt stage 4, as they were offered palliative care. Patients with relapsed disease were excluded.

Results: During the study-period, 334 patients with retinoblastoma were registered; 318 were evaluable as records were incomplete in 16. A diagnostic CSF was performed in 223 (70.1%) patients. The median age was 30 months (range: 2-108). The number of patients with stage 0, 1, 2, 3 and 4 were 16, 123, 12, 69 and 3, respectively. The number of patients with Group E disease were 92 (41%). The CSF was positive for malignant cells in 7/223 (3.1%) patients. None of the patients with stage 0, 1 or 2 had a positive CSF cytology for malignant cells. Six (8.7%) and 1 (33%) patient(s) with stage 3 and overt stage 4 disease, respectively had CSF metastasis.

Conclusion: None of the patients in this study with intraocular group E or stage 0, 1 or 2 disease had an evidence of CSF metastasis. A diagnostic CSF could be avoided in early stage retinoblastoma, if similar data is generated from additional centers.

P-0809 | Observation on Clinical Characteristics and Curative Effect of 8 Children with High Risk Retinoblastoma

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Background/Objectives: To analyze the clinical characteristics of diagnosis and treatment and efficacy and prognosis of high-risk group of retinoblastoma(Rb)in our center, and to share the experience in treatment.

Design/Methods: Clinical data of 8 paediatric patients(9 eyes)with Rb from 2014 to 2016 were analyzed retrospectively. The onset age, initial symptom, clinical tumour stage, treatment method and therapeutic effect were analyzed.

Results: The 8 cases of high-risk patients were followed up until March 2016. The average follow-up time is (10.5 ± 8.5) months, Boys 6, girls 2, male: female =3:1; 1 cases of age 2 years old, 7 cases of 2 years old. With the average age (39.5 + 19) months, the symptoms of initial diagnosis are Protrusion of eyeball or occupied. The shortest history was 1 months, the longest was 24 months. The clinical stage of 9 eyes showed: B stage 11.1% (1/9), D stage 33.3% (3/9), E stage 3.3% (3/9), extra ocular stage 22.2% (2/9). Enucleating in 6 cases, 4 cases of recurrence; 1 cases of bone marrow metastasis; disease-free survival of 4 cases, 2 cases during chemotherapy and radiotherapy, 2 cases of death, death due to intracranial metastasis.

Conclusion: The age of onset in children with high-risk neuroblastoma was older, the children were late treatment, most have occurred in local or distant metastasis, and eye treatment difficulties. At present, our hospital risk chemotherapy and recurrence therapy is safe and effective, and a few of the children can Eye protection. But with a high recurrence rate, once transferred to CNS has a poor prognosis.

P-0810 | What can Ophthalmological Local Treatment of Retinoblastoma do in Chemotherapy Insufficiency?

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Background/Objectives: Presently chemotherapy (CT) is recognized as the first line treatment for retinoblastoma (Rbl). However, significant number of cases of CT insufficiency requires additional local treatment – cryotherapy, laser thermotherapy, or brachytherapy. There is limited information concerning the effectiveness of these methods after completing the CT with the lack of effectiveness.

Design/Methods: A total of 388 tumors in 102 eyes of 82 children with insufficient response to systemic and local CT were included into the study. Bilateral retinoblastoma was in 63 children, 19 children were monocular. Twenty five eyes were group A, 33-group B, 23-group C, 21-group D. One hundred and eight tumors were treated with brachytherapy (Ru-106, Sr-90). In 28 eyes the plaques were relocated successively to irradiate two or three tumors. Two hundred sixty-seven tumors were treated with laser thermotherapy, 56 with cryotherapy. Ten eyes with resistant recurrent multiple Rbl were treated with the focal therapies simultaneously with intra vitreous melphalan injections (16 - 20µg).The follow-up is from 3 to 60 months (mean, 19).

Results: Ninety seven eyes (95%) were retained. The regression pattern types after each of the treatment methods are evaluated. Complete or partial regression was achieved in 90 tumors (83%) after brachytherapy, in 203 tumors (76%) after thermotherapy, in 49 tumors (87.5%) after

cryotherapy. There were 56 (21%) recurrences after thermotherapy, 4 (7%) after cryotherapy. There were no cases of metastases.

Conclusion: Local treatment is a necessary and effective part of Rbl treatment especially in chemotherapy insufficiency. Simultaneous intra vitreous CT seems to increase the effect of focal therapy.

SOFT TISSUE SARCOMAS

P-0811 | Outcome and Factors Affecting Survival in Children with Intermediate Risk Rhabdomyosarcoma: Children's Cancer Hospital Egypt 57357 Experience

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Background/Objectives: Treatment of childhood Rhabdomyosarcoma (RMS) needs a multidisciplinary approach, including surgical excision/radiotherapy for local control and chemotherapy for control of systemic disease. This study aimed to evaluate the outcome and factors affecting survival of Intermediate Risk (IR) RMS patients.

Design/Methods: This retrospective study included newly diagnosed patients with Intermediate Risk Rhabdomyosarcoma who were treated at Children's Cancer Hospital Egypt-57357 from August 2007 to June 2015, following IRS-V and subsequent COG treatment guidelines.

Results: A total of 219 patients were included, with a median age of 4 years. Of those patients, 154 (70.31%) were diagnosed with Embryonal-type RMS, and 65 (29.68%) had Alveolar-type RMS. Stage I disease was encountered in 35 patients (15.9%), while 38 (17.3%) and 146 (66.66%) patients presented in stages 2 and 3, respectively. The most common primary site was head and neck (parameningeal) which was seen in 33.3% of the patients, followed by urinary bladder and pelvic representing 15.1% and 17.8%, respectively. According to the assigned treatment protocols, 61 patients (39.61%) received early local radiotherapy at week 4 of treatment, while 93 (60.38%) received delayed radiotherapy at week 12. With median duration of follow up of 22.5 months, the 5-year Overall Survival (OS) was (66.8%) and Failure-Free Survival (FFS) was (57.8%) for the whole study population. When compared according to the primary site, poorer FFS was found in patients with pelvic RMS (48.1% at 5 years) and parameningeal RMS (53.1%), compared to 61.5% and 66% in bladder and non-parameningeal head and neck sites respectively (P=0.05). FFS and OS were significantly affected by the time of local radiotherapy (77.1% FFS in early radiotherapy group compared with 57.8% in late radiotherapy group, P=0.02).

Conclusion: Early local radiotherapy was associated with better outcomes in IR-RMS patients. Primary site at initial presentation significantly affects the survival in these patients.

P-0812 | Evaluation of Outcomes of Extra-Osseous Ewing Sarcoma Family of Tumors in Children: A Single Institution Experience

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Background/Objectives: Extra-Osseous Ewings sarcoma (EOE) is a rare clinico-pathologic entity within Ewing sarcoma Family of Tumors (ESFT), with few international reports addressing this tumour. In this study, we retrospectively reviewed the outcomes of EOE patients treated at our institute.

Design/Methods: Data for all patients with extra-osseous ESFT treated at Children's Cancer Hospital Egypt-57357 between February 2008 and December 2014 was analyzed. Patients were treated with chemotherapy surgery and/or radiotherapy as modality of local control.

Results: A total of 37 patients with EOE were included in the study, with a median age at diagnosis of 8 years (Range: 1 – 18 years). Twenty-six patients (70.2%) had localized tumors, while eleven patients (29.8%) had metastatic disease. The most common site was in the axial skeleton, and the median tumour size was 8 cm. With a median follow up period of 31.4 months, the 5-year overall survival (OS) and Event-Free Survival (EFS) were 76.3% and 67.8% respectively for localized tumors, while the 3-year OS and EFS were 42.9% and 36% respectively for patients with metastatic disease. Thirteen patients underwent surgery with or without radiotherapy, while twenty-four patients received radiation therapy only. At time of analysis, 22 patients were alive in complete remission. Median time to relapse was 42.2 months, 4 patients developed systemic relapse and 3 patients had local recurrence.

In univariate analysis, age < 8 years was associated with better outcome ($P=0.04$). Neither the gender, tumour extension, tumour size, site or local control modality had any statistical impact on survival.

Conclusion: In our study, the outcome for EOE was comparable to that reported for patients with osseous ESFT treated at the same time period with the same treatment protocol. Patient age was found to be the only significant prognostic factor affecting the outcomes of EOE.

P-0813 | Topotecan, Vincristine and Doxorubicin (TVD) for the Management of Relapsed or Refractory Rhabdomyosarcoma: The UK Experience

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Background/Objectives: Relapsed or refractory rhabdomyosarcoma (RMS) is incurable for most patients and its management remains challenging. A potential role for doxorubicin and topoisomerase I inhibitors in RMS has been identified in up front window studies. TVD is one of the available RMS relapse strategies in the UK and a good response rate has been reported previously. This report outlines UK experience to date.

Design/Methods: UK cases of relapsed/refractory RMS treated with TVD were identified through contact with all UK specialist paediatric oncology centres. Details of initial diagnosis and therapy were obtained from the European paediatric Soft tissue Sarcoma Group (EpSSG) database. Clinical details concerning the relapse and TVD response were obtained from the treating centres. Images were centrally reviewed.

Results: 5 patients (2 refractory, 3 relapsed) (2 locoregional, 1 local and metastatic) were identified. Histology was embryonal ($n=4$) and alveolar (PAX3-FOXO1 fusion gene) in 1. All patients had received initial chemotherapy (IVA) according to EpSSG RMS 2005. No other relapse therapy was received prior to TVD. Three patients received 1 cycle, 1 patient 2 cycles and 1 patient 6 cycles of TVD. Mean cycle-length was 25 (21-35) days. 1 patient (PAX3-FOXO1 positive, node only recurrence) achieved a complete response and subsequent radiotherapy. 1 had stable disease (after 1 cycle) and 3 experienced disease progression. The patient with CR had a further metastatic relapse 35 months following TVD. Patients experienced significant toxicity (grade IV myelosuppression ($n=4$), febrile neutropenia ($n=4$) and mucositis and grade III typhilitis ($n=1$)).

Conclusion: In this small group of patients objective response rate was only 1/5 (20%) albeit a CR. This differs from the previously reported response rate of 5/9. TVD may be most beneficial for a subgroup of patients with increased chance of salvage (small tumour, local relapse, no previous radiotherapy). Further evaluation of topoisomerase I inhibitor with anthracycline is warranted.

P-0814 | Dedifferentiated Chondrosarcoma in An Adolescent: Rare Bony Tumour with Long Term Survival

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Background/Objectives: Dedifferentiated chondrosarcoma is a highly malignant form of chondrosarcoma, characterized by biphasic morphology with a high grade non-cartilaginous sarcoma (dedifferentiated component) arising in a background of low grade chondrosarcoma. It is uncommon in the paediatric population with little published data and grim prognosis ranging from 7-24%.

Design/Methods: We report a 19-year-old male presenting with a 2 month history of left hip pain. Imaging showed an aggressive proximal femoral lytic lesion. The biopsy showed primitive spindle cells with fibrosarcomatous growth pattern, myxoid matrix, and weak S100 expression. The initial differential diagnosis included synovial sarcoma and malignant peripheral nerve sheath tumour. The molecular evaluation was negative for SS18/SSX1 and SS18/SSX2 fusion transcripts by RT-DNA amplification. No SS18 gene rearrangement was detected by FISH. Additional molecular tests argued against myxoid liposarcoma and Ewing/PNET family of tumors. A diagnosis of unclassified sarcoma was rendered, and he underwent wide excision of the proximal femur, joint capsule, and acetabulum with hip reconstruction, joint prosthesis, and bone grafting. Cytogenetics evaluation demonstrated a complex karyotype. Difficulties in classification prompted extensive sampling of the excision specimen which revealed a ~ 5 mm focus of low grade chondrosarcoma with abrupt transition to the non-cartilaginous primitive neoplasm, supporting a final diagnosis of dedifferentiated chondrosarcoma.

Metastatic work up confirmed localized disease. In contrast to classical osteosarcoma and Ewing sarcoma, experience with chemotherapy is very limited. There is no standard chemotherapy regimen for these patients and paediatric data are not available. He received chemotherapy as per the standard arm of Children's Oncology Group osteosarcoma protocol AOST0331 (euramos-1) including high dose methotrexate, cisplatin and doxorubicin. Chemotherapy was well tolerated. No radiation was administered.

Results: There is no evidence of recurrent or metastatic disease at 2.5 years post treatment. He is fully ambulatory and healthy.

Conclusion: Dedifferentiated chondrosarcoma may do well with complete surgical excision and chemotherapy.

P-0815 | Effect of Delaying Local Control Radiotherapy on Outcome of Localized Paediatric Bladder/Prostate Rhabdomyosarcoma

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Background/Objectives: Multidisciplinary treatment approach is used in treatment of bladder/prostate rhabdomyosarcoma (RMS), yet it is unclear, which treatment strategy is optimal for local control. Radiotherapy is one of the treatment local control methods. The study evaluate the impact of timing of radiotherapy (RTH) and Intensity modulated radiotherapy (IMRT) technique on cancer control outcomes for children with bladder/prostate RMS.

Design/Methods: Retrospective analysis of 29 patients treated as local control by RTH at Children's Cancer Hospital Egypt in August 2007-December 2015. Seventeen patients (58.6%) were treated by conformal radiotherapy and 12 patients (41.3%) treated by IMRT technique.

Results: Seventeen (58.6%) patients started Local radiotherapy before/at week 12 and 12 (41.4%) patients started after. Four years failure-free survival (FFS) and Overall survival (OS) for those who had early and delayed local control are ($94.1 \pm 7\%$ vs. $33.3 \pm 15.1\%$ $p=0.007$), (100% vs. $56.8 \pm 6.5\%$ $p=0.007$), respectively. Failure free survival for patients who treated Over treatment time (OTT) >5 weeks and < 5weeks is ($49.4 \pm 14\%$, $81.5 \pm 9.8\%$) respectively. Although they show difference, yet not statistically significant (0.6). Ten patients (83.3%) who had OTT <5 weeks were treated by IMRT.

Conclusion: Earlier local control was associated with better outcome in children with bladder/prostate RMS. IMRT shows tendency to improve survival profile due to decrease toxicity yet decrease OTT.

P-0816 | Peripheral Primitive Neuroectodermal Tumour (P-PNET) in Children; Single Center Experience from Karachi, Pakistan

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Background/Objectives: To study the clinico-pathological features and survival in children with peripheral primitive neuroectodermal tumour (PPNET).

Design/Methods: Retrospective review of peripheral primitive neuroectodermal tumour (PPNET) treated at our center from Dec 2001 -Nov- 2015. Children with PNET of kidney excluded because of referral to other centre. CT scan chest, abdomen and pelvis or MRI of other primary site, bilateral bone marrow and bone scan were done for staging work up. Diagnosis established with histopathology including immunohistochemistry. Age, sex, site and stage of the disease, type and courses of chemotherapy given, surgical and radiation treatment detail were recorded. Overall and event free survival was analysed.

Results: We had 30 previously untreated patients with PPNET, 17 with chest wall, 4 with urinary bladder and prostate, 2 pelvic and remaining other sites. Age range of whole group was 1 -18 years (median 13 years). Median age of chest wall PNET was 14 years, for other sites 6 years. Male to female ratio, 2.5:1. Majority presented with mass. Localized disease were 25/30 while 5/30 with metastatic disease. Upfront surgery done in 13/30 children, 17/30 received neo-adjuvant chemotherapy with VIDE (vincristine, ifosfamide, doxorubicin and etoposide) and recently compressed cycles of VCD/IE. Delayed surgery done mostly after 6 courses. Post operative radiation given to 14 cases with < 90% necrosis or positive margin. Total courses of chemotherapy were 14. Overall and event free survival was 57% with abandonment; 63% without abandonment with a median follow up of 8 years. Overall survival was better with chest wall primary (71%) vs other primary sites (54%).

Conclusion: In our series of Peripheral PNET chest wall is the most common site with better outcome while other peripheral sites are seen in younger age group with less favourable outcome.

P-0817 | Gemcitabine and Docetaxel in Paediatric Patients with Relapsed or Refractory Sarcomas. Experience in a Paediatric Center. Hospital de Niños Ricardo Gutierrez

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Background/Objectives: Report the experience in use of Gemcitabine/Docetaxel as rescue therapy in patients with refractory or relapsed paediatric sarcomas. Describe clinical response, toxicity according CTCAE/version 4.0 2010 and adherence to treatment.

Design/Methods: We evaluate outcome of paediatric patients with relapsed/refractory sarcomas treated with Gemcitabine/Docetaxel admitted to Hospital de Niños Ricardo Gutierrez between July 2009-March 2016. Patients have previously received 1 or 2 lines of chemotherapy according to histological type. Regimen: Gemcitabine 675mg/m²/d (days 1/8) and docetaxel 75mg/m²/d (day 8) every 3 weeks until disease progression.

Results: Twelve patients were treated. Median age: 12 years (9-17). Histologies: Osteosarcoma (6p), Ewing sarcoma (2p), malignant tumour of nerve sheath MTNS (1p), undifferentiated sarcoma (1p), alveolar rhabdomyosarcoma (1p), and pleomorphic sarcoma (1p). They received 58 cycles, median of cycles 5 (2-9). Outcome: One patient (8.3%) with metastatic osteosarcoma achieved complete response and is alive 8.5 months from relapse. Two patients partial response was achieved (17%) with metastatic lung osteosarcoma 6.5 and 5.1 months to progression, stable disease in 4p(33%): MTNS 3.5 months to progression, undifferentiated sarcoma 2.8 months to progression, Ewing sarcoma 3.5 months to progression, metastatic osteosarcoma 4.4 months to progression. Five patients (41%) progressed without response and died. Median time to progression was 3.4 months (0.21 -9).

Overall response rate (CR+PR):25% and disease stabilization was observed in 33% giving a disease control rate of 58% All patients presented grade 2 alopecia, 5p presented Grade 1 and 2 hematologic toxicity (2 neutropenia, 2 thrombocytopenia, 1 anemia), and 1p grade 2 arthritis. All patients had good adherence.

Conclusion: Gemcitabine/docetaxel resulted an option to handle patients with relapsed or refractory sarcomas which allowed good life quality with low toxicity. Despite the low number of patients it seem to be a good option particularly for patients with metastatic osteosarcoma given the complete and partial responses and longer time to progression in this cohort.

P-0818 | The Significance of Tumour Expression of Hypoxia Inducible Factor 1-alpha in Relation to Disease Advancement and Prediction of the Outcome in Paediatric Soft Tissue Sarcomas

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Background/Objectives: Hypoxia is a characteristic feature of most malignant solid tumors. Under hypoxic conditions an increased activity of hypoxia-inducible factor-1 alpha (HIF-1 α) occurs, which activates various processes favorable for cancer cells survival. Recently HIF-1 α has been proven to promote proliferation, invasiveness and resistance to therapy of many adult malignancies, including soft tissue sarcomas (STS). The prognostic role of HIF-1 α in paediatric STS is unknown.

The objective of the study was to analyze whether primary tumour HIF-1 α expression correlates with disease activity, course and final outcome in children with STS.

Design/Methods: The study included 91 children with STS (66 rhabdomyosarcoma, 25 non-rhabdomyosarcoma; M:F 53:38; median age; 105 months), treated with CWS protocols between 1992 and 2013 in Poland. In all patients the archival paraffin-embedded primary tumour samples and full clinical data were available. HIF-1 α expressions were assessed on tissue microarrays by immunohistochemistry, as low (L-HIF-1 α) and high (H-HIF-1 α), based on staining intensity and percentage of immunoreactive cells within the tumour. The study was approved by the ethics committee (NKBBN/449/2013).

Results: Most patients were diagnosed in advanced inoperable stages with poor response to CHT noted in 27.8% of them. The probabilities of 5-y-EFS and 5-y-OS were: 37.4 \pm 5.6% and 48.8 \pm 5.9%, respectively. H-HIF-1 α was detected in 48.3% of tumors and correlated significantly with more advanced STS stages (p=0.00336), lymph nodes metastases (p=0.00419), unfavorable histology (p=0.0147) and alveolar rhabdomyosarcoma subtype (p=0.00362). There was no relationship between HIF-1 α expression and age, gender, tumour size and invasiveness and response to CHT. However, H-HIF1 α correlated independently with poorer EFS and OS. The probability of 5-y-EFS and 5-y-OS in patients with H-HIF-1 α were 13.3 \pm 5.3% and 24.7 \pm 6.7% compared to 65.9 \pm 7.6% and 79.3 \pm 7.3% in patients with L-HIF-1 α (p=0.00001 and p=0.00000; respectively).

Conclusion: Detection of H-HIF-1 α in the tumour indicates its aggressive phenotype and independently predicts unfavorable course and outcome of paediatric STS.

P-0819 | Metastatic Mandibular Rhabdomyosarcoma in an Adolescent Presenting with Hypercalcaemia Secondary to Ectopic Parathyroid Hormone Expression

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Background/Objectives: Hypercalcaemia occurs in up to 30% of adult patients with cancer, but in children the incidence is only 0.4-0.7%. Unlike adult patients where hypercalcaemia often heralds a poor prognosis, in children it is most commonly observed at diagnosis. Mechanisms underpinning hypercalcaemia varies with tumour type. Tumour secretion of parathyroid hormone (PTH) is a very rare cause for hypercalcaemia associated with malignancy. Here we report a case of hypercalcaemia secondary to ectopic PTH secretion from childhood malignancy. A previously healthy 14-year-old male presented with a several month history of mandibular swelling, numbness and pain. Initial peripheral blood sampling demonstrated hypercalcaemia (Calcium Adjusted 3.89mmol/L, normal range 2.25-2.5mmol/L) with an elevated parathyroid hormone level (10.2pmol/L, normal range 1.6-6.9pmol/L), normal phosphate (1.28mmol/L, normal range 0.9-1.8mmol/L) but insufficient 25-hydroxyvitamin-D (66nmol/L, normal range >75nmol/L).

Design/Methods: Hypercalcaemia was acutely managed with hyperhydration therapy, loop-diuretics and intravenous bisphosphonates. Mandibular biopsy confirmed presence of alveolar rhabdomyosarcoma. Further imaging demonstrating with large metastatic lytic lesions in the axial skeleton. Ultrasonography did not reveal parathyroid adenoma. Chemotherapy according to the metastatic arm of the European Paediatric Soft Tissue Sarcoma Study Group 2005 protocol was commenced.

Results: Chemotherapy reduced the size of both primary and metastatic lesions. Initially demonstrating extensive bony damage with "floating teeth", the mandible showed evidence of bone reformation following several cycles of chemotherapy. Following initial management, hypercalcaemia did not return throughout the duration of his treatment, although electrolytes remained disturbed requiring replacement. After an initial decline, serum PTH levels peaked at

33.5pmol/L after the second cycle of chemotherapy before remaining elevated despite apparent resolution of disease on imaging.

Conclusion: Hypercalcaemia in malignancy is uncommon in children with cancer; hypercalcaemia secondary to ectopic PTH is exceptionally rare in this population. Although uncommon, recognising association between elevated PTH and hypercalcaemia of malignancy may aid early investigation into detecting a potential underlying malignancy.

P-0820 | Results of Treatment of Patients with Different Stages of Rhabdomyosarcoma (RMS) of the Orbit in Children

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Background/Objectives: Among all soft tissue sarcomas the most common is rhabdomyosarcoma (4%). The most frequent localization - head and neck, the orbit is 7%.

Design/Methods: 70 children with tumors of the orbit appealed to the Russian Cancer Research Center N.N. Blokhin (RCRC) from January 2000 to December 2014. Diagnosis of RMS is exposed for the first time in 49 cases (92.5%). Local recurrence 4 (7.5%) cases. The average age of patients 79.8 \pm 47.9 months. Four primary patients were not included in the research. The fate of 3 patients after treatment is unknown, 1 patient did not receive chemotherapy because of multiple malformations and died in a hospice. 1 of 45 patients came out from the study due to the refusal of parents of treatment. Surgery was performed on 44 patients: Only a biopsy -18, conserving surgery - 15, exenteration 11.

Results: Relapse-free survival in primary RMS group, depending on the program chemotherapy with an average follow-up of 106.8 \pm 12.4 months. Using VA -50.9 \pm 1.33%. Local protocol (Carb/VCR/Cis/Doxo) 81.3 \pm 9.8%.

Overall survival in the group of untreated patients (n = 44) was 97.7 \pm 2.3%, with an average follow-up of 153.5 \pm 3.4 months. Survival in patients with recurrent fetal RMS (n = 4) was 50%.

Conclusion: The preferred method of organ-saving treatment at the present stage is chemoradiotherapy with a rational approach to the selection of the mode of chemotherapy and radiotherapy. The main factors influencing the disease-free survival: are the ability to remove the primary tumour and adequate choice of chemotherapy program. Organ-operation in orbit is preferably carried out initially, if this is feasible, otherwise - just at the height of the chemotherapy effect and are designed to ensure: a radical removal of the tumour within the healthy tissue, maximum safety of orbital structures.

P-0821 | Ewing Sarcoma Family of Tumors (ESFT): Experience in the Last Ten Years of Treatment at the Instituto Nacional De Enfermedades Neoplasicas (INEN)

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Background/Objectives: ESFT is a group of malignant tumors of bone and soft tissues, with an average age of presentation of 15 years. Multimodal therapy has shown improvement in survival for these patients. To determine the clinical-pathological characteristics and disease-free survival (DFS) in patients with ESFT diagnosis.

Design/Methods: This is a descriptive, longitudinal and retrospective study. A total of 51 patients with ESFT, under 15 years of age, were evaluated during the past 10 years. Clinical parameters taken into account were: age, sex, tumour location, treatment protocol, post-treatment tumour reduction. DFS was calculated with the Kaplan Meier method.

Results: The average age was 9 years, 51% were males. Bone presentation 78.4%, extraosseous 21.6%. Pain was present in 80.4%, lymph node involvement 27.5%, functional limitation 72.5%, fever 15.7%. Metastasis at diagnosis 27.5%, with the lung as the most common site (19.6%). Chemotherapy produced toxicity with grade 2 and 3 neutropenia in 29.4%; grade 4 thrombocytopenia in 21.6%; and grade 3 and 4 anemia in 31.4%. Correlation between neoadjuvant chemotherapy and decrease of tumour size showed significant difference (p=0.008). DFS at 5 years was 65% in patients receiving full treatment and 25% in those with incomplete treatment.

Conclusion: Clinical characteristics included tumoral involvement, predominantly in the bone. Pain was the most common symptom and the lung was the most common site for metastasis. Patients who completed therapy showed improved DFS.

P-0822 | Use of Precision Medicine to Inform Treatment of Relapsed, Refractory, or Rare Paediatric Soft Tissue Sarcomas

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Background/Objectives: Due to the poor prognosis of paediatric patients with relapsed or refractory soft tissue sarcomas, discovery and implementation of innovative approaches to therapy is an urgent need. This pilot study evaluated the feasibility of using a personalized approach to guide the therapy of children with relapsed sarcomas to improve paediatric patient outcomes.

Design/Methods: A retrospective review of medical records and molecular diagnostic analysis from 10 paediatric subjects with relapsed, refractory, or rare soft tissue sarcomas was completed. The clinical molecular diagnostic report obtained from Paradigm[®], a next-generation sequencing cancer diagnostic testing company, provides recommended cancer therapies and potentially contraindicated therapies based on the individual's tumour genetic variants, copy number variants, gene fusions, mRNA expression, and protein expression. The therapeutic recommendations included in the clinical molecular diagnostic report were compared to the cancer therapies each subject received and the outcome of overall survival was ascertained.

Results: Two subjects received therapies aligned with the genomic diagnostic report recommended therapies. Six subjects received therapies not aligned with the report recommendations. Two subjects received potentially contraindicated therapies. A Cox regression model analysis revealed improvement in overall survival (hazard ratio = 0.48, $p = 0.2$) among subjects who received therapies consistent with tumour molecular testing compared to those who received inconsistent or potentially contraindicated therapies. For example, a 16 year-old male with metastatic alveolar soft part sarcoma had tumour molecular profiling at diagnosis. Results from the genomics report confirmed the highly neoangiogenic nature of the tumour and supported the use of sunitinib malate. The patient has improved to stable disease 18 months after diagnosis.

Conclusion: While our results are preliminary, this study indicates the positive impact of using precision cancer diagnostics to provide a basis for informed treatment of children with relapsed, refractory, or rare sarcomas and, ultimately, for improving outcomes of children with the most aggressive cancers.

P-0823 | Sarcomatoid Carcinoma in Xeroderma Pigmentosum : Efficacy of Immunotherapy

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Background/Objectives: Xeroderma Pigmentosum (XP) is a rare congenital DNA repair defect that causes multiple skin tumors. We report the case of a 6-year-old girl, from Mayotte, with XP, who developed a huge, nonoperable scalp tumour with meningeal invasion, who was treated with anti-PD1 molecule.

Design/Methods: In September 2014, the patient presented with a 30mm diameter sarcomatoid carcinoma of the scalp. Despite multiple resections, the tumour recurred and grew up to 149 × 104mm a year later. She was transferred to the Reunion Island for additional treatment. The tumour was very haemorrhagic and odorous with bone lysis and meningeal contact. The cerebral cortex was not involved and CSF was free of tumoral cells. Pathological exam showed a sarcomatoid carcinoma with Epithelial Membrane Antigen (EMA) and muscle actin focal positive staining. Two courses of chemotherapy (5FU – Cisplatin) were administered without any improvement. We therefore initiated an anti-PD1 molecule (Nivolumab) treatment at the dose of 3 mg/kg every 2 weeks.

Results: Owing to a better understanding of the interactions between the immune system and tumour cells, immunotherapy has emerged as a promising therapeutic strategy with objective response rates of approximately 30% in stage IV melanoma with molecules targeting PD1. When used as first-line treatment, it has also shown an improvement in overall survival in comparison with dacarbazine in BRAF wild-type melanoma. This is why we proposed Nivolumab for our patient. After 6 courses, we observed a dramatic tumour response (65% volume shrinkage) thus rendering surgery possible. Clinical and biological tolerance was excellent. Treatment is still ongoing with promising evolution.

Conclusion: There is little data about the use of Nivolumab in children. We report rapid clinical efficiency on an unresectable sarcomatoid carcinoma in a child with XP. These data are encouraging but further investigations are warranted.

P-0824 | ALK Status Determination and Crizotinib Therapy in High Risk Neuroblastoma and Soft Tissue Sarcoma

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Background/Objectives: Survival rates of high risk neuroblastomas and soft tissue sarcomas (STS) could be improved by using novel treatment options. ALK inhibitor therapy seems to be a potential new strategy. Anaplastic lymphoma kinase (ALK) is expressed only during the embryonal development of the nervous system, which makes it an ideal anti-tumour target. The presence of the ALK mutation is known in ALCL, some STS and neuroblastomas. The ALK inhibitor, crizotinib is effective in ALK positive tumors and its side effects are well tolerated. The aim of this work is to investigate the different ALK mutations in some solid tumors and to determine the potential advantage of crizotinib.

Design/Methods: 37 samples from children with STS (18 samples) and neuroblastoma (19 samples) were analyzed for ALK mutation by fluorescent in situ hybridization (FISH) break-apart probe and immunohistochemistry (IH). ALK positivity was not only detected, but the results of the two different methods were compared. Tumour samples were analyzed at diagnosis and at relapses, to identify potential changes in the ALK status.

Results: 3/18 STS samples were ALK positive by IH and 4/18 by FISH. 16/19 neuroblastoma samples were ALK positive by IH and 4/19 by FISH. The difference between the two methods can be explained by different types of ALK mutations (amplification, translocation, point mutation). Immunohistochemistry samples were evaluated manually and digitally as well. Crizotinib

treatment was initiated in 6 ALK positive patients. 1 complete remission, 3 partial responses, 1 stable disease and 1 progression was observed after initiating the therapy, however 4 from the initially responder cases progressed after couple months. The side effects were tolerable in all cases.

Conclusion: Our findings suggest the possible benefit of ALK status (ALK translocation, amplification or point mutation) screening in high risk neuroblastoma and STS patients. Crizotinib treatment can be beneficial in children with ALK positive solid tumors.

P-0825 | Late Relapse in Rhabdomyosarcoma. Report from GDL Sarcomi Parti Molli

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Background/Objectives: Prognosis in paediatric patients with relapsed rhabdomyosarcoma is not good. Studies show that the sooner is the relapse, the worst is the outcome. It is not known if further classes of risk can be defined, among relapsing patients. The aim of this study is to evaluate the patients' outcome according to time interval from diagnosis to relapse.

Design/Methods: 819 patients under 21 years old, with histologically confirmed RMS were diagnosed from 1979 to 2011 and enrolled in RMS79, RMS88, RMS96, EpSSG2005 study. Only recurrence of the disease after primary remission was considered. 217 (26%) relapsed after a minimum 36 months-follow up. Patients were categorized in three groups considering the time interval from diagnosis to relapse: early relapse (ER), patients relapsing < 18 months from diagnosis, late relapse (LR) from 18 to 36 months, very late relapse (VLR) > 36 months.

Results: Overall 217/819 had a relapse, 55% were male. Embryonal histology, tumour > 5 cm, T2 stage were prevalent. Considering the relapse, 61% was local, 18% metastatic. According to time interval to relapse, 114 (53%), 79 (36%), 24 (11%) patients were categorized as ER, LR, VLR, respectively. 24% were alive at the time of last follow-up. 10-year overall survival (OS) rate was 16.4% (95% CI 10.2-23.8) among patients with ER, 33.3% (95% CI 22.6-44.3) for the patients who relapsed after 18 to 36 months, 42.7% (95% CI 22.2-61.8) among patients with a VLR ($p < 0.0001$).

Conclusion: It is known prognosis of patients with ER is worse than that of patients relapsing > 18 months. Results of our report confirm the poor prognosis of patients with ER, and highlight the same poor prognosis of patients recurring after 36 months. This data could be considered to tailor treatment considering also time interval to relapse and could suggest different biological characteristics of recurrent disease.

P-0826 | Combined Chemotherapy and ¹²⁵I-Partial Implantation for Treatment of Children with Head and Neck Soft Tissue Sarcomas Improve the Short-Term Efficacy

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Background/Objectives: To evaluate the efficacy of chemotherapy combined with ¹²⁵I seed implantation in treating paediatric head and neck soft tissue sarcomas.

Design/Methods: The clinical characteristics, overall survival rate, local control rate and event free survival rate of patients treated with chemotherapy and ¹²⁵I seed implantation were studied retrospectively.

Results: There were 12 males and 2 female patients. Age at diagnosis ranged between 1.0-10.7 years, and the median age is 4.9 years. Only 3 of the patients had localized disease, the other 11 patients had metastatic disease. The follow up time ranged from 8 to 30.5 months, median follow up time was 12.3 months. The overall response rate (complete response, very good partial response and partial response; CR, VGPR and PR) for all 14 patients was 85%, including 6/14 patients with CR, 1/14 patient with VGPR, 5/14 patients with PR. 2/14 patients had progressive disease. The overall local control rate was 85%, with a median LC time 18.9 months (95% CI: 16.4 to 21.3 month). The overall survival rate in this group of patients was 100%. The overall survival time was 8 to 30.5 months. The event free survival rate was 85%, with a median EFS time 18.9 months (95% CI: 16.4 to 21.3 months). Hematological toxicity was the most common side effects of chemotherapy. 7 of 14 patients suffered from grade 1 or 2 skin reaction after seed implantation.

Conclusion: Chemotherapy combined with ¹²⁵I seed implantation is a feasible treatment for children with head and neck sarcomas, with high local control rates and event free survival.

P-0827 | Low Grade Non Rhabdomyosarcoma Soft Tissue Sarcoma: What is Peculiar for Childhood

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Background/Objectives: Nearly half of Soft tissue sarcomas (STS) are non rhabdomyosarcoma (NRSTS).The low grade (LG) form is a heterogeneous group of diseases that rarely metastasize but known for local recurrence. **Aim:** to retrospectively evaluate paediatric LG-NRSTS as regard demography, survival and factors affecting outcome in Egyptian patients. Normal 0 false false false EN-US X-NONE AR-SA.

Design/Methods: The study reviewed 66 NRSTS patients presented to the Pediatric Oncology Department, National Cancer Institute, Cairo University between January 2008 and December 2013.

Results: Out of the reviewed cases 32 patients had low grade tumors and were eligible for analysis. The male to female ratio was 1:1 and the median age was 7.5 years (range: 1mo-18 yr). Desmoid fibromatosis (N=18) showed frequent local recurrence and nearly half of this group were alive without disease. No recurrence of the disease occurred in the non fibromatosis group (n=14) and all patients were alive free of disease. The 5 year overall survival (OS) was 88% for the entire study patients versus 45% event free survival (EFS). Tumors >5 cm in diameter and fibromatosis histology subtype were associated with lower EFS.

Conclusion: LG-NRSTS is of generally good prognosis with OS survival reaching 90%. However, aggressive fibromatosis usually runs a poorer course in form of high incidence of local recurrence and lower survival rates. This necessitates to be further assessed in larger prospective studies including novel therapies in addition to the current conventional modalities.

P-0828 | Impact of Preformed Metal Crowns on MRI Surveillance in Paediatric Head and Neck Oncology Patients Over A 10 Year Period

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Background/Objectives: MRI image quality can be dramatically degraded by artefacts caused by dental materials and these artefacts can obscure imaging of pathology (Klinke et al, 2012). The artefacts generated by metals used in medicine and dentistry on MRI have been investigated (Klinke et al, 2012), with contradictory results reported for different dental materials in laboratory-based studies (Tymofiyeva 2013). The impact of metal restorations in children who require ongoing MRI surveillance has not previously been reported.

Design/Methods: A retrospective review of 250 paediatric head and neck oncology cases identified 40 patients who required placement of preformed metal crowns (PMCs) under general anaesthetic to treat dental decay. Thirty three of the 40 patients had MRI carried out after placement of PMCs. The radiology reports were reviewed to determine the impact of the crowns on the subsequent imaging.

Results: Reports for 2 of the 33 patients noted the presence of PMCs. The first patient had a diagnosis of parapharyngeal rhabdomyosarcoma and the artefact from the crowns was noted but this did not interfere with imaging the area of interest. The second patient's diagnosis was of oropharyngeal embryonal rhabdomyosarcoma and the area of interest could not be examined due to the extent of artefact in this small child. This patient had the PMCs replaced by non-ferromagnetic zirconia crowns and repeat MRI successfully carried out.

Conclusion: In our sample the use of PMCs for treatment of dental caries did not cause problems imaging the majority of head and neck tumour patients. In only one case did the artefact caused by the PMCs impede adequate MRI imaging.

P-0829 | Treatment Outcome of Neurofibromatosis Type 1 Associated and Sporadic Malignant Peripheral Nerve Sheath Tumour

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Background/Objectives: Malignant peripheral nerve sheath tumour (MPNST) is one of soft tissue sarcoma. MPNST occur spontaneously or associated with neurofibromatosis type 1 (NF1). There are some disputes about prognostic differences between sporadic MPNST and NF1 associated MPNST.

Design/Methods: Ninety five patient charts were reviewed for retrospective study for NF1 associated MPNST. In addition to comparison NF1 associated and sporadic MPNST, patient characteristics, resection margin, pathology and stage were investigated for identifying prognostic factors.

Results: Median age of patients was 40.7 years and patients with NF 1 showed median age of 35 years. Frequent recurrent location was extremity(48.4%), then trunk(34.7%), and head&neck(16.8%) were less frequent sites. Tumour size in NF1 associated patients(9.3cm) were greater than in the other patients(5.74cm). About half of patients underwent wide resections.(49.5%) Resection margin free(R0) surgery was taken on the 35 patients(36.5%) and the other patients(59 patients,63.5%) was taken margin positive surgery.16 patients(16.8%) had taken isolated chemotherapy, 34 patients(35.8%) had taken radiotherapy only and 11 patients(11.6%) had both. 10 year overall survival(OS) of patients in MPNST was 51.1±6.1%. 10 year OS was 56.2±7.3% in sporadic MPNST patients and 40.1±10.8% in NF1 MPNST patients, the data revealed p-value = 0.045 and significant difference between 2 groups. In addition, resection margin and metastasis had effect on overall survival significantly(P-value=0.037 in 10yr OS and <0.001 in 5yr OS). On multivariate analysis, only metastasis was poor prognostic factor on OS[Odd ratio = 3.11, 95% confidence interval (CI) 1.22-7.95].

Conclusion: NF1 had effect on overall survival in MPNST and there are many characters which affect on life style and survival, such like multiple neurofibroma, tendency for malignant progression. For better management NF1, we need to have general consensus follow up periods, methods and study genetic factors to influence on malignant progression.

P-0830 | Intensified Induction Chemotherapy Followed by High-Dose Chemotherapy for Children with Group 3 Alveolar Rms and Group 4 RMS

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Background/Objectives: Whether intensified chemotherapy including high-dose chemotherapy with stem cell rescue improves the survival rate in high-risk rhabdomyosarcoma (RMS) still remains to be elucidated. Japan Rhabdomyosarcoma Group (JRSG) conducted a phase II trial.

Design/Methods: Patients with group 3 alveolar RMS and group 4 RMS were eligible (0-17 years). Induction chemotherapy consisted of two regimens, Regimen A: cyclophosphamide, etoposide, pirarubicin, cisplatin, Regimen B: ifosfamide, etoposide, dactinomycin. Three courses of Regimen A and two courses of B were repeated alternatively. Tumour resection was performed after three courses of chemotherapy if indicated. Finally, patients undertook high-dose chemotherapy (double-conditioning regimen with thiopeta and melphalan) with peripheral stem cell rescue. Enrolment was open from May 2004 to September 2008.

Results: Thirty-four patients were enrolled. CR and PR were achieved in seven and nine patients, respectively at the end of induction chemotherapy. 5-year PFS and OS were 47.1% (95% CI: 29.8%-62.5%) and 70.6% (95% CI: 52.2%-83.0%), respectively. In 11 with group 3 alveolar RMS, 5-year PFS and OS were 54.5% (95% CI: 22.9%-78.0%) and 72.7% (95% CI: 37.1%-90.3%), respectively. In 23 with group 4, 43.5% (95% CI: 23.3%-62.1%) of 5-year PFS and 69.6% (95% CI: 46.6%-84.2%) of 5-year OS were observed. 11 of 15 group 4 patients with 0-2 adverse prognostic factors are alive (44-84 months). No treatment-related death was observed. Although no organ failure was observed, grade 3 pharyngitis with pain requiring opioids was frequently observed after high-dose chemotherapy.

Conclusion: Dose reduction of thiopeta/melphalan is required to reduce severity of pharyngitis. This treatment strategy is worth to be further evaluated in patients with high-risk RMS.

P-0831 | Primary Rhabdomyosarcoma of the Breast

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Background/Objectives: Primary breast malignancies are extremely rare in children. Albeit rare, hematologic neoplasms such as lymphoma and soft tissue sarcomas especially rhabdomyosarcoma (RMS) are the most common tumors that may be seen as primary or metastatic neoplasms in the breast. We report an adolescent girl with primary rhabdomyosarcoma of the breast and discuss the treatment.

Design/Methods: The single case with primary rhabdomyosarcoma of the breast within a cohort of 210 children and adolescents with RMS diagnosed and treated in our institution during 1990-2015, was assessed retrospectively. There were three more adolescent girls with alveolar rhabdomyosarcoma and breast metastasis that were detected at diagnosis in two and during follow up in one, in the same cohort (presented in SIOP 2015).

Results: A twelve year old girl presented with a palpable 8 cm mass on the retroareolar area of the left breast that had grown within the last three months. A tru-cut biopsy was obtained. The pathology was consistent with alveolar rhabdomyosarcoma. Axillary lymph node involvement was detected in the ultrasound, MRI and PET-CT. There were no distant metastasis. Chemotherapy (vincristine, actinomycin D, cyclophosphamide) was initiated, with a partial response after three courses. After seven courses of chemotherapy mastectomy, axillary dissection and placement of an expander was performed. The pathology revealed residual viable tumour in the primary site and 1/16 lymph nodes was positive. There were no tumour cells in the surgical margins. The patient received adjuvant radiotherapy to the left breast and axilla. Chemotherapy is being continued. She is under treatment for 11 months from diagnosis.

Conclusion: Primary rhabdomyosarcoma of the breast is very rare. Multidisciplinary approach in treatment is crucial. Psychological effects of metastasectomy in adolescents should be considered. Placement of an expander in the area resulting in better cosmetic results without hampering treatment should be considered in these patients.

P-0832 | MET/ERK2 Pathway Regulates the Motility of Human Alveolar Rhabdomyosarcoma Cells

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Background/Objectives: Rhabdomyosarcoma (RMS) is a soft tissue sarcoma that is subdivided into two major types, namely, alveolar RMS (ARMS) and embryonal RMS (ERMS). Most ARMS can be distinguished based on the presence of PAX3-FOXO1. ARMS containing this fusion protein are the most difficult to treat clinically because of their metastatic potential. MET, a receptor of hepatocyte growth factor (HGF), functions downstream of PAX3-FOXO1 and is a key mediator of RMS metastasis. There are currently no studies investigating the details of signaling pathways downstream of MET in ARMS even though HGF and MET are suggested to be deeply involved in the invasiveness of ARMS. Although HGF and MET are suggested to be responsible for the invasiveness of ARMS, MET-induced signaling pathways in ARMS cells have not been investigated to date.

Design/Methods: This study included three human ARMS and ERMS cell lines each. Migration of ARMS cells treated with ERK1/2 inhibitor, mTOR inhibitor, or ERK1/2 siRNAs was determined by performing wound-healing and migration assays.

Results: MET expression was higher in ARMS cell lines than in ERMS cell lines, as determined by performing QPCR and western blotting. HGF stimulation did not enhance the proliferation of ERMS and ARMS cell lines, as determined by cell growth and cell cycle analyses. Wound-healing and migration assays showed that migration of HGF-stimulated ARMS cell lines was completely and partially inhibited by ERK1/2 inhibitor and ERK1 or mTOR inhibitor, respectively. Further, migration of HGF-stimulated ARMS cells was not inhibited after transfection with ERK1 siRNA but was inhibited after transfection with ERK2 siRNA.

Conclusion: Our results suggested that HGF/MET signaling promoted the migration of ARMS cells mainly through ERK2 signaling. Therefore, a specific inhibitor of ERK2 phosphorylation might serve as an anti-cancer agent to inhibit the invasion and metastasis of ARMS.

P-0833 | Treatment of High Risk Soft Tissue Sarcomas in Children in Developing Country: Survival and Quality of Life

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Background/Objectives: Significant amount of patients with soft tissue sarcomas present with unresectable or disseminated disease, which confers a poor prognosis and is associated with a high mortality and morbidity rate. The choice of treatment strategy in the case of widespread local or advanced metastatic disease remains unclear.

Design/Methods: A retrospective chart review of 58 children with high risk soft tissue sarcomas of different histological subtypes treated and observed from 2006 to 2015 was performed. The risk stratification was assessed due to European Pediatric Soft Tissue Sarcoma Group guidelines. Quality of life was assessed due to extent of four types of disorders: mental, neurosensory, movement, and cytopenic complications of cytotoxic treatment.

Results: The largest cohort were patients with rhabdomyosarcoma – 67%. Primary metastatic disease was observed in 20% of patients. Patients received multimodal treatment: ifosfamid-doxorubicin chemotherapy followed by primary tumour surgery and distant beam radiotherapy. Most patients received maintenance chemotherapy with vinorelbine.

At the end of 2015, with a median follow-up of 36 months, the 3-year overall survival is 56%. The 3-year event free survival is 47%. The overall survival in patients with primary metastatic disease was 12.5%. The most frequent adverse events that worsened the quality of life of patients were associated with neurosensory and movement disorders after tumour excision.

Conclusion: Aggressive local therapy after initial partial or complete tumour response to neoadjuvant chemotherapy improves the survival in high risk soft tissue sarcomas. Wide tumour excisions and radiotherapy influenced the quality of life of survivors. In the case of progression or stabilization of disease during treatment surgery should be carefully considered to avoid quality of life impact.

P-0834 | Alterations of the Oxidative Phosphorylation Complexes in Rhabdomyosarcomas

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Background/Objectives: Rhabdomyosarcoma (RMS) is an aggressive neoplasm characterized by metastatic invasion and rapid growth. Since many tumors present a shift from oxidative phosphorylation (OXPHOS) to aerobic glycolysis (Warburg effect), the aim of the present study was to investigate whether RMS present alterations in the OXPHOS complexes.

Design/Methods: Paraffin-embedded tissue samples from 27 human RMS (alveolar, embryonal and pleomorphic) and normal healthy muscle tissues were stained by immunohistochemistry (IHC) for porin and complex I to V of the OXPHOS. Frozen RMS (n=3) and normal muscle tissues (n=10-28) were analyzed for enzymatic activity of citrate synthase and OXPHOS complexes. Ptc^{+/+} (Patched) transgenic mice expressing a constitutively active Hedgehog (Hh) signaling pathway develop RMS. These mice were treated with different Hh signaling inhibitors to investigate if these compounds could stimulate or reverse the Warburg effect in RMS.

Results: The activity of all OXPHOS complexes was low in human RMS samples. Compared to control muscle, specific and significantly lower complex I levels were observed in RMS, whereas the amount of the other complexes as well as the mitochondrial membrane protein porin was similar to unaffected muscle. Only embryonal RMS presented in addition very low complex II levels.

RMSs developed by Ptc^{+/+} mice presented similar OXPHOS features as human embryonal RMS. Treatment of Ptc^{+/+} mice with Hh inhibitors was not able to alter the OXPHOS system.

Conclusion: The low activity of citrate synthase and OXPHOS complexes in RMS can be explained by the high abundance of stroma/connective tissue. In addition, RMS showed a very small cytoplasm with a very limited space for mitochondria.

Hh pathway-inhibition with Smo-inhibitors does not affect OXPHOS expression, suggesting that the Hh axis in RMS is not involved in the regulation of the Warburg effect.

P-0835 | Can Baseline Body Mass Index Predict Treatment Outcome in Paediatric Rhabdomyosarcoma?

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Background/Objectives: Rhabdomyosarcoma (RMS) accounts for 7% of childhood malignancies and for over 50% of all soft tissue sarcoma. RMS risk stratification is based on clinical

staging and surgical grouping. The aim was to investigate the influence of using baseline body-mass index (BMI) to better stratify RMS.

Design/Methods: Kaplan-Meier curves and regression models were used to evaluate the association of the baseline BMI percentile with survival in a cohort of 55 paediatric RMS patients ≥ 2 and < 18 years old treated with cyclophosphamide-based first-line treatment at Children's Cancer Hospital-57357. They were recruited from July 2007 until December 2012 and were followed up to the end of March 2015.

Results: The mean \pm (SD) body weight, height, and surface area were 25.1 ± 17.6 kg, 115.7 ± 27.8 cm and 0.86 ± 0.39 m², respectively. Six patients (10.9%) were underweight (BMI $< 5^{\text{th}}$), another 6 patients (10.9%) were at risk of becoming obese (BMI $> 95^{\text{th}}$), while 9 cases (16.4%) were overweight (BMI $\geq 85^{\text{th}}$ & $< 95^{\text{th}}$), and 34 cases (61.8%) had ideal BMI (BMI $> 5^{\text{th}}$ & $< 85^{\text{th}}$). Comparing patients with an overweight or at risk of overweight BMI versus those with underweight or ideal BMI, they had significant better response rate (73.3% versus 42.5%, p-value = 0.04), their mean overall survival was 68.1 months (95% CI, 60.6-75.8) versus a mean of 54.6 months (95% CI, 45.2-60, p-value = 0.042), and their mean event-free survival was 56.7 (95% CI, 43.7-70) versus a mean of 36.8 months (95% CI, 28.2-45.6, p-value = 0.033), respectively.

Conclusion: Baseline BMI has a significant association with survival outcome in RMS. Baseline obese or overweight BMI had a significantly better survival. Future studies might investigate effect of body weight change during treatment on the clinical outcome.

P-0836 | Metastatic Paratesticular Pleomorphic Rhabdomyosarcoma - A Case Report

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Background/Objectives: Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma in children and adolescents. The common histological variants in children are the embryonal and alveolar sub-types, while the pleomorphic variant is mostly seen in the adult age group. Treatment with surgery and chemotherapy with or without radiation is the mainstay of treatment.

Objective: To describe a rare case of metastatic paratesticular pleomorphic RMS in an adolescent male.

Design/Methods: Case report.

Results: A sixteen year old Indian male presented with painless left testicular swelling for 3 months. Ultrasound abdomen showed a left paratesticular swelling suggestive of left epididymal adenomatoid tumour. The patient underwent high inguinal orchidectomy. Histopathology showed spindle cells exhibiting moderate pleomorphism. Immunohistochemistry was positive for vimentin, skeletal muscle myogenin (myf-4), focally for desmin, smooth muscle actin and muscle specific actin suggestive of pleomorphic rhabdomyosarcoma. PET CT scan showed loco-regional lymph node metastasis to transverse abdominis muscle and left para aortic lymph node as well as skeletal metastasis. He received chemotherapy with Vincristine, Actinomycin, Doxorubicin and Ifosfamide. Follow up scans showed resolution of metastatic lesions. Radiation was proposed as a consolidation therapy but family refused. The patient is now 3 years post end of therapy and in good health with no evidence of relapse.

Conclusion: Paratesticular Embryonal rhabdomyosarcoma is known to occur in young males, but the pleomorphic variant is rare, with only one prior reported case in the paediatric age group. The differentiation of subtypes of rhabdomyosarcoma requires the expertise of an experienced pathologist. Pleomorphic RMS is treated similar to its embryonal counterpart and responds poorly to chemotherapy when compared to the embryonal and alveolar subtypes. The appropriate diagnosis of pleomorphic RMS is significant as it is a high-grade sarcoma, with an aggressive clinical course.

P-0837 | The 5-Year Survival Rate of a Cohort Matched Study through Iranian Paediatric Sarcoma Population

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Background/Objectives: Sarcoma, a malignant tumour with mesenchymal origin, makes a serious issue in the paediatric health system of Iran. In this way, there should be a big effort in improving the epidemiological evaluations and database of these patients. This study designed to consider the 5-year survival rate of patients with Sarcoma who referred to MAHAK Pediatric Cancer Treatment and Research Center (MPCTRC) for diagnosis and treatment.

Design/Methods: Children less than 15 years old (n=258) who diagnoses at MPCTRC as Sarcoma cases during 2007 to 2014 enrolled in this study. This retrospective simple sample size study conducted according to gathering and analyzing epidemiological data. The 5-year survival rate of patients was achieved based on different disease' categories of patients. The data analyzes were done by SPSS software version 22.

Results: The percentage of cases in each disease category based on pathology reports were as: Ewing sarcoma family of tumors: 35.2%; Rhabdomyosarcoma (RMS): 28.2%; Osteosarcoma: 22.5% and Non Rhabdomyosarcomatous Soft Tissue Sarcoma (NRSTS): 14%. The 5-year survival rate of these categorized patients were: RMS: 55%; NRSTS: 51.9%; Ewing sarcoma: 38.8%; Osteosarcoma: 31.6% respectively.

Conclusion: The most important issue in improving the management of children with sarcoma is increasing the duality of early diagnosis, treatment and follow up. In this way with better planning and suggestions can lead to a better 5-year survival rate of these cases.

P-0838 | Rhabdomyosarcoma of the Limbs: Results Obtained from the AIEOP Soft Tissue Sarcoma Committee

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Background/Objectives: Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma in children, and in 14% of cases occurs in the limbs.

To evaluate the characteristics of limbs-RMS, the results obtained in the various protocols and the prognostic factors.

Design/Methods: From 1979 to 2012, 135 patients were enrolled: 90 with localized RMS (RMS-loc) and 45 with metastatic RMS (RMS-mts). As initial surgery, biopsy was performed in 64% of cases and nodal exploration only in 34% of patients. Chemotherapy consisted in the administration of IVA cycles +/- anthracyclines. 63% of patients received radiotherapy.

Results: Patients with RMS-mts, compared to whom with RMS-loc, presented more often alveolar histology (87% vs 67% in the), major invasivity (T2: 53% vs 20%) and tumour size > 5 cm (76% vs 54%). 10y-OS (Overall Survival) and PFS (Progression Free Survival) were respectively 65% and 50% in RMS-loc, 33% and 24% in RMS-mts. Over the years, PFS has significantly improved RMS-loc: RMS79 47% vs RMS2005 95%. Prognosis of patients with RMS-mts remains negative, particularly in case of unfavorable seat (distal seat PFS 11%), alveolar histology (PFS 18%) and in presence of bone metastasis and/or bone marrow involvement (PFS 9%).

Conclusion: The prognosis of patients with RMS-loc has improved in recent protocols. The treatment of RMS-mts remains one of the major challenges for paediatric oncology. Some subgroups of patients (distal site of the tumour, > 1 MTS seats, bone/bone marrow MTS) with very poor prognosis (SLP <15%) may be candidate for innovative therapies, already as first-line treatment.

P-0839 | Aldehyde Dehydrogenase Inhibitor Disulfiram Suppresses the Growth of Cancer Stem Cells in Embryonal Rhabdomyosarcoma through the Inhibition of Angiogenesis

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Background/Objectives: We previously reported that aldehyde dehydrogenase I (ALDH1) is a potential marker of cancer stem cells (CSCs) in embryonal rhabdomyosarcoma (ERMS), and recent studies have demonstrated that disulfiram (DSF), an inhibitor of ALDH, suppresses CSCs in various cancers. In this study, we examined whether DSF can eradicate a subpopulation of cells with high ALDH1 activity (ALDH1^{high} cells) in ERMS.

Design/Methods: We employed two human ERMS cell lines, RD and KYM-1. The cells were sorted into ALDH1^{high} cells and a subpopulation with low ALDH1 activity (ALDH1^{low} cells). To demonstrate that DSF suppresses ALDH1^{high} cells, we performed a sphere-formation assay *in vitro* and a tumour-formation assay *in vivo*. In the sphere-formation assay, the cells were incubated with DSF. In the tumour-formation assay, 5 mm cubes of KYM-1 tumour masses were transplanted into nude mice and then either a vehicle (DMSO) or DSF was injected into the mice. The tumour sections were analyzed by immunohistochemical and immunofluorescence staining.

Results: The ratio of ALDH1^{high} cells was significantly reduced when treated with DSF *in vitro*. In the sphere-formation assay, the DSF-pretreated RD and KYM-1 cells formed significantly less spheres than the untreated cells. Regarding the efficacy of DSF *in vivo*, the tumour size of untreated mice and DSF-treated mice for three months was 632.4±432.0 mm³ and 185.5±86.2 mm³ (p<0.05), respectively, indicating that DSF significantly suppressed the tumorigenicity of ALDH1^{high} cells. According to the immunohistochemical and immunofluorescence staining of the xenograft tumour sections, fewer ALDH1-positive cells were observed in the DSF-treated mice than in the untreated mice. Furthermore, there were significantly fewer VEGF- and CD31-positive cells in DSF-treated mice, indicating that DSF has anti-angiogenic activity.

Conclusion: Our results indicate that DSF is a promising therapeutic agent for the eradication of CSCs in ERMS by suppressing the activity of ALDH1 and angiogenesis.

P-0840 | Treatment and Outcome of Childhood Metastatic Rhabdomyosarcoma: Ten Years Single Institution Experience

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Background/Objectives: Introduction: Optimal use, timing and intensity of surgery, chemotherapy and radiotherapy, in the treatment of metastatic RMS, must be planned with regard to the age of the patient, site and size of the primary tumour, extent of disease and pathological subtype.

Aim: presentation of our experience in the treatment of children suffering from metastatic rhabdomyosarcoma.

Design/Methods: Patients and methods: evaluation of seven patients with metastatic rhabdomyosarcoma (5 girls and 2 boys) treated between 2004 and 2014. Their age ranged between 4 and 18 years. Chemotherapy consisted of the treatment scheme for primary metastatic soft tissue tumours. One patient with bone marrow involvement was underwent high dose chemother-

apy. In four patients rhabdomyosarcoma embryonale and in three patients rhabdomyosarcoma alveolare was diagnosed. All patients had primary tumour in unfavorable site. Five patients had regional nodal involvement, two patients had two sites of metastatic disease, and one patient had bone marrow involvement. Six patients were irradiated and three patients underwent marginal resection.

Results: estimated outcome for all patients, four patients died during chemotherapy (including patient who underwent high dose chemotherapy) because of the progression of disease, but three of seven patients are alive with median follow up of 28 months. Two of three alive patients had regional nodal involvement and they were treated with chemotherapy, irradiation and surgery. The third patient had regression of pulmonary metastases during chemotherapy and local control was achieved with radiotherapy without surgery because of mutilation.

Conclusion: The results of treatment for children with metastatic RMS remain so poor and patients with very poor prognosis need new, more effective therapy strategies. Optimal treatment strategies for metastatic RMS may open many controversial issues such as duration of therapy, value of high dose chemotherapy, the consequences of local therapy and surgery of metastases.

P-0841 | A Review of Treatment Outcomes of Kaposi's Sarcoma in Children Attending Hospice Africa Uganda and its Implications for the Provision of Palliative Care

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Background/Objectives: Kaposi's sarcoma (KS) is one of the two major malignancies associated with HIV infection in African children. However, there is limited data on treatment outcomes of HIV infected children with KS. Within the provision of palliative care, the treatment of malignancies such as KS and the palliative of symptoms associated with it are important aspects of care.

Design/Methods: A chart review of 10 children with HIV/AIDS and KS at Hospice Africa Uganda was carried out. All the children had been on programme for at least a month prior to review.

Results: Of the children reviewed, six (60%) were male and four (40%) were female. The age of the children ranged from three to fifteen years with the mean age being 9.4 years. In reviewing their histology, the most common presentation was lymphadenopathic KS. Five of the children were receiving treatment in terms of both chemotherapy and Anti Retro-viral Drugs (ARVs) whereas the other five were unable to start either treatment. Three out of the five children receiving chemotherapy had earlier shown signs of clinical improvement but following treatment default, they had presented with rapidly progressing symptomatically. The three children did not respond to re-treatment courses of chemotherapy with one registered fatality.

Conclusion: Children commonly get lymphadenopathic KS which is common in the older children. Although this review is small in scale, it does seem to suggest that combination of chemotherapy and ARVs is beneficial. On the other side, treatment default can lead to rapidly progressing symptoms, poor response to re-treatment regimens and possibilities of high fatality rates. Within the provision of palliative care, this has implications for both management of KS but also for the palliation of symptoms associated with both treatments for the disease as it progresses. Bigger sample studies are recommended in the paediatric population to study this in more depth.

P-0842 | Desmoplastic Small Round Cell Tumors (DSRCT) in Children and Adolescents – Experience of the CWS Study Group

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Background/Objectives: DSRCT is a rare sarcoma of young age with a very poor prognosis. Data of patients with DSRCT treated in 3 prospective CWS-trials were analyzed to assess the outcome, identify prognostic factors and analyze treatment strategies.

Design/Methods: Forty-two patients < 21 years registered between 1996 and 2014 were eligible for this analysis. They received 4 to 6 drugs chemotherapy regimen (ifosfamide, Vincristine, Doxorubicin, Actinomycin-D, Carboplatin, Etoposide), depending on risk group. Local therapy consisted of surgery and/or irradiation. In some cases high-dose-chemotherapy with stem cell rescue, hyperthermic intraperitoneal chemotherapy (HIPEC) or hyperthermia with systemic chemotherapy were applied as individual treatment decision by treating center.

Results: Median age was 13.6 years. Male/female ratio was 31/11. 40/42 (95%) of tumors were localized in abdomen/pelvis. 2/42 (5%) of tumors were < 5cm. 29/42 (69%) had primary metastatic disease. Only 17/42 (41%) of patients achieved complete remission. 5-year event-free survival (EFS) and overall survival (OS) were 12% and 16%, respectively.

All 3 patients with primary resection (IRS I and II) survived, thereof the two patients with tumors <5cm, in contrast to 2/39 with IRS III/IV. The median follow-up for survivors was 5.1 years (2.3-10.6).

Conclusion: Patients with primary resected tumors had the best chance for survival. The role of the administered intensive chemotherapeutic regimes seems debatable. Therefore, innovative therapeutic approaches are needed for this group.

P-0843 | Synovial Sarcoma of the Tongue in a 14 year Old Child. Report of a Case

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Background/Objectives: Synovial sarcoma (SS) is a malignant neoplasm arising from primitive mesenchymal cells resembling synoviocytes. Is the third most common soft-tissue sarcoma in adolescents and young adults. Median age is 30 years. Males are more commonly affected. Characteristic t(X;18) translocation is seen in 90% of cases.

Primary sites are lower (60-75%) and upper extremities (15-20%). Head and neck involvement is rare (6-7%). Oral SS has been described in adults. Tongue tumors present insidiously with progressive painless growth and few other symptoms. Tumour size and depth are important to evaluate excision, since survival depends on complete resection.

Design/Methods: Case Report: A 14-year-old boy presented with a 2cm cystic mass in the tongue. Surgical excision revealed monophasic synovial sarcoma. Family did not accept primary re-excision to clear margins. Underwent alternative treatment with magnets and herbs, and returned a year later with a massive tumour affecting tongue, floor of mouth, neck from vertebrae to hypopharynx, and lung nodules.

Results: Tracheostomy and gastrostomy were placed. Chemotherapy shrunk the tumour and a partial glossectomy with neck dissection was carried before radiotherapy. Patient remained disease-free for a year, until an extensive local recurrence appeared. He did not consent for radical surgery, so a second partial glossectomy and neck dissection was performed, covering a large neck defect with a pectoral flap. He developed an oro-cutaneous fistula after adjuvant chemotherapy. Remained disease-free during two years, until a second recurrence ensured and he again refused surgery. Palliative care was given. At 5-year follow-up he died with disease, due to aspiration during alternative treatment with ozone.

Conclusion: SS of the tongue is exceedingly rare with no case previously described in children. Growth is insidious and complete surgical resection is essential for cure. Local and distant recurrence is common. Magnets, herbs and ozone treatment are ineffective. Partial glossectomy allowed this child a better quality of life.

P-0844 | Angiomatoid Fibrous Histiocytoma in Children - Clinical, Histopathological and Surgical Aspects

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Background/Objectives: Angiomatoid fibrous histiocytoma (AFH) is a rare soft-tissue tumour with intermediate malignant potential that mostly affects children and young adults. First described in 1979 and classified as "malignant fibrous histiocytoma". It was renamed as AFH because of its infrequent malignant behavior with low rates of recurrence and metastases.

The aim of the study was to define clinical and histopathological findings of AFH and to describe therapeutic approaches utilized and follow up.

Design/Methods: A retrospective study was performed of patients ≤18 years old, with AFH, admitted to our institution between 1997 and 2016. Data collected from medical records were: age, sex, location of the tumour, clinical history, findings on physical examination, imaging exams and histology findings.

Results: There were 11 patients (6 males and 5 females), with a median age of 13 years old (range: 8 to 17). All tumors were in soft tissue, located in the lower extremities (n=5/11), shoulder girdle (n=4/11) and trunk (n=2/11). Systemic symptoms as fever, anemia and weight loss were present in 4 patients. Tumour size ranged from 1.4 to 13.5 cm. At diagnosis, eight patients had localized disease, one with local relapse and two with distant metastases (lungs). The treatment was surgery in all patients: complete resection (n=3), primary re-excision (n=8) due to unknown margins at primary surgery. Three patients received chemotherapy and two, radiotherapy. One patient was lost to follow up. The median follow up was 7 years (range: 2y-16y), 9 patients are alive without evidence of disease (one patient had local recurrence submitted to surgical resection). One patient died of disseminated disease.

Conclusion: AFH is a rare disease and often initially misdiagnosed. Correct diagnosis is fundamental to ensure that the patient receives proper treatment. Usually the surgery is the only treatment needed. Local recurrence or metastases are rare, but can occur insidiously and long-term monitoring is recommended.

P-0845 | Clinical Characteristics of Infants with Rhabdomyosarcoma

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Background/Objectives: Rhabdomyosarcoma (RMS) is the most common soft-tissue sarcoma in children, and about 90 cases of RMS were developed in Japan per year. Prior studies indicated that the treatment outcome of infant (under 1-year-old) patients with RMS was poor compared with the outcome of older (1-9-year-old) patients. Here, we analyzed the characteristics of infant patients with RMS who were diagnosed and treated in our institute.

Design/Methods: We analyzed the characteristics, treatment outcomes of infant patients with RMS retrospectively in reference to medical records of our institute.

Results: Fifty-three patients with RMS were treated from 1971 to 2015. Among these patients, 7 patients were infants. Median age at diagnosis was 6 months (2-10 months). Tumour histology included embryonal (85.7%) and alveolar (14.3%). Primary tumour sites included bladder or prostate (28.6%), limb (14.3%), head (14.3%), trunk or retroperitoneum (28.6%) and para-testis

(14.3%). Metastasis was detected in 1 patient (14.3%) at diagnosis. Five year overall survival rate was 66.7%, which was not significantly different from 76.2% of survival in older patients (p=0.885). All 4 infant patients who were diagnosed after 1990 are alive without disease, thus treatment outcome seems to be improved recently.

Conclusion: Treatment outcome of infant patients with RMS was not significantly different from the outcome of older patients in our institute. It has been reported that inadequate local treatment might have associated with poor treatment outcome in infant patients. Our results suggest that adequate combination therapy of chemotherapy, surgery and radiation is required to achieve good outcome of even in infant patients with RMS as well as in older patients.

P-0846 | Irinotecan and Temozolamide for Relapsed Solid Tumors: Mahak Paediatric Cancer Treatment and Research Center Experience

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Background/Objectives: The poor prognosis of relapsed solid tumors and lack of standard treatment are still remaining as prominent medical concern. Recently promising outcomes have been described in various relapsed adult and paediatric solid tumors, using the combinations of irinotecan and temozolamide (IRN/TMZ). In this study we share our experience using the combination therapy of IRN/TMZ for treating relapsed solid tumors at Mahak Pediatric Cancer Treatment and Research Center.

Design/Methods: In this study, 19 patients with relapsed solid tumors who received the combination of irinotecan and temozolamide therapy between July 2011 and October 2015 at MAHAK Pediatric Cancer Center were retrospectively evaluated.

Patients' medical information, treatment, toxicities, outcome, responses and survival were registered and analysed using spss version 22.

Results: Nineteen patients with relapse solid tumors received 103 courses of IRN/TMZ. The overall objective response rate of 31.6% was achieved. Stable disease was observed in three (15.8%) patients. 10 patients had PD(52%). One year overall and event free survival of 31% and 23% was obtained. The mean and median survival times were 8.8 and 7 ±7.1 (range from 1 to 25 months) respectively. Median and mean time to progression of disease were 4 and 5.2 ±5.5 months. Better survival were observed in patients with one or two relapse rather than those with three or more relapses. Among 103 courses of IRN/TMZ, the most common toxicity was diarrhea occurring in 22 courses and only 9 courses required hospitalization. Thrombocytopenia and neutropenia was developed in 14 and 16 courses respectively and febrile neutropenia was occurred in only five courses. Colitis was observed in 7 courses and one resulted in hospitalization.

Conclusion: Irinotecan and temozolamide combination could be well tolerated for treatment of relapsed solid tumors. However, more investigations are required to define the efficacy and influence of this regimen on paediatric relapsed solid tumors.

P-0847 | A Spectrum of Fibromatosis-Like Tumours Affecting the Airway. A Tertiary Centre Experience

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Background/Objectives: Aggressive Fibromatosis (AF) and Inflammatory myofibroblastic tumours (IMTs) are rare types of soft tissue tumour. Whilst not strictly cancers, they are classed as intermediate-malignant tumours. Aggressive fibromatosis is a monoclonal proliferation of fibroblasts, with a tendency towards local aggression. IMTs show myofibroblastic proliferation intermixed with inflammatory cells and have a tendency to recur. Surgery alone can be curative, but definitive airway surgery comes with an associated operative risk, and long term compromises to function and appearance. We describe 3 cases where weekly vinblastine and methotrexate chemotherapy have been used to avoid such surgical morbidity.

Design/Methods: Our local tumour directory was scrutinised for cases of aerodigestive fibromatosis. Three cases were identified between 2014 and 2016. Case-notes and investigations were examined. Chemotherapy followed the NRSTS 2005 (Non-Rhabdoid Soft Tissue Sarcoma) Protocol.

Results: A 5-year old boy with severe stridor was found to have a tracheal mass occluding 80% of the tracheal lumen and extending into surrounding soft tissues. He underwent an emergency microlaryngoscopy, with laser reduction of the luminal tumour. Despite this, his stridor recurred after just 4 weeks. Histological interpretation was complex, but ultimately consistent with an ALK-negative myofibroblastic lesion. Vinblastine and methotrexate chemotherapy stabilised the extra-tracheal mass and later led to a sequential reduction in luminal tumour. A 7-year old boy presented with voice change. A vocal cord nodule of fibromatosis was excised at left lateral cordotomy. Symptoms recurred after 18 months, and a chemotherapeutic approach has now been adopted. A 3 year old boy with a mandibular lesion was found to have aggressive fibromatosis. Surgery carried a high risk of poor functional outcome, and he has commenced chemotherapy.

Conclusion: Chemotherapeutic treatment of lesions across the spectrum of fibromatosis has been validated for recurrent or inoperable disease in a Phase II trial. These cases illustrate its use in situations with high surgical morbidity.

P-0848 | Sacrococcygeal Teratoma: Our Experience with Intrapelvic Subtypes

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Background/Objectives: Sacrococcygeal teratoma (SCT) is the most common solid neoplasm in neonates with an estimated prevalence of 1 in 40000 live births. The purpose of this study is to review the clinical characteristics and determine the outcome of surgical treatment for Altmann type III & IV and compare it with TYPE-I & II.

Design/Methods: A retrospective review of all patients treated for SCT at one paediatric surgery unit, from July 2010 to June 2014 was conducted and the results were analyzed.

Results: In all, 7 children were treated over the study period. Four patients had extrapelvic type (group-A) and three had intrapelvic type (group B). All the patients of group A presented with sacrococcygeal mass and 25% had urinary difficulty, whereas in group B 67% urinary complaints and 34% had difficulty in passing stool. 75% cases of in group A were presented within & days of life where as all the patients in group B presented after infancy. Minor post-operative complication (wound infection, discharge from wound) was more common in group A. None had associated anomaly and none had wound dehiscence or anal incontinence. Two patients in group B were operated with chevron incision and specimen was retrieved via abdominal incision while in one case surgery was initiated via abdominal approach but later was changed to PSARP incision for complete removal and specimen was retrieved via abdominal incision. None of our patients had malignant component on histology and there was no recurrence after almost 2-6 years of follow up.

Conclusion: Presentation of subtype III & IV is delayed, high index of suspicion is needed for prompt diagnosis. We suggest the surgery should be initiated via chevron incision rather abdominal incision especially for subtype III though detailed study is needed for appropriate results.

P-0849 | A Prospective Assessment of Health-Related Quality of Life (HRQoL) Outcomes in Patients with Rhabdomyosarcoma Treated with Proton Radiotherapy

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Background/Objectives: HRQoL outcomes are not well described for children with rhabdomyosarcoma. We report the child-self-report (CSR) and parent-proxy-report (PPR) PedsQL HRQoL Core and Cancer module scores in a proton treated cohort.

Design/Methods: Children with rhabdomyosarcoma enrolled on a prospective HRQoL protocol were assessed during proton therapy (baseline) and annually from 2005-present. Mean QoL scores were compared with published data from healthy controls using Student's t-test. Linear mixed effects models were generated to determine longitudinal trajectory of PedsQL scores, dichotomized by age (>/≤3 yo), treatment delay from toxicity (>/≤2 days), GTV volume (>/≤15cc), tumour location (head/neck vs. other), IRS group (1-2 vs. 3-4) and maximum grade acute and late toxicity (CTCAE v3.0).

Results: Patients/parents with rhabdomyosarcoma (n=63, 38% Female, 64% head/neck/orbit tumors) were enrolled. Median follow-up was 3 years for 39 evaluable patients (≥1 year follow-up). Baseline mean Total Core Scores (TCS) were lower compared to controls (CSR: 76.9 vs. 83.8, p=0.05; PPR: 71.2 vs. 82.7, p<0.001), but this difference normalized at follow-up (CSR: 83.1 vs. 83.8, p=0.75; PPR: 81.4 vs. 82.7, p=0.60). Mixed effects modeling predicts an increase of 0.29 points/year for CSR TCS (p=0.62) and 1.8 points/year for PPR TCS (p=0.001). Patients ≤3 yo at treatment had slower increases in follow-up PPR TCS, 0.25/year vs. 3.8/year (p = 0.001). There was no correlation with severity of late toxicity, however PPR TCS decreased at follow-up for patients with ≥Grade 3 toxicity during treatment (p=0.001) and for IRS Group 1-2 patients who underwent surgery prior to radiotherapy (p=0.001).

Conclusion: Children with rhabdomyosarcoma treated with proton therapy had lower QoL scores during treatment compared to healthy controls, but these scores increased after treatment and became indistinguishable from healthy controls. Younger age, surgical resection prior to radiotherapy, and severe toxicity during treatment had a negative effect on survivors' HRQoL.

P-0850 | Effect of Combined Intra-Arterial Chemotherapy and Systemic Chemotherapy as Neo-Adjuvant Therapy for Paediatric Invasive Bladder and Prostate Rhabdomyosarcoma

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Background/Objectives: To evaluate the therapeutic effects of combined intra-arterial chemotherapy (IAC) and systemic chemotherapy as neo-adjuvant therapy for invasive bladder/prostate rhabdomyosarcoma (RMS) in children.

Design/Methods: From November 1999 to December 2013, 6 patients (4 boys and 2 girls; median 5.4 years, range 0.5-14.4 years) with invasive bladder/prostate RMS were treated with preoperative IAC combined with systemic chemotherapy. Tumour arising from bladder in 4 patients and from prostate in 2. Four patients had stage 3, one stage 2, and one stage 4 disease according to TNM pretreatment clinical staging system. Patients underwent bilateral internal iliac artery infusion with cisplatin, pirarubicin, and vindesine. Intravenous chemotherapy with vindesine, ifosfamide, and etoposide administered 3 weeks after IAC. IAC and intravenous chemotherapy repeated 2 cycles with 3-week interval. Bladder-sparing surgery was carried out after of neo-adjuvant therapy, followed by consolidate intravenous chemotherapy. Five patients had additional radiotherapy.

Results: No cardiotoxicity, renal insufficiency, or hepatic dysfunction were found in all patients. Grade III myelosuppression developed in 2 patients. Partial response (PR) was observed in all of 6 patients. Bladder-sparing surgery was carried out in all patients: partial cystectomy in 4, partial prostatectomy plus partial cystectomy and total prostatectomy plus partial cystectomy each in 1. Five patients achieved complete surgical remove of the tumour

and 1 had microscopic residual disease. All patients were followed up until December 31, 2015 (median length of 8.1 years, range 3.6-16.1 years). Five patients were recurrence free survival with functioning bladder. One patient had pelvic cavity tumour recurrence 12 months after surgery.

Conclusion: Neo-adjuvant IAC combined with systematic chemotherapy for the treatment of invasive bladder and prostate rhabdomyosarcoma in children is safe and effective with the advantage of bladder preservation.

STEM CELL TRANSPLANTATION AND HEMAIOLOGICAL DISEASES

P-0851 | Outcomes of Langerhans Cell Histiocytosis Using An Alternative Vincristine Based Regimen in Vietnam

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Background/Objectives: In many low to middle income countries (LMIC) cost and general availability of treatment options can lead to significant morbidity and mortality in populations compared to higher income countries. Alternative regimens used in LMIC's are less well represented in the published literature as well. In this study, the lack of available vinblastine necessitated the use of its chemical analog in the treatment of Histiocytosis in Vietnam.

Design/Methods: A retrospective chart review was undertaken at Children's Hospital #2 in Ho Chi Minh City Vietnam. 23 patients age less than 15 years old were diagnosed during March 2012 to September 2014, treated with a modified LCH2009 protocol as first-line treatment, and followed through until March 2015. The modified regimen closely resembled the standard LCH2009 but used vincristine 1.5 mg/m2 instead of vinblastine 6 mg/m2.

Results: The survival rate of the Risk Organ (RO) RO(+) group was 50%, while the survival rate of RO(-) group was 100%. Overall survival (OS) of the treated group was 68.4%. Reactivation rate in RO(+) group of our study was higher than that of LCH2009 (33.33% vs 25%). In contrast, reactivation rate in RO(-) group of our study was lower (14.28% vs 37%). The overall reactivation rate of 26.3% was similar to that of Pollono et al, 2007 (29.7%). Compared with LCH2009, RO(-) patients had excellent survival rate in both regimens (99% vs 100%). However, survival rate of RO(+) group in our study was quite limited compared with that of LCH2009 (50% vs 87%).

Conclusion: We found that the use of a VCR-based regimen to treat histiocytosis was inferior to published comparisons of LCH2009. While substitution of Vincristine for Vinblastine may provide some benefit in lower risk patients, further intensification of therapy and/or use of other available agents may need to be studied in higher risk groups within LMICs.

P-0852 | Thrombosis Associated with Childhood Solid Tumors: A Single Center Experience

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Background/Objectives: Tumors are known as one of the important acquired risk factors of thrombosis.

Design/Methods: In this study we aimed to retrospectively evaluate the clinical findings, genetic risk factors, treatment modalities and the clinical outcomes of the 29 patients who have thrombosis with an underlying solid tumour out of 560 patients diagnosed with thrombosis between January 2005 and March 2016 at Hacettepe University Faculty of Medicine Department of Pediatric Haematology.

Results: There were 17 (59%) boys and 12 (41%) girls with a median age of 156 months (5 - 228 months). The most common underlying malignancies were non-Hodgkin lymphoma (n:6), glioma (n:4), neuroblastoma (n:3), osteosarcoma (n:3), rhabdomyosarcoma (n:2), pleositic astrocytoma (n:2) and other malignancies (n:9) respectively. The location of the thrombosis was lower extremity DVT in 10 patients, upper extremity DVT in 5 patients, cardiac thrombosis in 5 patients, cerebral thrombosis in 3 patients and other locations for the other 7 patients. Factor 5 Leiden mutation was found to be heterozygous in 4/20 patients and normal in 16/20. Homozygous prothrombin 20210A mutation were detected in 1 out of 20 and 4/20 were heterozygous. Homozygous MTHFR C677T and MTHFR A1298C mutation was found in 1/20 and 3/13 respectively and PAI-1 4G/4G homozygous mutation and heterozygous mutation was found in 2/10 and 2/10 respectively. Most of the patients (65.5%) were treated with low molecular weight heparin (LMWH) and recurrent thrombotic episode developed in 3 of them. The median follow-up period was 6 months (1- 84 months). Seven patients (24%) died and the cause of the death was found to be primary disease for 5 of them and primary disease and thrombosis for the other 2 patients.

Conclusion: Thrombosis is a life threatening important problem that should be kept in mind for the children with solid tumors.

P-0853 | Clinical Profile and Outcome of Langerhans Cell Histiocytosis in Children-Experiences from a Tertiary Care Centre of Bangladesh

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Background/Objectives: The clinical presentation and outcome of treatment for LCH are very variable, ranging from an isolated spontaneously remitting bone lesion to a multisystem disease with life threatening organ dysfunction. The study was conducted to see clinical profile and outcome of LCH treating according to Histiocyte Society Guideline – 2009.

Design/Methods: This prospective observational study was conducted over three years - January 2013 to December 2015 at BSMMU, Dhaka, Bangladesh. Total 15 children with diagnosis of Langerhans Cell Histiocytosis (LCH) included consecutively in the study. LCH was diagnosed from clinical, radiological and histopathological examination. After pretreatment clinical evaluation, disease was stratified, then systemic chemotherapy started according to Histiocyte Society Treatment Guideline-2009. Initial treatment response in each patient assessed after 6 week of induction therapy; follow-up is being continued according to Guideline-2009.

Results: Age range of studied children was 4 months to 13 years with M: F 3:2. Among 15 studied children 12/15 (80%) had multiorgan (MS-LCH) and 3/15 (20%) had single organ (SS-LCH) involvement. Bone lesion 66.7%, skin lesion 66.7%, liver involvement 40.0%, lymphadenopathy 26.7%, diabetes insipidus 20.0%, otorrhoea 20.0%, chronic diarrhea 6.7%, and bone marrow involvement in 6.7% cases.

Risk organ involvement found in 40% (6/15) cases having commonest risk organ liver (6/12). CNS-risk lesion was 53.3% (8/15).

After enrollment, 14/15 (93.3%) started therapy with refusal 1/15 (6.7%). After 6 weeks, better response 85.7% (12/14) and worse response 14.3% (2/14). Among better response group, 2/12 (16.7%) reactivate disease during maintenance therapy; 4/12 (33.3%) patient developed relapse (2 in lymph node and 2 in pituitary gland) and 6/12 (50%) maintaining remission after completion of therapy. Overall mortality is 28.6% (4/14).

Conclusion: The study found excellent initial response (85.7%) to initial 6 weeks of induction therapy but high rate of relapse and reactivation (50%) thereafter.

P-0854 | Small Fiber Neuropathy in Paediatric Patients with Chronic Graft-Versus-Host Disease after Allogeneic Hematopoietic Stem Cell Transplantation- Preliminary Results of a Prospective Study

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Background/Objectives: Neurological complications in chronic GVHD can affect central or peripheral nervous system and can produce severe clinical problems with significant morbidity and mortality. Small fiber neuropathy (SFN) is of great interest in many neuropathic pain syndromes affecting peripheral nerves. A significant number of cGVHD patients experience painful muscle cramps and neuropathic pain (NeP). SFN may be the cause of NeP and muscle cramps and can be diagnosed with quantitative sensory testing (QST). QST may be valuable diagnostic tool in diagnostics of cGVHD patient with NeP or cramps.

Design/Methods: QST is diagnostic procedure designed for SFN detection. Eight paediatric patients with cGVHD were examined and QST was performed. Patients also filled the Pain Detect Questionnaire (PDQ) with final goal to diagnose the NeP.

Results: Two out of 8 paediatric patients reported muscle cramps at the time of presentation and both of them met the criteria for NeP according to PDQ. In patients with NeP the QST disclosed affection of C and A-delta fibers (elevated threshold for pain, heat and cold sensation). Isolated A-delta SFN was diagnosed in 4 patients without NeP.

Conclusion: Neuropathy in cGVHD may have various causes and patterns and it is possible that SFN may have important role in NeP development and muscle cramps in a proportion of paediatric cGVHD patients. According to our preliminary results, it is possible that A-delta fibers in cGVHD are affected first, in the period before NeP, while the affection of C and A-delta fibers presents later, after patients develop NeP. Neuropathy and pain in cGVHD may have major impact on the functional status, quality of life and long term outcomes of cGVHD patients. Early recognition and proper diagnostics of SFN and NeP may contribute to the better treatment of pain in cGVHD patients.

P-0855 | The Necessity for a Paediatric Transplant Programme in a Developing Country

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Background/Objectives: In a country still grappling with a legacy of inequality, haemopoietic stem cell transplant (HSCT) programmes have not been prioritised. In preparation for the opening of a custom-built cellular therapies unit at the Nelson Mandela Children's Hospital in Johannesburg, an audit of past practices was conducted.

Design/Methods: A retrospective analysis of children undergoing HSCT at a state-academic and a private-academic hospital was performed. Descriptive statistics, Kaplan-Meier survival curves and Cox regression analysis were calculated.

Results: From January 1980 to December 2015, 39 stem cell transplants were performed on patients diagnosed in our unit, including 19 autologous and 20 allogeneic transplants. The majority of patients (31/39) came from Gauteng Province while six were referred from other provinces and two patients came from Zimbabwe for treatment. Median age was 4.6 years (range 2.8 months to 16 years) and no patients were HIV positive. Indications for transplant included haematolymphoid malignancies (13), solid tumours (15) and non-malignant haematological conditions (11). Twenty-three procedures were performed in our combined unit while 16 patients were referred elsewhere. Sixteen patients (41%) are alive and disease-free, four are alive with disease, 15 died from relapsed disease and four (10.3%) died of treatment-related mortality (TRM). Three patients developed second malignant neoplasms, one of whom demised. The median follow-up period was 624 days (range 44 days to 15.6 years). Five year

overall survival (OS) from transplant was 52.7% with no difference detected between indication for transplant ($p=0.79$) or geographical location of transplant ($p=0.38$).

Conclusion: Limited resources and expertise have resulted in poor access to a life-saving and achievable treatment modality. Despite the lack of a dedicated programme, OS and TRM rates are considered acceptable for the historical period under study. Implementation of a dedicated HSCT programme will increase access for children with high risk malignancies, both locally and country-wide.

P-0856 | Results of Allogeneic Stem Cell Transplantation (SCT) in Children with Acute Lymphoblastic Leukemia in a Public Hospital from a Middle Income Country

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Background/Objectives: ALL can be cured in 80-85% of children with chemotherapy protocols. However, a sub-group requires more intensive modalities. Median Disease Free Survival (DFS), Cumulative Incidence of Relapse (CIR) and Treatment Related Mortality (TRM) for SCT ranges between 0.60-0.70%, 0.24-0.30% and 5-12% respectively.

Our purpose is to review, analyze, and communicate the retrospective results of SCT performed at our Public Institution.

Design/Methods: From 8/1998 to 11/2015, 65 children with ALL received SCT. Male/female ratio was 2:1. Median age was 9.7 years (r3-17). 31 pts. were in 1st CR, 32 in 2ndCR and 2 in 3rdCR. All donors were full match; 90.7% were related and 9.3% unrelated (URD). Bone marrow, peripheral blood and cord blood (CB) were used in 22(29.5%), 40(61%) and 3 pts respectively. Children older than 4-years-old received total body irradiation and etoposide (95.3%), younger pts received busulfan and cyclophosphamide (4.7%).Graft vs host disease (GVHD) prophylaxis included methotrexate and a calcineurin inhibitor (CNI) until day+180. CB pts received methylprednisolone and CNI. ATG was added in URD.

Results: Thirty seven (56%) of pts are alive, 28 (44%) died: 15 of progression, 7 of infection and 6 of toxicity. At a median follow up of 71 months the DFS is 0.51% (r0.38-0.65)(SE0.095); DFS in pts transplanted in 1stCR is 0.58%(SE0.11) in 2ndCR 0.48% (SE0.095) and in 3rdCR 0%(P 0.049).CIR is 0.23%(r0.19-0.32)(SE0.075) and TRM is 7.7%. Sixty-one pts.(93.8%) engrafted, 4 pts failed(6.2%). Median time for neutrophils and platelets engraftment was 16 and 23 days respectively. Twenty-nine pts. (44.6%) developed acute GVHD; grade I/II/IV in 62%. Thirteen pts. (20%) had chronic GVHD and was systemic in 61.5%. Mean total nuclear cells were 6.37×10^8 /kg and mean CD34, 6.36×10^8 /kg.

Conclusion: These 17-year results are acceptable, considering our less privileged socioeconomic population. Our practices can be reassured because outcomes are concordant with those reported by high-income countries.

P-0857 | The Necessity of Hla-Typing for Some Childhood Malignant and Benign Hematological Disorder

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Background/Objectives: Allogeneic hematopoietic stem cell transplantation (HSCT) has been established as a mode of curative therapy for hematologic malignancies, some benign hematologic and immune disorders. The chance that any one sibling would be a perfect match is 25%. Our Objectives are to find percentage of HLA-matching, how many proceed into HSCT and how many awaiting. The reasons for non-processing to HSCT in some patients who have matching siblings.

Design/Methods: Retrospective data at hospital molecular lab for patients who had HLA-typing studies from paediatric haematology oncology unit over one year; March 2015- 2016.

Results: Eight out of nine patients have fully HLA histocompatible match (89%). Those who had HSCT are 2/8 patients (25%); relapsed acute lymphoblastic leukaemia (ALL) and severe aplastic anemia (SAA). Those awaiting HSCT are 2/8 (25%); sickle cell disease with stroke and Diamond Blackfan Anemia (DBA). Other 4/8 (50%), 2 Down syndrome (DS); relapsed ALL and refractory acute myeloid leukaemia (AML) are rejected by referral center. Patient with AML 1/8 refused transplant by parent, HSCT was canceled in patient with late combined relapsed ALL 1/8 who had negative minimal residual disease post reinduction. One out of nine had no HLA-match died from sepsis despite remission of secondary hemophagocytic lymphohistiocytosis (HLH) and the other patient died from refractory AML with DS, Overall outcome 7/9 (78%).

Conclusion: This study emphasis on high incidence of finding HLA-matching donor among Saudi children compared to the literature. HLA-typing is essential for all children diagnosed with AML at diagnosis and relapsed ALL. It is essential in; Fanconi anemia, SAA, DBA. It is required in hemoglobinopathies with specific indication.

P-0858 | Coagulation System Alterations in Children after Allogeneic Stem Cell Transplantation

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Background/Objectives: The coagulation cascade is disturbed by several mechanisms due to conditioning treatment and allogeneic stem cell transplantation (SCT). The aim was to study the effect of SCT on the maturing coagulation system in children.

Design/Methods: Twenty children underwent SCT for a haematological malignancy after myeloablative conditioning. In fifteen patients, conditioning included total body irradiation therapy. The patients were evaluated for prothrombin fragment F1+2, thrombin-antithrombin complexes (TAT), fibrin degradation products (FiDD), for coagulation factors V, VII, VIII, von Willebrand factor, and for natural anticoagulants antithrombin and protein C prior to conditioning (baseline), after conditioning but prior to SCT, and at 2 and 4 weeks after SCT.

Results: As a sign of thrombin generation, F1+2 increased two weeks after SCT ($p < 0.05$), whereas TAT remained stable. Prior to conditioning and prior to SCT F1+2 and TAT correlated positively with each other ($p < 0.01$), but the correlation was lost after SCT. There was a trend towards higher FiDD two weeks after SCT ($p = 0.07$), and at that time F1+2 correlated with FiDD ($R = 0.60$, $p = 0.01$). Factor V and von Willebrand factor increased already after conditioning ($p < 0.05$). FV remained elevated until two weeks, vWF until four weeks after SCT. FVIII was stable but at elevated levels after conditioning (median 185%; reference range 52–148%) until 4 weeks after SCT (median 195%). Fibrinogen increased two weeks after SCT ($p < 0.05$). Antithrombin and FVII were lower two weeks after SCT when compared with the respective four week samples ($p < 0.05$). Protein C remained stable throughout the study period.

Conclusion: SCT caused distinct alterations in coagulation system with many coagulation factors increasing already after conditioning and remaining elevated up to four weeks after SCT. Thus, a procoagulant state, which led to enhanced thrombin formation and fibrin turnover prevailed after SCT.

P-0859 | HLA-Haplotypes in Children with Oncohaematological Diseases

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Background/Objectives: Efficient selection of suitable donor for transplantation in patients with oncohaematological diseases becomes possible due to the accumulation of HLA frequency data in different populations. According to the latest data, the match in donor's and recipient's HLA-haplotypes improves the transplantation outcome, so the research of HLA-haplotypes distribution in healthy donors and patients with blood diseases seems to be essential.

Design/Methods: We analyzed HLA-typing results of 160 children with B-ALL, aged 0.5–17 years (mean 8.3 ± 4.6), 48 with CML 3.5–18 aged (mean 11.5 ± 4.8), 57 with AML, aged 0.5–17 years (mean 8.9 ± 5.2), 43 with AAA, aged 2–17 years (mean 10.7 ± 4.1). The control group was consisted of 502 cord blood samples from healthy newborns. For haplotype estimation we carry out the HLA-typing of patient's parents and siblings, as well as the mothers of newborns in the control group. HLA-typing was performed by SSOP and SSP. HLA-haplotypes frequencies were calculated by direct counting. Statistical analysis was performed using χ^2 -test.

Results: We haven't found significant difference in distribution of the most common HLA-A/B/DRB1-haplotypes between controls and patients in each group. In B-ALL group vs controls we obtained high frequency of rare combinations A*33/B*58/DRB*15 ($f = 0.0256$ vs $f = 0.00131$; $p = 0.0039$) and A*32/B*15/DRB*04 ($f = 0.0132$ vs $f = 0.000832$; $p = 0.026$). In patients with ALL the frequency of A*02/B*27/DRB*01 was increased ($f = 0.0175$ vs $f = 0.0029$; $p = 0.0031$). Interestingly, A*26/B*38/DRB*11 was observed in patients with ALL only, but not in control group. In CML group we haven't found any distinctions in three-locus HLA-haplotype frequencies, so we analyzed A*/B* and B*/DRB1*-combinations. Our studies revealed a significant increase of A*02/B*57 ($f = 0.0416$ vs. $f = 0.0090$; $p = 0.041$) in patients with CML. Patients with AAA had significantly higher frequency of A*24/B*07/DRB1*15 vs control group ($f = 0.034$ vs $f = 0.0069$; $p = 0.009$).

Conclusion: Our results are preliminary, and the study must be extended on a larger cohort of patients as data become available for efficient search of suitable donor.

P-0860 | Use of Plerixafor for Peripheral Blood Stem Cell Mobilization in Children

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Background/Objectives: Granulocyte colony stimulating factor (G-CSF) and chemotherapy are generally used for peripheral blood stem cell collection. Plerixafor, a CXCR4 receptor inhibitor along with G-CSF has been used as a second line mobilizing agent in adults.

Design/Methods: We retrospectively evaluated the cases of two children who received Plerixafor along with G-CSF for peripheral blood stem cell collection. Data including demographics, primary diagnosis, previous chemotherapy, radiation and harvest outcome were analysed.

Results: Two children, the former aged 3 years and with relapsed Neuroblastoma (patient A) and the latter aged 4 years with relapsed metastatic Wilms tumour (patient B), received Plerixafor along with G-CSF for peripheral stem cell mobilization. Both were to receive high dose chemotherapy followed by stem cell rescue. Both patients received prior chemotherapy and surgery for relapsed disease and patient B received whole lung radiation as well prior to this. Patient A failed peripheral stem cell mobilization twice, once with G-CSF alone and later with cyclophosphamide, steroids and G-CSF and had inadequate collection from bone marrow harvest. Both patients received G-CSF 10 mcg/kg three days prior and during stem cell collection. Plerixafor 0.25 mg/kg subcutaneously was given on each day of the collection. Peripheral stem cells were collected over three days. The total collection for patient A and B were 4.76×10^6 cells/kg and 3.12×10^6 cells/kg respectively. No adverse reactions were seen in both the patients.

Conclusion: Data using Plerixafor as a mobilizing agent for peripheral stem cell collection in paediatric population is scarce. Plerixafor along with G-CSF is an effective peripheral blood stem cell mobilizer.

P-0861 | Post-Transplant Lymphoproliferative Disorder in Children: The Irish Perspective - A Single Centre Experience

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Background/Objectives: Post-transplant lymphoproliferative disorder (PTLD) is a serious complication of solid organ and haematopoietic stem cell transplantation. The disease spectrum varies from an infectious mononucleosis-like type illness to aggressive lymphoma. The incidence of PTLD has increased due to the use of more potent immunosuppressive regimens. Optimal therapy for this disease has not yet been established. This study reports on the treatment and outcome of ten patients who were diagnosed with PTLD at Our Lady's Children's Hospital Crumlin (OLCHC) in Dublin between 2004 and 2015.

Design/Methods: Clinical and laboratory data were collected by retrospective review of patient medical records and hospital radiology management systems.

Results: There were 10 cases of PTLD diagnosed over an 11 year period. Both solid organ and haematopoietic stem cell transplants were represented. In addition to a reduction in immunosuppression, all patients were treated with rituximab alone or in combination with systemic chemotherapy. All cases were of B cell origin and were CD20 positive. Nine out of the 10 children are currently alive and disease free. There was no treatment related mortality and no loss of solid organ grafts.

Conclusion: Many therapies for paediatric PTLD have been explored but few multicentre collaborative studies have been published. Treatment of children with PTLD at OLCHC has yielded a 90% survival with a median follow up of 1078 days (range 55–4031 days). This is superior to internationally reported results, albeit in a small patient cohort. These results support the use of reduction of immunosuppression with single agent rituximab alone or in combination with systemic chemotherapy in the treatment of this malignancy.

P-0862 | Allogeneic Related Transplant in Children with Leukemia with Myeloablative Conditioning Without Radiotherapy at the Instituto Nacional de Enfermedades Neoplásicas (INEN)

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Background/Objectives: In August 2012, the INEN reactivated the hematopoietic precursor transplant program and the immunosuppressed patient service. In 2014, the first allogeneic transplant was carried out; so far five paediatric transplants have been performed.

Objectives: Evaluate the process of allogeneic related donor transplant at the INEN.

Design/Methods: Case series. Five patients with allogeneic related transplant, from a compatible sibling have been evaluated. The source was peripheral blood. Four boys and one girl with acute leukaemia (Lymphoblastic: one in first remission, one in second remission, one in third remission; myeloid: one in second remission; biphenotypic one in first remission) Conditioning with: busulfan, cyclophosphamide, thiotepea (2 lymphoblastic, 1 myeloid); busulfan, cyclophosphamide, etoposide (one very high risk lymphoblastic); busulfan, fludarabine, thiotepea (one biphenotypic with history of hypertransaminasemia prior to transplant). Radiotherapy was not employed for conditioning, being substituted with intrathecal chemotherapy at one month post transplant for 6 applications.

Results: Time to recovery for neutrophils was 11 days and for platelets 9 days. The most frequent complication was febrile neutropenia (5 cases). Bacteremia was documented in 2 cases (E. coli; Campylobacter sp.); one patient had gastroenteritis due to Clostridium difficile after day 100 post transplant. One patient presented grade 1 cutaneous graft versus host disease. Chimerism post transplant was 96–100% The follow-up period is 3 to 21 months. All children are in complete morphologic and molecular remission with no transplant related complications.

Conclusion: The results obtained are promising; we expect to perform autologous and unrelated allogeneic transplants in the near future

P-0863 | Haploidentical Hematopoietic Stem Cell Transplantation in Acute Myeloid Leukemia with RUNX1 Mutation – A Case Report

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Background/Objectives: Acute Myeloid Leukaemia (AML) with RUNX1 mutations is associated with resistance to therapy, inferior event free survival, relapse free survival (RFS) and overall survival. Allogeneic hematopoietic stem-cell transplantation (HSCT) has a favorable impact on RFS in RUNX1-mutated patients.

Objectives: To describe the role of Haploidentical HSCT in a case of AML with RUNX1 mutation.

Design/Methods: Single case report.

Results: A four year boy born to a non consanguineous parentage presented with fever and skin bleeds. He had anemia, thrombocytopenia, hyperleucocytosis with blasts. His father who died at 39 years was diagnosed with Myelodysplastic Syndrome (MDS) with secondary AML and had undergone HSCT. Child's aunt underwent HSCT for MDS-AML. His brother had easy bruisability and there is history of anemia in paternal family. The boy was diagnosed with AML M4 with unconfirmed underlying bone marrow failure syndrome or a genetic mutation. He received two courses of chemotherapy with Fludarabine, Cytarabine with G-CSF

following which high dose cytarabine was given. He had delayed count recovery and Minimal residual disease (MRD) continued to be positive. Conventional and stress cytogenetics were normal. Genomics report revealed **RUNX1 MUTATION**. Hence HSCT was planned and mother was chosen as the donor with 8/10 HLA match. His brother was also tested positive for the same mutation. Another course of chemotherapy with Cytarabine, Doxorubicin and Etoposide was given and MRD reduced. He underwent HSCT with Reduced Intensity Conditioning with Busulfan, Cyclophosphamide and Fludarabine. Neutrophil engraftment was achieved on Day 15 of transplant. He achieved complete chimerism. Last chimerism done is 95% donor and 5% recipient (1 ½ years post transplant). He has no graft versus host disease. RUNX1 mutation is negative in bone marrow and positive in somatic cells.

Conclusion: Allogeneic hematopoietic stem-cell transplantation (HSCT) is required to improve the RFS in RUNX1-mutated AML patients.

P-0864 | Analysis of Food Intake of Paediatric Patients Submitted to Hematopoietic Stem Cell Transplantation

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Background/Objectives: Conduct an analysis of food intake of paediatric patients undergoing Hematopoietic Stem Cell Transplant (HSCT).

Design/Methods: A retrospective study of patients younger than 18 years who underwent HSCT from October 2015 to March 2016.

Results: In the study 16 patients were analyzed, with an average age of 8.26 years, 11 female and 5 male. Among the types of HSCT were performed 3 Autologous, 4 tandem, 4 Allogeneic Related, 3 Allogeneic Unrelated and 2 Haploidentical. The patients had average food intake of 87.47% of their daily energy nutritional needs. The patients who underwent Tandem HSCT had the highest percentage of food intake (123.51%), followed by Allogeneic Unrelated HSCT (93.53%), Autologous HSCT (78.07%), Haploidentical HSCT (69.07%) and the HSCT Allogeneic Related (66.75%). Between the periods of HSCT the highest percentage of observed adequacy was between Day (D) -14 to D -8 Allogeneic Related HSCT (171.92%) and the lowest was between D 0 and D +6 of Haploidentical HSCT (26.86%). In general, the higher uptake was observed between D -14 to D -8 (152.69%), and lowest among the D 0 and D +6 (72.62%).

Conclusion: Adequate food intake during HSCT is essential to decrease protein catabolism in these patients and reduce the risk of any associated complications. Knowing the expected evolution of food intake provides data for performing indication alternative nutritional therapies such as through supplements or enteral tubes for complementation of nutritional support.

P-0865 | Hematopoietic Stem Cell Transplantation: An Institutional Experience of 27 Cases

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Background/Objectives: Stem cell transplant (SCT) is a therapeutic option for many patients with different pathologies. In oncology, 15% of children might need a SCT. The aim of this review was to present a single center experience in children with hematopoietic stem cells transplantation (HSCT).

Design/Methods: We conducted a descriptive, cross-sectional and analytic study in Hospital Infantil de México "Federico Gomez" between March 2011 to May 2014. This retrospective review was conducted by reviewing medical records of 27 patients with HSCT.

Results: Mean age of the population was 10 years (y) 9 months (mo) ± 4 y, being the youngest patient 2y 2mo and the oldest, 17y 10mo. Distribution by gender was 59.2% (16/27) male and 40.8% (11/27) female.

Of the 27 patients, 22 (81.4%) had an oncological diagnosis and 5 (18.5%) had a benign hematological diagnosis. Of those 22 patients with oncological diagnosis, 20 (90.9%) had a hematological malignancy. The most common malignancy was acute lymphoblastic leukaemia (ALL) (12/22; 54.5%), followed by acute myeloid leukaemia (AML) (6/22; 27.2%), chronic granulocytic leukaemia (2/22; 9%) and solid tumors (2/22; 9%) (neuroblastoma and Ewing sarcoma). Finally, all five remaining patients with benign hematological diagnosis had severe aplastic anemia. Transplants performed were as following: a) allogeneic related donor (15/27; 55%), b) haploidentical (8/27; 29.6%), c) autologous (2/27; 7.4%), d) syngeneic HSCT (1/27; 3.7%) and e) unrelated donor HSCT (umbilical cord) (1/27; 3.7%). Overall survival was 39% at 39.3 mo. Depending on the type of transplant, survival was 57% at 39.3 mo in allogeneic HSCT, 43% at 15.5 mo in haploidentical and 0% at 11 months in autologous.

Conclusion: A significant proportion of children with relapsed ALL and AML can be cured, even those with early relapse. Children who receive re-induction therapy, enter remission and proceed to SCT can achieve a cure rate of 30%.

P-0866 | Use of Exome Sequencing for Evaluation of Molecular Signatures or Pathways Involving Germline and Hsct-Induced Mutations Associated with Paediatric Hsct-Therapy and Patient Outcomes

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Background/Objectives: Hematopoietic stem cell transplantation (HSCT) is a therapeutic procedure for patients with malignant and non-malignant disorders. While this procedure is considered high risk, it is the only curative therapy for some patients. Evaluating genetic asso-

ciations based on HSCT patient outcomes may provide information to significantly impact their care. Establishing effective strategies to prevent toxicities and improve outcomes after HSCT is critical. Whole exome sequencing was utilized to identify molecular signatures that correlate with germline and HSCT-induced genetic mutations relative to HSCT-patient outcomes.

Design/Methods: A retrospective study involving whole exome sequencing of DNA collected both pre and post HSCT from six paediatric subjects with autologous HSCT was performed. All six subjects underwent myeloablative conditioning regimen involving carboplatin in combination with standard of care agents. Pre and post HSCT DNA sequences were compared to identify mutations induced by exposure to anti-cancer therapy. To gain further insight on these specific mutations, canonical ingenuity pathway analysis[®] (IPA) was performed.

Results: Whole exome sequencing was exploited to assess genetic mutations in 9,433 genes among all six paediatric subjects pre and post HSCT. Approximately 10% of those genes (959 genes) were commonly mutated among all six subjects when comparing gene mutations pre and post HSCT. Canonical IPA analysis using hypergeometric test illustrated these common genetic mutations in pre versus post HSCT may be relevant in mechanisms involving DNA damage response and repair pathways ($p=0.000078$, and $p=0.00017$, respectively). This data-rich analysis also revealed thirty-five other statistically significant biological pathways for future investigative research.

Conclusion: These key preliminary findings highlight the importance for further exploring associations between paediatric germline genotypes and HSCT-induced genetic mutations involved in relevant biologic pathways which may correlate with patient prognosis. Future studies may elucidate molecular signatures for developing personalized treatments for HSCT therapy to properly manage HSCT-induced toxicities, optimize clinical outcomes, and improve standard of care.

P-0867 | Management of Acquired Aplastic Anemia in a Resource Poor Setting and Role of Hepatitis C Virus: Experience from a Developing Country

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Background/Objectives: Acquired aplastic anemia is a major cause of hematologic morbidity in children. Stem cell transplant offers cure but most of the patients in developing countries are unable to afford it, and immunosuppressive therapy is an alternative in this situation. These children are also vulnerable to acquire various transfusion associated infections.

Design/Methods: The records of children with acquired aplastic anemia treated at the division of paediatric hemato-oncology at King Georges' Medical University, Lucknow from January 2007 to June 2015 were reviewed retrospectively.

Results: Total 122 patients were diagnosed with acquired aplastic anemia during study period, out of which 22 were excluded as they refused treatment. Data of remaining 100 patients was analysed. Mean age of these children was 9.23 years (1.5 to 17 years) and majority was male (69%). The most common clinical manifestation was fever (77%) followed by bleeding (62%) and pallor (61%). Seventeen (17%) patients had very severe disease.

Sixty four (64%) patients received antithymocyte globulin (ATG) and cyclosporine, 15 (15%) only cyclosporine and remaining 21 patients received no/other treatments. Overall survival was 50%. Children treated with immunosuppressive treatment had a better overall survival (58.2%) compared to patients given other/no treatment (18.1%). Survival of patients in ATG group was comparable to those given cyclosporine alone (43.8% vs 53.8%, p value = 0.88). Three children were hepatitis C positive at presentation, and they died within 3 months of presentation, despite ATG being given to 2 of them. Thirteen acquired hepatitis C during treatment, out of which 7 (53.8%) died. Overall survival was poorer in hepatitis C positive children (37.5%) as compared to children who were negative (51.4%).

Conclusion: Immunosuppressive treatment is a suitable alternative to stem cell transplant in resource poor settings. Survival is comparable whether cyclosporine is used alone or with ATG. Acquisition of hepatitis C infection increases the mortality in these children.

P-0868 | Concentrations of Peptides Regulating Gastro-Intestinal Tract in Paediatric Stem Cell Transplantation

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Background/Objectives: Gastro-intestinal functions are regulated by numerous peptides, which secretion can be modified by severe inflammation. The goal of the study was determination of chosen peptides concentrations profile in children treated with stem cell transplantation.

Design/Methods: Plasma ghrelin, cholecystokinin (CCK), glucagon-like peptide-1 (GLP-1) and fibroblast growth factor 21 (FGF-21) concentrations were measured in fasting state in 44 children 1.5–19 (average 9.9) years old, 31 boys and 13 girls, referred to hematopoietic stem cell transplantation (HSCT) due to neoplastic-32 (73%) and non-neoplastic-12 (27%) diseases. The HSCT group was studied twice – before transplantation (44 children) and 7 months in average after transplantation (27 of 44 children). All children in having two collections were treated with allogeneic HSCT. Graft versus host disease was diagnosed in 52% of patients. Healthy control group - consisted of 26 children 4.3–16 (average 12.2) years old, 11 boys and 15 girls.

Results: All children in post-HSCT group were without immunosuppressive treatment and without any signs and symptoms of the primary disease. Mean percentiles and SDS BMI did not differ significantly between studied groups and control. Mean percentiles BMI after transplantation (64.3+/-29.5) was significantly ($p=0.05$) lower comparing to before procedure (53+/-34.4). Median concentrations and AUC values of ghrelin, CCK and GLP-1 were significantly ($p<0.05$) lower and FGF-21 significantly higher before transplantation in comparison to control group. Similar profile was observed after transplantation. Paired comparison of

peptides concentrations before and after transplantation showed significant decrease of all studied peptides after transplantation.

Conclusion: Decrease of peptides regulating of gastrointestinal functions in peritransplantation period indicate dysfunction of the system in patients referred to procedure and progression of its injury after transplantation.

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P-0869 | Identifying and Treating Eosinophilic Cystitis after Allogenic Stem Cell Transplant: A Case Report

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Background/Objectives: Eosinophilic Cystitis (EC) is a rare condition. Its etiology is associated with allergies, neoplasms, and chemotherapeutic agents. The association of EC and stem cell transplant (SCT) has been reported but few case reports have discussed successful treatment options. We hope to add a new perspective on the disease's presentation, as well as its potential treatments.

Design/Methods: This is a single case report at Texas Children's Hospital in Houston, Texas.

Results: The patient is an eighteen year old male with relapsed acute lymphoblastic leukaemia who received a mismatched (9/10) unrelated allogeneic stem cell transplant. He received conditioning with TBI/cyclophosphamide and cytarabine. Graft Versus Host Disease (GVHD) prophylaxis included tacrolimus and methotrexate. Six months post-transplant, he developed gross hematuria and transfusion dependence. Cystoscopy demonstrated diffuse transmural eosinophilic infiltrates. Viral studies including BK virus, CMV, EBV, HHV6-8, adenovirus and JC virus were negative. Other infectious etiologies were also negative. No medication was identified as an inciting agent. The patient was treated with systemic steroids, montelukast and cetirizine. In addition, two one-week courses of intravesical dexamethasone were given. He improved briefly but relapsed shortly after completion of therapy. Subsequently, he underwent cystourethroscopy with cauterization of focal hemorrhage sites, followed by intravesical aminocaproic acid. After initial improvement, he again developed recurrent hematuria. Given initial improvement with steroids, the patient was restarted on systemic steroids at one mg/kg/day and intravesical dexamethasone which have continued on a tapering schedule over twelve weeks. He has since been symptom free on that regimen.

Conclusion: Several treatment options have been reported for EC in individual case reports, including antihistamines, intravesical steroids, anti-fibrinolytic agents, and cauterization; however treatment success is not uniform. EC as seen here can continue to recur without multifaceted, long-term treatment regimens. We discuss this case to broaden existing case descriptions and help establish a novel treatment algorithm for future patients.

P-0870 | Allogenic Transplant for Paediatric Leukemias and Myelodysplastic Syndrome: Outcome Data from a Tertiary Care Centre in India

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Background/Objectives: Pediatric ALL merits a consideration for Allogeneic Hematopoietic stem cell transplant (HSCT) in CR1 for high-risk cases and certain subgroups of relapsed ALL in CR2 based on time to relapse, site of relapse and Immunophenotype. For AML, Allogeneic HSCT is recommended for high and very high-risk cases in CR1 and all AMLs in CR2. Allogeneic HSCT is curative for majority of the paediatric MDS cases. For paediatric patients with Ph+CML, allogeneic HSCT, possibly in the first year after diagnosis, remains the treatment of choice, provided that a well-matched donor is available. We present here the data from our institute for 9 patients of ALL, CML and MDS who underwent Allogeneic HSCT at our centre.

Design/Methods: We retrospectively analysed the data of patients who underwent Allogeneic HSCT at our centre for Leukaemia/MDS) from November 2013 to March 2016.

Results: 9 patients (M:F:1.25:1) (age range:3.5-19y;mean age10.5y)(Relapsed Ph+ALL:1, ALL in CR2:3, ALL in CR3:1, CML in CP1:2, MDS:1, MDS with leukemic transformation:1) underwent Allogeneic HSCT at our centre from November 2013 to March 2016. The type of Allogeneic transplant was- Matched sibling donor(MSD):4, Matched related donor:1, Haploidentical HSCT:3, Double cord:1. Stem cell source was Umbilical cord:1, Peripheral blood stem cell:8. Status at D+100 post HSCT was Complete-remission (CR):8, Relapse:1. The mean duration of follow-up was 324.3days (range:87-705days). The outcome of these patients at last follow-up: death:2 (attributable to sepsis:1 & relapse:1), alive:7 (relapse:1, CR:6). Acute GvHD occurred in 5 (Gr1:1, Gr2:3, Gr3:1) (skin alone-1, skin&gut-3, gut&liver-1) & chronic GvHD in 1(extensive, involving skin).

Conclusion: Allogeneic HSCT is now becoming an integral part of management of certain categories of paediatric leukaemia and MDS patients contributing to improved overall and disease free survival. MSD HSCTs are becoming more and more safe and alternate donor HSCT more and more possible with newer techniques, protocols, regimens and better supportive care.

P-0871 | Acute Hepatic Injury in Children with Hemophagocytic Lymphohistiocytosis

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Background/Objectives: In Vietnam, hemophagocytic lymphohistiocytosis (HLH) is a rare and fatal hematological syndrome. We investigated clinical features and response to the first 8 weeks of treatment by the HLH-2004 protocol in children with HLH and acute hepatic injury (AHI) with the group who did not have this complication.

Design/Methods: A cohort study was conducted at the Children's Hospital 1 from 2010 to 2012. Clinical characteristics and laboratory features during the diagnosis and the first 8 weeks of immunochemotherapy were followed up.

Results: Ninety-three children fulfilled the diagnostic criteria of HLH. Among them, 57.4% had AHI. The median age of the group with AHI was 26 (IQR: 15-45) months compared to 32 (IQR: 12-68) months in the group without AHI ($p>0.05$). There was no significant difference about sex, gastrointestinal hemorrhage, central nervous system involvement, duration of fever and time from diagnosis to treatment between the two groups. The proportion of patients with HLH and AHI had the time from admission to diagnosis < 5 days was 80% compared to 60.5% among the group without AHI ($p=0.03$). The proportions of patients with HLH and AHI had neutrophil count <500/mm³, triglyceride >5mmol/l, ferritin >10,000mcg/l, LDH >2,000U/L were significantly higher than those without AHI. Patients with HLH and AHI had a higher proportion of infection by EBV (56.3%) compared to the group without AHI (29.3%, $p=0.011$). After first 8 weeks of initial treatment, the proportions of complete response (46% vs. 27.9%), incomplete response (20% vs. 34.9%), and death (34% vs. 37%) were similar between the two groups with and without AHI.

Conclusion: AHI is a major complication during the course of HLH. However, AHI does not appear to be predictive of poor outcomes. The early diagnosis and management of children with HLH and AHI can potentially save life of these severe patients.

P-0872 | Ferritin/Fibrinogen Ratio is a Potential Marker for Childhood Hemophagocytic Lymphohistiocytosis

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Background/Objectives: Among diagnostic parameters of Hemophagocytic lymphohistiocytosis (HLH), cut-off value of serum ferritin level, 500ng/mL, has been under discussion, due to its low sensitivity. Since outcomes can be improved if HLH development is diagnosed or predicted at admission, goal of this research is to investigate the value of serum ferritin level at admission in HLH prediction.

Design/Methods: Patients hospitalized in Beijing Children's Hospital between Sep 2009 and Jul 2012 were included, if their serum ferritin tests were ordered at admission. Patients with systemic juvenile idiopathic arthritis (SJIA) were excluded because macrophage activation syndrome (MAS), which often happens in SJIA, has characteristics overlap those of HLH. All clinical or laboratory features were collected at admission. ROC curves were created with SPSS version 13.0; Areas under the curve (AUCs) of combined parameters were performed with SAS.

Results: Ninety patients were studied (35 female, 55 male), 36 of which were diagnosed HLH or developed HLH. The age range was 0.1 to 14 years, with a median age of 4. Forty four patients had splenomegaly, 36 had cytopenia affecting 2 or 3 lineages. The median value of serum ferritin levels was 9164ng/mL (193.2 ng/mL-311,700 ng/mL). Although admission ferritin level alone couldn't predict HLH occurrence ($P=0.146$), Ferritin/ fibrinogen ratio ($P=0.007$) and Ferritin/ neutrophil absolute count ratio ($P=0.000$) showed significant results in HLH predicting. AUC of fibrinogen improved from 0.718 to 0.729 after combining ferritin level.

Conclusion: Peaks of serum ferritin levels can appear when HLH develops, rather than admission point in some patients. Plus, as a result of immune activation, elevation of serum ferritin can be triggered by multiple reasons. Specificity of ferritin in HLH indicating could be improved when combined with parameters which are decreased in HLH, such as ferritin/ fibrinogen ratio.

STEM CELL TRANSPLANTATION TECHNIQUE AND SUPPORTIVE CARE

P-0873 | Outcome of Paediatric Patients with Hematopoietic Stem Cell Transplantation who Require Intensive Care Support: A Single Institution Experience

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Background/Objectives: Allogeneic hematopoietic stem cell transplantation (HSCT) is a potentially curative treatment for hematological malignancies. Patients with life threatening complications may need admission to the paediatric intensive care unit (PICU) for further support.

Design/Methods: We performed a retrospective single-center study on 129 consecutive HSCT patients in a third-level hospital during 2014 September - 2016 March and analyzed the outcome and factors prognostic of PICU admission.

Results: A total of 129 HSCT [127 allogeneic (matched sibling/family donor=54, matched unrelated donor=51, haploidentical donor=22) and 2 autologous] were carried out. Forty-four PICU admissions were observed in 31 patients (24%). All of them had received allogeneic HSCT (matched sibling/family donor=7, matched unrelated donor=15, haploidentical donor=9). The underlying conditions were acute leukaemia (n=7), thalassemia (n=8), bone marrow failure (n=8), immune deficiencies (n=4) and the others (n=4). Causes of PICU admission were mainly respiratory failure (34%), neurological problems (30%) followed by septic shock requiring vasoactive drugs (9%). Vasoactive drugs support was used in 48%, mechanical ventilation in 61%, noninvasive ventilation in 34%, renal replacement therapy in 30% of PICU admissions. Plasma exchange was performed in 30% and ECMO was done in 4.5% of PICU admissions. Sixteen patients died in the PICU, with a PICU mortality rate 51.6%. Mechanical ventilation, renal replacement therapy, vasoactive drugs support, occurrence of an active graft versus host disease (GvHD) and duration of PICU stay had significant effects on in PICU mortality ($p<0.05$).

Conclusion: The incidence of HSCT-related complications requiring PICU admission was 24%, with a PICU mortality rate of 51.6%. Needs of mechanical ventilation, renal replacement therapy, vasoactive drugs support, occurrence of an active GVHD and duration of PICU stay are main predictive factors of mortality.

P-0874 | Comparison of Virus Infection in Paediatric Allogeneic Hematopoietic Stem Cell Transplantation from Matched Related/Unrelated and Haploidentical Donors in Children

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Background/Objectives: Haploidentical stem cell transplantation (haplo-HSCT) has been developed as an alternative transplant strategy for children with hematological disorders without a HLA matched donor. Whereas infectious complications, in particularly viral infections in the early and intermediate posttransplantation phase, remained an issue primarily due to slow and impaired immune recovery due to T cell depletion. The aim of our study is to compare the incidence of virus infections and outcome in children who underwent allogeneic HSCT from matched related/unrelated and haplo donors.

Design/Methods: A hundred and twenty paediatric patients (median: 6.3 years) who underwent allogeneic HSCT were included in this retrospective study. There were 49 matched related donor (MRD), 50 matched unrelated donor (MUD), and 22 haploidentical donor transplantation with $\alpha\beta$ T cell depletion. All patients received acyclovir prophylaxis against viral infections until discontinuation of immunosuppression. Intravenous immunoglobulin was given weekly during inpatient treatment and thereafter according to immunoglobulin G level < 6 g/L. PCR screening for BK virus, Adenovirus, Epstein-Barr virus, Parvovirus B19, Human herpes virus 6 and Cytomegalovirus (CMV) were performed routinely weekly. Analysis on immune reconstitution was performed monthly until day 180 in haplo transplant patients. Lymphocyte count $> 1,000/\text{mm}^3$ and lymphocyte count at day 100 were analyzed in all patients.

Results: Adenovirus, BK virus, CMV virus and Parvovirus B19 reactivations were significantly low in MRD transplant patients ($p=0.045$, $p=0.043$, $p=0.001$ and $p=0.032$ respectively). Comparison of 9/10 and 10/10 matched transplants for virus infections showed also significantly low CMV, Parvovirus B19 and BK virus infections ($p=0.001$, $p=0.019$ and $p=0.001$) in 10/10 matched transplants. Incidence of all virus infections between MUD and haplo transplantation was found statistically not different.

Conclusion: These data indicate that haplo-HSCT is comparable with MUD transplantation in the setting of viral infections. A larger study group and prospective studies are needed to confirm this observation.

P-0875 | HSCT for Myeloid Sarcoma - Case Report and Summary of the Literature

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Background/Objectives: Myeloid sarcoma is a rare disease in the paediatric age group, and often refractory to chemotherapy with significant mortality and morbidity. We describe a young male with myeloid sarcoma of the upper limb successfully treated with autologous stem cell transplant and a review of published literature

Design/Methods: The NS evidence database was used to search Medline, CINAHL and Embase. We're relevant, terms were matched to the database of each thesaurus.

Results: Limited literature exists regarding the use of HSCT in the treatment of myeloid sarcoma in this age group. Adjunct treatments such as radiotherapy are often common depending on the location and burden of disease.

Conclusion: Discussion: It is imperative that experience on the use of HSCT to treat paediatric myeloid sarcoma are shared, including data on longer term outcomes such as late effects and treatment related morbidity.

P-0876 | Autologous Hematopoietic Stem Cell Transplantation : First Experience of Paediatric Haematology and Oncology Center (Rabat, Morocco)

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Background/Objectives: The autologous peripheral hematopoietic stem cell (HSC) is used as a support to the restoration of hematopoiesis in paediatric haematology-oncology.

The objective of this work is to report the experience of Rabat paediatric haematology and oncology service about autologous hematopoietic stem cells transplant.

Design/Methods: A retrospective study was conducted at the Pediatric Haematology and Oncology service of Rabat on a period of sixteen months (November 2014 - March 2016). Eight children were grafted using autologous peripheral hematopoietic stem cells during this period.

Results: 6 boys and two girls were treated during this period by intensive chemotherapy followed by autologous hematopoietic stem cell transplantation; the median age at the time of transplant was 9 years (with extremes ranging from 4 years to 15 years). The indication of the intensification by high-dose chemotherapy followed by autologous was the high-risk neuroblastoma in 5 cases and Hodgkin lymphoma in 3 cases (2 cases of relapse and a case of resistance to treatment). According to data from the literature, the deadline of post-transplant aplasia output is two to four weeks earlier to the white line; this deadline was 15 days on average in our study. Several authors reported that post-transplant infectious complications are common during the period of neutropenia (mucositis, sepsis, and diarrhea). In our study, infectious complications

are dominated by mucositis and febrile neutropenia. Two patients presented a tumoral relapse respectively after five and six months post-transplant, with a case of death post-relapse in a child followed for a high-risk neuroblastoma.

Conclusion: Through these observations, we present the experience of Pediatric Haematology and Oncology service of Rabat (SHOP) for intensive chemotherapy with autologous HSCT. For the success of this procedure, it is necessary to contribute efforts between various stakeholders such as parents, the paediatric oncologist, nurse, biologist, hematologist, the intensivist, dentist, dietician, psychologist and the social worker.

P-0878 | Comparable CD34+ Cell and Viability Despite Decreased Tnc Data between Pre-Freezing and Post-Thawing Cord Blood

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Background/Objectives: Cell dose is the most important factor determining the clinical outcome of cord blood (CB) transplantation. Therefore, total nucleated cell (TNC) and CD34+ cell doses are primary determinants for CB selection. Some physicians distrust the banking data because of the discrepancy of cell doses between pre-freezing data from CB banks and post-thawing data from transplant centers.

Design/Methods: We retrospectively analyzed the transplanted CB units regarding their pre-freezing and post-thawing cell doses and viabilities, which were registered in KoreaCORD from August 2001 to December 2010.

Results: Paired pre-freezing and post-thawing data were compared for TNC counts in 285 units from 7 Korean CB banks, for CD34+ cell counts in 200 CB units from 5 banks, and for viability in 35 units from 4 banks. Compared to pre-freezing data from CB banks, the TNC counts after thawing from transplant center were significantly decreased from 10.6×10^8 to 9.2×10^8 ($P < 0.001$). However, the CD34+ cell counts and viability revealed no significant changes, respectively, between data of pre-freezing from CB banks (43.7×10^4 , 85%) and post-thawing from transplant centers (39.1×10^4 , 91%), respectively.

Conclusion: We observed that the CD34+ cells and viability were comparable before freezing from CB banks and after thawing from transplant centers, while the TNC counts were decreased after thawing.

P-0879 | Karyotype Analyses of Bone Marrow Mononucleated Cells before and after Cryopreservation

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Background/Objectives: The karyotype analysis is important for the study of hematological malignant disorders as well as for the diagnosis of various diseases. The ability to perform chromosome analysis of cryopreserved bone marrow or peripheral blood cells is important for future retrospective studies. This study is performed to evaluate the type of chromosomal abnormalities and to compare the karyotypes of the cells after cryopreservation using programmed controlled-rate freezing system in a single hospital.

Design/Methods: Total 15,340 chromosome analyses were performed from bone marrow samples as well as peripheral blood lymphocytes, amniotic fluid cells, or other tissues at the cytogenetic laboratory in this Hospital from May 1981 to August 2014. Bone marrow samples (BM) are obtained by 6,563 referred patients for diagnosis or monitoring of hematological malignancy and other bone marrow disease. Of the cryopreserved BM, twelve matched BM, stored for 1 ~ 6 months, were thawed and cytogenetic analyses were done for each sample.

Results: From karyotype analysis with BM, the aberration rate was 19.9% (1,309/6,563). The frequent aberrations were t(8;21), -Y, t(15;17), +8 in AML; t(9;22), hyperploidy, -19 in ALL; t(9;22) in CML; +8, -7, dup(1q), dup(7q), del(20q) in MDS. For the cryopreserved BM, the chromosomal analyses were not successful due to poor quality of banding pattern and mitosis of cells.

Conclusion: The karyotype analysis is important for the study of hematological malignant disorders. Although this study has some limitation of the sample distribution and small sample number, the karyotype analysis of BM after cryopreservation as well as chemotherapeutic treatment has some limitations and needs further study for the future to get information from the stored diagnostic samples.

P-0880 | Some Challenges in Finding Stem Cell Transplant Donors Amongst Black South Africans

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Background/Objectives: There is an increasing need for hematopoietic stem cell transplant (HSCT) in South Africa for treatment of patients with various hematological disorders.

Design/Methods: Since 1991, more than 1000 preliminary searches were done on the South African Bone Marrow Registry (SABMR) for donors. Between 1997 and 2012, 254 South African patients received HSCT from matched unrelated donors. Only 25% of HSCT in South Africa are from local donors and 75% were from international donors. This is because of lack of HLA-typed donors on the SABMR and partly because there is not enough black donors on the registry.

Black people are under represented on the SABMR for donors. There are more than 65,000 people on the SABMR of which 71% are white, 8% asian, 6% colored and only 5% black. As a result, black patients don't fully benefit from Stem cell transplant (SCT) as the odds of finding a matched donor are higher amongst people who are geographically and racially matched.

Results: Black people don't donate blood products because of lack of education regarding blood products donations and benefits thereof. Many black people in South Africa deeply value cultural and religious beliefs and have attached them to their body parts and therefore are unable to donate or receive stem cells.

Most black people from rural areas are not aware of the need for HSCT as medical centers that provide HSCT are few, centralized and mainly situated in Gauteng and Western Cape provinces. Furthermore, black patients from rural areas that could benefit from HSCT are often diagnosed late and die before their families and communities are exposed to the reality of the desperate need for black HSC donors. This makes it even more difficult to convince black people, especially from the rural areas to donate stem cells or any other blood products.

Conclusion: More awareness and exposure needed.

P-0881 | Using Practice Development Methodology to Advance Paediatric Nursing Practice in Haematopoietic Stem Cell Return Within Children's Haematology Unit, Royal Belfast Hospital for Sick Children

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Background/Objectives: From practice experience the ward manager identified the need for staff training in haematopoietic stem cell return. Three senior paediatric nurses within the unit were selected to advance their nursing practice within this area by attending an education day facilitated by the adult transplant co-ordinator previously responsible for this procedure. Following the education day, in order to successfully incorporate the changes required to clinical care, the trainees were invited to attend a practice development workshop.

Design/Methods: The workshop created a formal approach for the use of practice development tools such as: values clarification and claims, concerns and issues, to create ownership within the process and an action plan to guide the implementation of the paediatric nurse led procedure. As the trainees were new to practice development tools, each of the tools were introduced to allow the participants to have a full understanding of their overall aim. Any potential challenges were explored with the resources required to overcome these identified. Through the workshop it was identified that the new developments within practice required the collaboration of medical and pharmaceutical teams, and so they were invited to discuss our findings through a team meeting and education session.

Results: Both medical and pharmacy teams appreciated the depth of exploration of the factors with rationalised decision making evident through the use of tools and creation of action plans. All teams agreed to the service developments with little of the anticipated resistance and challenges. Further ongoing education of staff in this area will be required.

Conclusion: The extension of the nursing role within this area created a sense of motivation within the paediatric nursing team. The practice development tools, action plan and a shared vision were used to create an improved holistic child and family centred procedure.

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P-0882 | Changing Trends in the Use of Granulocyte Transfusions in Neutropenic Children with Sepsis

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Background/Objectives: Advances in antibiotic and antifungal therapy help provide optimal supportive care in chemotherapy and HSCT. Granulocyte transfusion is an additional agent being used to reduce mortality due to sepsis in high risk children.

Design/Methods: A retrospective observational analysis of children undergoing treatment for cancer and HSCT at our centre from 2007 to 2015, who received granulocytes. We divided children into two groups - the first group being those receiving granulocytes from January 2007 till December 2013 and the second group being those receiving granulocytes from January 2014 till December 2015. This division is based on the change in our policy to use granulocytes within 48 hours of septicemia as the incidence of drug resistant bacterial strains had increased at our centre.

Results: Data on 72 children with 230 granulocyte infusions were analysed. From 2007 to 2013 (n=48/72) we had 27/48 (56%) culture proven sepsis of which 14(51%) were carbapenam resistant gram negative bacilli. Of the 27, 11 children survived the crisis (41%).

We then changed our policy to transfuse granulocytes early during sepsis. From 2014 to 2015 (n=24/72) 22 patients had culture proven sepsis (91%) of which 20 had carbapenam resistant gram negative bacilli and 12/22 (54%) with culture proven sepsis survived the episode. The survival rate had improved from 41% in first group to 54% after early intervention with granulocytes (P value is 0.0347) Relative risk = 0.6839 and 95% Confidence Interval: 0.5068 to 0.9229.

Conclusion: Granulocyte transfusion is essential to tide over neutropenic sepsis when faced with resistant bacterial infections. Despite the increased incidence of resistant bacteria during the period of 2014 to 2015, the survival rate improved from 41% to 54%. Clearly, this intervention cannot be taken in isolation and needs to be offered early and in parallel with appropriate antibiotics.

P-0883 | Profile of Infections in Paediatric Hematopoietic Stem Cell Transplant Patients: Experience from a Tertiary Care Centre in India

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Background/Objectives: Hematopoietic stem cell transplantation (HSCT) is the definitive treatment modality for several malignant, non-malignant and primary immunodeficiency conditions in children. Though the success rates are increasing in leaps and bounds, infections are still a major cause of morbidity & mortality in patients undergoing HSCT.

Design/Methods: We retrospectively analysed the profile of infections in paediatric patients who underwent HSCT at our centre from February 2012 to December 2015.

Results: 53 patients underwent 61 HSCTs between February 2012 to December 2015 (9autologous and 52allogenic). M:F ratio 2.53:1 and average age 7.74years(range:5months-22years).Graft source:bone marrow(BM):11/61(18.1%), G-CSFmobilized peripheral blood stem cells(PBSC)-41/61(67.2%), BM+PBSC-8/61(13.2%),umbilical cord blood-1/61(1.6%). Indications for BMT:thalassaemia major(24.6%), sickle cell anemia(9.8%), severe acquired aplastic anemia(5%), congenital marrow failure(9.8%),primary immunodeficiency(14.7%), relapsed ALL(8.2%), CML(3.3%), MDS(3.3%), relapsed/refractory solid tumors(6.5%),relapsed/refractory neuroblastoma stage4(11.6%), RefractoryNHL (1.6%),others(Epidermolysis bullosa dystrophica)(1.6%). Patients received prophylactic antifungal, antiviral and prophylaxis against Pneumocystis jiroveci. There were 53 documented infections in 61 transplants during and post HSCT;spectrum:34bacterial (5ESBL,10Klebsiella pneumoniae, 1Pseudomonas aeruginosa, 4Acinetobacter boumani, 7MRSA, 2Enterococcus faecalis,1Enterococcus faecium,1Stenotrophomans maltophilia,1CONS, 1Morganella morgani, 1Edwardsiella tarda), 14viral(7CMV,1EBV, 2BKV, 1Adenovirus, 1JC virus, 2Varicella), 3fungal(1Aspergillus, 1Candida tropicalis, 1Candida dubiliniensis) and 2BCGiosis. Distribution of occurrence of infections: 29-pre-engraftment, 20-post-engraftment upto D+100 postHSCT and 4-postD+100 of HSCT. Median time of occurrence of infection:10days postHSCT(rangeD-9toD+341) and mean time of Neutrophil engraftment:15.5days postHSCT(range9-26days) (9-non-engraftment,1-engraftment pending,1-rejection post-engraftment). Mortality attributable to infection occurred in 8/61(13.1%).

Conclusion: Infections in HSCT setup contribute to significant morbidity & mortality. Preventive & pre-emptive strategies should be sought for and applied wherever feasible to reduce the frequency of infections and improving outcomes for these patients.

P-0884 | Results from an Open National Public Health Insurance Program in Hematopoietic Progenitor Cells Transplant Implemented at a Private Tertiary Hospital in Mexico: A Success Story

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Background/Objectives: Transplantation of hematopoietic progenitor cells (THPC) is an effective treatment strategy for children with immunological, hematological and oncological conditions. The number of accredited institutions to perform transplants in Mexico is insufficient. Cooperation with private institutions is essential to meet the needs.

We report a case series of THPC patients treated through a public-private cooperation.

Design/Methods: This study represents a retrospective, descriptive, and longitudinal case series of patients treated with THPC between January 2009 and December 2014. Data on age, gender, diagnosis, and type of transplant, as well as conditioning, graft, transplant, and infectious complications were recorded. Disease-free and overall survival were calculated through Kaplan-Meier.

Results: Twenty-eight women and 41 men were included. Median age was 8.3 ± 5.19. Diagnosis included Acute Lymphoblastic Leukaemia (17), Acute Myeloid Leukaemia (4), lymphoma (7), Chronic Myeloid Leukaemia (5), Neuroblastoma (9), Medulloblastoma (8), Ewing Sarcoma (7), and others (12). Transplantation was autologous in 37 patients, allogenic in 30, and haploidentical in 2. Median number of cells infused was 5.81x10⁶. Median time to engraftment was 18 days. Mucositis occurred in 88% (grade III). Neutropenic colitis in 32%. 25% had acute graft vs. host disease (GVHD) (grades II-IV). Two had sinusoidal obstruction syndrome, 4 had cytomegalovirus infection and 1 had a BK virus infection. Chronic GVHD was seen in 15% of patients. The 48-month overall survival was 85%. Disease-free survival was 62%. Grade IV GVHD decreased survival to 32%.

Conclusion: HSPT in children and adolescents increases the overall and disease-free survival for immunologic, hematologic and oncologic conditions, although it is certainly not free of severe complications. Early detection and management of such complications decreases the mortality risk. A healthcare program implemented in private institutions with public funds represents an appropriate strategy to improve results, and allows access to care for children that require HSPT in Mexico.

SUPPORTIVE CARE/PALLIATIVE CARE

P-0885 | Health Related Quality of Life of Egyptian Children Survivors of Childhood Hematological Malignancies

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Background/Objectives: Health related quality of life (HRQOL) has been increasingly acknowledged as an essential health outcome measure in children with cancer. For various reasons, developing countries including Egypt have under-used these outcomes. The aim of this study was to describe the HRQOL in short term survivors of childhood hematological malignancies by comparing their scores with a healthy control.

Design/Methods: A cross section study of HRQOL was conducted on 65 children survivors of hematological malignancies and their parents (aged 5-15 years). All patients were in remission for 1 to 3 years. The PedsQL 4.0 Generic Core Scales and The PedsQL 3.0 Cancer Module was administered to the patients and their parents. The generic Core Scales was administered to the control group. The control group consisted of 60 sex and age matched healthy children.

Results: HRQOL were assessed in 65 (37 males, 28 females) survivors of hematological malignancies. The age ranged between 5-15 years (mean = 8.6 years, median = 9 years), this constitute 72% of eligible subject participated. Significant positive correlation between the children and their parents reports as well as the PedsQL 4.0 Generic Core Scale and the PedsQL 3.0 Cancer Module. Better HRQOL was reported by the child than the parents. Most of the survivors reported moderate to good HRQOL, however HRQOL in survivors was significantly lower than the control subjects ($p < 0.001$). The type of hematological malignancies did not have important effects on HRQOL. Impaired female survivors HRQOL is greater than males especially for emotion, worry and cognition. Anxiety, communication and school sub scales were more impaired in older children ($p < 0.05$).

Conclusion: HRQOL in survivors of hematological malignancies in Egypt is significantly lower than the population norms. Males have better HRQOL than females. Efforts to improve HRQOL of survivors is needed for these children especially in the psycho-social domains.

P-0886 | Difficulties in Providing Palliative Care in Rural India (West Bengal) – Experience of an NGO

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Background/Objectives: As in any developing countries state of West Bengal in India has a huge burden of cancer patients in advanced stage coming from rural area where awareness regarding the usefulness of palliative care is rather poor. Our goal is to give a pain free good quality of life in these advanced stage cancer patients. Objective of this study is to identify the main difficulties in achieving the above goal in a rural village setting in India.

Design/Methods: Advanced cancer patients in need of palliative care in various villages in of rural India were selected for this study. Their symptoms and managements in that rural surroundings were evaluated by an NGO (under the guidance of a senior palliative care specialist) working in that area. An attempt was made to identify the main obstacles in getting proper palliative care in a rural setting.

Results: Pain, fatigue are the main symptoms effecting these patients. In most patients pain and other symptoms control were grossly inadequate due to lack of properly trained manpower in the rural India. However regular homecare visits by a group of social workers were of immense help in the last few months of life. NGO team was well guided by a palliative care specialist.

Conclusion: There is a wide gap of trained manpower in this filled in rural areas of India. Dedicated groups from rural area itself need encouragement and proper training, so that difficult symptoms can be managed locally along with necessary social and psychological support to these patients.

P-0887 | Palliative Care for End Stage Cancer Patient in Rural India

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Background/Objectives: Due to financial incapability and absence of manpower poor families often fail to carry their advanced cancer patients to the nodal centres. This pilot study will explore whether communication by mobile phone can lessen this burden. To identify and try to solve to the extent possible the main difficulties in giving palliative care to the terminal cancer patients of the area.

Design/Methods: Initially a plan was generated regarding management of an advanced cancer patient in a nodal centre at District Head Quarter. Subsequently every two week a trained social worker attached to nodal centre will follow up and give necessary advice and emotional support to the patients and their families through their registered mobile phone number. Patient's family were also encouraged to communicate with the team by phone in case of fresh complain and urgency in between.

Results: Since initiation cancer patients were contacted by mobile phone every two weeks to enquire about their difficulties. In 76% of the situation trained social workers could give necessary advice by phone regarding management of their physical symptoms. Moreover patient's family were really overwhelmed by the emotional support offered by the team over phone. Only 24% of cancer patients has to attend the nodal centre for expert advice from Palliative Care specialists.

Conclusion: This novel approach helped

- In providing regular physical and emotional support to the patients and their families.
- In significantly reducing the financial and manpower problems of carrying patients to the nodal units.
- In improve the quality of life of patients by continuous guidance.

More and more team members can take help of this new strategy for better communication and uninterrupted care.

P-0888 | Safety & Cost-Effectiveness of Short Hydration Protocol (SHP) in the Outpatient Setting for Patients Receiving Cyclophosphamide: A Single Center Experience

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Background/Objectives: Cyclophosphamide (CTX) in doses higher than 1000mg/m²/dose may lead to renal impairment, hematuria, or hemorrhagic cystitis. To avoid this, mesna and super hydration are used for which patients must be admitted or have long infusion times in the outpatient setting. We looked at our single center experience using a short hydration protocol (SHP) with CTX and evaluated the complications, safety, and potential cost saving of this approach.

Study Objectives

1. Identify the incidence of renal impairment, hematuria, and hemorrhagic cystitis with the use of SHP/CTX
2. Correlate risk factors that may contribute to the incidence of complications.
3. Perform a cost comparison of outpatient vs inpatient administration of CTX.

Design/Methods: Patients age 0-14 years diagnosed with solid tumors from January 2005 until December 31, 2012 who received CTX doses 1200mg/m²/dose- 2200mg/m²/dose were included. The incidence of complications including renal impairment, hematuria, and hemorrhagic cystitis in this group were reviewed. Comparison of cost of services in the outpatient vs inpatient was undertaken.

Results: Eighty seven patients with solid tumors received CTX using a SHP: 36 (41%) had Rhabdomyosarcoma, and 51 (59%) Ewing Sarcoma. The age at diagnosis was categorized in to three sub-groups: Group-I (0 to 3 years), Group-II (3 to 7 years) and Group-III (7 to 14 years). There were 20 (23%), 29 (33%), and 38 (44%) patients in Groups I, II, and III respectively. CTX related complications were seen in 43 patients (48%); 38 (88%) had hematuria whereas only 2 had hemorrhagic cystitis (5%). 56% of the patients with complications were Group-I and II. A significant cost benefit was realized using the SHP.

Conclusion: In our setting, CTX is safely administered in the outpatient setting with SHP even in small children. There was no incidence of increased complications requiring hospitalization for these patients. This approach is convenient for the patient/ family and more cost effective.

P-0889 | Central Line Associated Bloodstream Infection in Paediatric Oncology Patients in Qatar: A Prospective Study

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Background/Objectives: Central Line-associated Bloodstream Infection (CLABSI) is associated with high morbidity and mortality. The study aim is to assess CLABSI rate and its risk factors in hospitalized paediatric oncology patient in Qatar.

Design/Methods: A prospective observational study was conducted at Pediatric Oncology Department, Hamad Medical Corporation, Qatar between January 1, 2013 and December 31, 2014. All children less than 14 year of age with malignancy who required a central line catheter were included.

Results: Thirty seven subcutaneous tunneled catheters were inserted. Majority of patients were younger than 10 years of age (88%), and male to female ratio was 1.3 to 1. Leukaemia was the most frequently encountered diagnosis. The overall mean central venous catheter (CVC) infection rate was 4.12 days per 1000 CVC days. Thirteen catheters were infected (35.1%), of which 11 catheters were porta-A-cath and 2 catheters were Hickman double lumen line. Gram negative bacteria were found in 69.2% of CLABSI cases but no fungal infection was detected. Gender, age, type of disease, and type of catheter were not associated with increased risk for CLABSI ($p > 0.05$). Mean number of days with neutropenia was more in patients who had CLABSI 73.5±44.5 compared to patient who did not have CLABSI 48.9±52.1, but the difference did not reach statistical significance ($p = 0.203$). The mean number of infected days was 11 days per 1000 total line days in patients with port-A-cath compared to 2 days per 1000 total line days in patients with Hickman lines ($p = 0.498$).

Conclusion: CLABSI incidence rate continues to be a concern in hospitalized paediatric oncology patients in Qatar. This study showed that mean CVC infection rate was 4.12 days per 1000 CVC days. Gram negative bacteria CLABSI were the dominant organism in this group of patients and catheters.

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P-0890 | Difficulties in Proving Paediatric Palliative Care among Health-Care Professionals at a Japanese Children's Hospital

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Background/Objectives: In order to deliver quality palliative care, knowing difficulties with paediatric palliative care among health-care professionals (HCPs) is important. The aim of this study was to describe HCPs' difficulties at one of the largest children's hospitals in Japan.

Design/Methods: Self-reported questionnaires were developed for this study with some modifications to Palliative Care Difficulty Scale (PCDS). A single-page instrument was distributed to 623 HCPs working at Shizuoka children's hospital in February 2014. The questionnaires consisted of 21 items in 5 domains, including "alleviation of symptoms", "communication", "clinical ethics", "community coordination" and "death/dying". HCPs were asked to rate their difficulty on a 4-point Likert scale (never, sometimes, often, or always) for each of the items. In this study, "often" and "always" ratings were considered to represent difficulty.

Results: A total of 370 instruments were returned, for response rate of 59.4%. Most of respondents were nurses (66%) and medical doctors (9%). The rest consisted of physical/occupational therapists, pharmacists, radiologists, social workers, dieticians, clinical psychologists, child life specialist, child care workers and teachers. In 3 of the 21 items, more than 70% represented difficulty, that is, "After parents are informed of bad news, it is difficult to talk", "It is difficult to get support from experts about psychological symptoms" and "It is difficult to get support from

experts about physical symptoms". In 2 of the 21 items, less than 40% represented difficulty, that is, "It is difficult to communicate about the goal of treatment/care in multi-professional team" and "Necessary education is not received about communication".

Conclusion: HCPs at a children's hospital felt considerable difficulties with paediatric palliative care. Educational programs including communication skill training and expansion of palliative care team activities may contribute to alleviating HCPs' difficulties.

P-0891 | Nutritional Challenges During Chemotherapy: A Multiple Case Study of Paediatric Oncology Patients

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Background/Objectives: Nutrition remains a major area of concern at the time of diagnosis, treatment and survivorship of childhood leukaemia (Acute Lymphoblastic Leukaemia-ALL). Nutritional problems may be present at diagnosis, or start after the first few doses of chemotherapy. However, lack of research in the area hinders timely identification, assessment and management of children who experience nutritional problems.

The objectives of this multiple case study research was to identify nutritional challenges faced by a child undergoing chemotherapy, to explore how parents dealt with those challenges, to learn what recommendations parents have received from their medical caregivers to deal with dietary side effects and to explore the benefits of given dietary recommendations in improving intake of a child.

Design/Methods: This study qualitatively explored such nutritional challenges and the coping strategies from children with ALL and their parents. Moreover, this study looked into the trends of nutrition status through diet recall, growth charts and hospital records stating nutritional problems from start of chemotherapy.

Results: The results of this study revealed that each of three cases faced nutritional challenges during the initial intensive phases of chemotherapy but gradually they started improving their intake. These challenges were evident from their medical record and growth charts analysis, diet recalls and in depth interviews. All three cases received detailed counselling on nutritional challenges and parents shared their strategies for dealing with these challenges. However, ongoing counselling and dietary recommendations were missing in all three cases.

Conclusion: Adequate nutrition enables a child to cope better with detrimental effects of chemotherapy whereas poor nutrition can lead to increased risks of infections, decreased tolerance to chemotherapy, poor survival, and higher chances of relapse. The need for nutritional assessment of all paediatric oncology patients and dietary counselling sessions along with large scale research studies to guide practice are evident.

P-0892 | Fever in Neutropenia in Children and Adolescents with Cancer: Risk Prediction Based on Data Covering Two Decades in a Single Center

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Background/Objectives: Fever in neutropenia (FN) is the most frequent potentially life threatening complication of chemotherapy in children with cancer. Risk prediction of FN would allow for targeted prophylaxis during chemotherapy. This study aimed to develop a prediction rule for FN risk and to evaluate its performance versus previously published rules.

Design/Methods: This retrospective cohort study in children and adolescents diagnosed with cancer before 17 years covered two decades (1993 to 2012) in a single institution.

Results: During 692 years of cumulative chemotherapy exposure time in 583 patients, 712 FN episodes were diagnosed (annual rate 1.03; exact 95% CI. 0.95-1.11). 154 of them with bacteremia (0.22; 0.19-0.26). The risk for FN (rate ratio per decade, 0.97; 0.72-1.30) and FN with bacteremia (0.88; 0.38-2.04) did not change over time.

In multivariate mixed Poisson regression, the risk for FN was independently associated with 6 of 11 characteristics studied: chemotherapy intensity, bone marrow involvement, central venous catheter, prior FN, time since diagnosis, and relapse. Three of these characteristics significantly changed over time, and four of them had significant changes of associations with FN over time (interaction). The risk prediction rule derived from this multivariate model explained 19% of the variance for FN. In external validation, a previously published risk score based on 5 characteristics explained 9% of variance, and a clinically used rule with 1 characteristic (acute myeloid leukaemia versus other diagnoses) explained 4%.

Conclusion: The predictive performance of rules predicting FN during chemotherapy, including the one derived from this dataset, was poor. Significant changes of characteristics and their associations with FN over time may partially explain this. Adding laboratory results or restricting the spectrum of diagnosis might increase the predictive performance of future rules.

P-0893 | Prilocaine-Induced Methemoglobinemia During Central Venous Catheter Insertion

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Background/Objectives: Central Venous Catheters (CVC) and ports are used very commonly in the treatment of malignancies for venous access. They are routinely implanted under local anesthesia safely. Prilocaine is a lidocaine homologue local anesthetic which is biotransformed by hepatic amidase to aminophenol metabolites (ortho-toluidine and N-propylalanine), which can oxidize hemoglobin to methemoglobin.

Prilocaine-induced methemoglobinemia is rather rare, depending on treatment dosage. Even low doses (1-2mg/kg) may cause this problem in children. Methemoglobin levels above 10%

may result in clinical anoxia, and above 60% can cause stupor, coma, and death. Primary treatment is oxygen. If the methemoglobin level is more than 20%, intravenous methylene blue must be applied.

In this retrospective study, five cases to whom CVC was inserted and later developed methemoglobinemia were presented to stress the importance of choosing local anesthetics especially for paediatric patients during minor interventions.

Design/Methods: Five consecutive cases, with a median age of 8 years (Range : 2/2/12-17/11/12 years) and have malignancies (2 ALL, 2 Hodgkin Disease, 1 Wilms tumour) had minor surgical interventions (3 insertion of CVC, 1 change of CVC and 1 removal of CVC). During follow-up, all of them had cyanosis, hypoxia unresponsive to oxygen and low peripheral oxygen saturation (sPO2 : 80-90%) in 1-2 hours.

Results: Chest x-rays evaluated for pneumothorax were normal. A venous blood sample revealed a methemoglobin level of 9%-27%. All patients received intravenous methylene blue (1 mg/kg) for high levels or clinical persisting symptoms. In one hour after treatment, methemoglobin levels were normalized (1.6-2.3%). All patients recovered fully without any further problems.

Conclusion: Prilocaine is a commonly used agent that may cause methemoglobinemia, even at therapeutic doses; thus, appropriately calculated doses should be used and after prilocaine application, patients should be observed for at least an hour for clinical findings. If needed the local anesthetics should be changed accordingly.

P-0894 | Efficacy and Safety of Oral Aprepitant in the Treatment of Nausea and Vomiting Induced by Chemotherapy in Mexican Paediatric Patients with Cancer

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Background/Objectives: Objective: To assess the efficacy and safety of Aprepitant in the treatment of CINV in children with cancer.

Design/Methods: We Included in a clinical trial, patients aged 1 to 17 years. Prior to chemotherapy administered: oral Aprepitant in < 10kg: day 1, 40 mg, 2 and 3, 20 mg; 10.1 to 20kg: day 80 mg 1, 2 and 3, 40 mg.; 21 to 40 kg:day 1, 2 and 3, 80 mg > 40.1kg: day 1, 125 mg, 2 and 3, 80 mg and Ondansetron IV (5 mgm2BS) c / 8 h day 1-5 all received dexamethasone (2.5mgm2do/8hr). We consider efficiency if the level of NYVIC was less than 3 of the WHO agreement for 5 days, without medical recue, also evaluating the local and systemic tolerance.

Results: We evaluated 60 patients, male 16 (26.7%) and female 44 (73.3%) average age of 104 years, 15 with leukaemia (25%) and 45 solid tumour (75%), 18 highly emetogenic chemotherapy (30%) and 42 (70%) moderately emetogenic chemotherapy. Efficacy was seen in 24 / 30 which received aprepitant vs 14 / 30 in those with ondansetron (47%), p 0.007. No local or systemic adverse events were reported. The number of rescues was significantly higher in patients with ondansetron.

Conclusion: Adequate control of Nausea and Vomiting Induced by Chemotherapy (CINV) is a cornerstone in cancer treatment. Aprepitant is an inhibitor of substance P effective in the treatment of CINV of adults, there is poor experience in children under 8 years. Aprepitant may be an alternative for the control of CINV in paediatric patients of all ages.

P-0895 | Study of Cost-Benefit of Prophylactic Treatment of Febrile Neutropenia with Pegfilgrastim vs. Filgrastim in Paediatric Patients with Solid Tumors

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Background/Objectives: Analyze the cost-benefit of prophylactic treatment of febrile neutropenia with pegfilgrastim vs. filgrastim in paediatric patients with solid tumors.

Design/Methods: A study of cost-benefit, which analyzed complete clinical records of paediatric patients with solid tumors and NF who received prophylactic treatment with pegfilgrastim vs. filgrastim, were considered variable clinical and demographic, NF events, days of hospital stay as well as related complications and the global cost related search for differences by students t and X 2.

Results: A total of 106 courses of chemotherapy in 26 patients were included. 14 patients (53.8%) were given filgrastim and 12 patients (46.1%) received pegfilgrastim. The 57.6% of male gender. The average number of days of hospital stay and cost significantly higher in the Group of Filgrastim with respect to pegfilgrastim(p<0.001).

Conclusion: Febrile neutropenia (FN) is one of the major complications of cancer patients, exponentially increasing the costs of treatment. Pegfilgrastim is the Pegylated filgrastim and may reduce the severity and duration of the febrile neutropenia as well as the costs, the use of pegfilgrastim decreased the number of events of neutropenia and fever, the days of hospital stay and costs in approximately 30%.

P-0896 | Effectiveness of Glycyrrhetic Acid Gel + Polyvinylpyrrolidone as Adjuvant in the Treatment of Mucositis in Mexican Paediatric Patients with Cancer

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Background/Objectives: To determine the efficacy of gel glycyrrhetic acid + polyvinylpyrrolidone (Gelclair®), as adjuvant in the treatment of mucositis in paediatric cancer patients, conventional treatment compared (Philadelphia solution) in children with cancer and mucositis.

Design/Methods: A controlled clinical trial open type, which included 60 patients who were treated with glycyrrhetic acid + polyvinylpyrrolidone (Gelclair®), comparing paired with a historical cohort of paediatric patients diagnosed with grade 3 mucositis was designed and 4. the efficacy and safety of both treatments according to the local response (remission) was evaluated and tolerance to liquids and solids as well as the presence of local and systemic adverse effects, and the presence of complications. Descriptive statistics were performed using measures of central tendency and dispersion as well as students T test for difference of proportions.

Results: It showed that glycyrrhetic acid + polyvinylpyrrolidone (Gelclair®) is more effective and safe in treating mucositis in children with cancer, with 60.5% of cases in which there was clinical remission vs 39.5% of patients were Philadelphia treated solution. The most frequently used chemotherapeutic prior to the episode of mucositis was methotrexate, and the most frequent complication was associated with neutropenia and fever; evolution time ranged from 4-10 days, patients had higher frequencies of adverse events were treated with Philadelphia solution.

Conclusion: The oral mucositis in cancer patients occurs in 30-50% of patients undergoing chemotherapy and up to 90-100% of patients receiving radiotherapy to the oral cavity. Previous studies have reported efficacy and safety of glycyrrhetic acid gel + polyvinylpyrrolidone in adult patients. We believe that glycyrrhetic acid gel is more effective and safer than, Philadelphia solution in the adjuvant treatment, mucositis in children diagnosed with cancer.

P-0897 | Palliative Care in Children with Cancer. Experience of a Hospital in the Center of Mexico

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Background/Objectives: To report the experience in palliative care given to our paediatric patients with cancer.

Design/Methods: We included in a cohort, patients of Pediatric Oncology of the HMI service that its palliative care. We evaluate clinical and demographic variables, diagnosis, reason for admission to palliative care, care provided specific: chemotherapy, radiotherapy and unspecific as analgesia, pain management, time of duration of such care, palliative care home and hospital, as well as the death and site of the same.

Results: In the study period (2005 January-2015 December) 65/591 patients with childhood cancer (11%) its palliative care, 58% male and 55% corresponded to acute leukaemia relapse 3rd, prevalence in preschool children, 80% lived in urban areas, chemotherapy was the care palliative specific more used (46%) and pain the nonspecific (95%) with duration of 3 months, the most frequent death cause was bleeding and 55% died at his home.

Conclusion: In Mexico the law from 2012 indicates the right to palliative care giving and dignity to the process of dying, the Hospital Materno Infantil ISSEMYM is a reference Center for children with cancer in our Institute of Social Security. In Mexico there are few reports related to palliative care. The multidisciplinary treatment of cancer in our center includes palliative measures specific and unspecific, the proportion of patients who die hospitalization still is very high, and so it should have an impact in the implementation of the home care that requires a specific unit of paediatric palliative care.

P-0898 | Efficacy and Safety of Transdermal Buprenorphine as an Adjuvant in the Treatment of Chronic Pain in Children with Cancer of Toluca Valley

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Background/Objectives: To assess the efficacy and safety of transdermal buprenorphine as an adjunct in the treatment of chronic pain of children with cancer.

Design/Methods: In a Quasi-experimental study, manage, transdermal buprenorphine 3-6 mcg/kg, 35 mcg/hour to children with cancer and chronic pain. We evaluated gender, type of cancer, using Visual Analog Scale Pain level every 8 hours, for children, vital signs for 5 days, response to treatment and side effects more frequently, tests of renal and hepatic function, local tolerance: pruritus, Erythema and edema. They were rescued with tramadol.

Results: We include 25 patients, 10 male and 5 female. 40% with acute lymphoblastic leukaemia. The most common reason for pain was the progression of the disease. The intensity of the pain on day one had an average of 8 and 1 seventh. Only 29% warranted rescue with tramadol. Vital signs remained normal for the age. Adverse effects were Nausea at 19%, constipation, urinary retention in the 6% to 6%.

Conclusion: Pain affects the quality of life of children with advanced cancer. Buprenorphine is a semi-synthetic opioid, 30 times more potent than morphine, its properties facilitate its transdermal penetration. Chronic pain in children with cancer is a challenge due to its complex biological nature, the causes are multiple and require a fast and effective treatment. Transdermal buprenorphine has few adverse effects, allows a controlled dosing and activity without relying on teams to relieve your pain, and increases the quality of life in our children.

P-0899 | Continuous Infusion Ondansetron for the Management of Nausea and Vomiting in Patients Receiving Cisplatin

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Background/Objectives: Chemotherapy-induced nausea and vomiting (CINV) significantly impairs quality of life despite our advances in antiemetic prophylaxis. Ondansetron is administered in 8-hourly boluses to prevent CINV, but highly emetogenic agents such as cisplatin often cause breakthrough nausea and vomiting. At British Columbia Children's Hospital (BCCH) ondansetron has been used for many years as a continuous infusion in cases of poorly controlled CINV. Our objective was to review the efficacy of ondansetron given as a continuous infusion in the management of emesis in patients receiving cisplatin.

Design/Methods: We performed a retrospective study of the medical records of all children who received cisplatin at BCCH during a 5-year period from 1 January 2010 to 31 December 2014. Data included patient demographics, type of cancer, dose of cisplatin, ondansetron given as infusion vs bolus, use of other antiemetics, and number and volume of emesis charted in the nurses' notes.

Results: Preliminary results on 26 patients (12 female, median age 4.2 years) were obtained. Cancers included intracranial tumours (n=13), neuroblastoma (n=4), osteosarcoma (n=3), hepatoblastoma (n=4) and adrenocortical carcinoma (n=2). Median cisplatin dose was 60mg/m². Among 25 chemotherapy cycles (5 day cycle) in patients who received ondansetron via bolus administration there were 135 events of emesis, with a total volume of 11,233mL (83mL/event). Among 27 chemotherapy cycles in patients who received ondansetron via continuous intravenous infusion there were 160 events of emesis, with a total volume of 8,300mL (52mL/event). Patients experienced more emesis-free days while on continuous infusion therapy (40 vs 34%). Concomitant antiemetics were used more often during bolus therapy.

Conclusion: Despite an increase in the frequency of vomiting, there is a reduction in the volume of emesis and more emesis-free days in patients receiving ondansetron via continuous infusion. Concomitant antiemetics may be confounding the lower frequency of emesis in bolus therapy patients.

P-0901 | Empowering Bereaved Parents in the Development of a Comprehensive Bereavement Program

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Background/Objectives: The death is incredibly difficult. Parents' and caregivers' grief journeys are unique and ongoing; however, common themes and support systems help to define successful bereavement services. Bereaved parents who have experienced the loss of a child have special insight and can help to identify the key components necessary for the development and implementation of a comprehensive bereavement program. We utilized bereaved parents in our strategic planning and implementation of our bereavement program. The purpose of this abstract is to describe the process and early outcomes of this bereavement initiative.

Design/Methods: The bereavement program at St. Jude Children's Research Hospital begins with anticipatory bereavement services prior to death. Following the child's death, a specially trained bereaved parent mentor is offered and available. Additionally, bereaved parents have created a resource manual with parent and sibling with recommended books, websites, and other helpful references. Parents developed a booklet containing reflective pieces and video describing difficult moments in their grief journey to provide a support to other parents and staff. Finally, they designed and illustrated communication cards to be sent to all bereaved families at key time points during the first 13 months after a child's death.

Results: Data about each of the steps will be shared and the actual documents and multimedia resources used in the program will be available to share with participants. A total of 15 bereaved parent mentors are trained and provide support to 75 mentees currently. At the time of this publication, there have been 157 documented encounters, with over 200 contacts from mentors to mentees.

Conclusion: The innovative nature of this program with multiple components of the parent-driven comprehensive bereavement program can serve as a paradigm for the development of other programs and for the field of paediatric oncology as a whole.

P-0902 | Can "Small Mince Pies" Traditional Food of Ireland Play Role in Cell Cycle Arrest and Apoptosis

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Background/Objectives: In spite of the significant progress in the development of anticancer therapies the incidence of cancer is still on its rise worldwide. Due to limited role of chemotherapy, radiotherapy and surgery, cancer patients who already got crippled with this disease followed by burden of drug induced toxic side effects have now turned to seek help from complementary and alternative medicine. Daily everybody is ingesting a cocktail of phytochemicals from vegetables, fruits, spices etc however most of the population is unaware about its biochemical, physiological and pharmacological therapeutic inputs. About 25000 different chemical compounds occur in fruits, vegetables and other plants eaten by man. Out of 121 prescription drugs in use for cancer treatment, 90 have been derived from plant species. Small mince pies filled with cinnamon, cloves and nutmeg and hot mulled wines are traditional foods eaten during holiday season in Ireland. This compilation was intended to showcase and focus on some of the components of daily traditional diet that have been shown to work on different target sites for anticancer activity.

Design/Methods: Search was made for various spices and fruits known to have an active component effective in preventing cancer through cell cycle arrest and apoptosis.

Results: From extensive meta-analysis of studies done, it was possible to pinpoint the target sites of as many as 25 spices and fruits that could be included in diet for preventing cancer.

Conclusion: From the meta-analysis it can be concluded that spices and fruits can be better employed for cancer prevention with better patient compliance and can improve the quality of life.

P-0903 | Advance Care Plans in Paediatric Oncology

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Background/Objectives: Advance Care Plans (ACP) are finding widespread application within paediatric and adult palliative care, but with variable success in their uptake within paediatric hospitals and hospices. Demonstrable benefits included maintaining communication between clinicians and dying children and their parents, as well providing opportunities for discourse as the child's symptoms and journey evolve. The aim of this study was to explore published research describing barriers to delivering ACP in the paediatric oncology setting.

Design/Methods: The NHS evidence was used to search the cinahl embase medicine and psychinfo using predetermined search terms.

Results: Articles were included if they were English, paediatric data, and related to children dying Sent from my iPhone.

Discussion: ACP have proven benefit improving discussions around end of life care in children dying from cancer. Further research is needed to fully understand if these can impact upon improved standards of clinical and outcomes for patients. Significant barriers remain in place to their widespread application in the clinical environment and their remains a responsibility for all clinicians and health care professionals to explore and eliminate them in their own institutions.

P-0904 | Uncharted Territory: Life after Cancer for Young Adults

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Background/Objectives: Similar to survivors of childhood cancer, young adult (YA) survivors have distinct and complex medical and psychosocial needs. However, there are no specific follow-up guidelines for patients who were diagnosed as a young adult. Most YA survivors receive inadequate survivorship care with minimal surveillance for late effects. This study aims to examine the concept of survivorship care planning and determine what aspects of post-therapy care is most needed.

Design/Methods: Two focus groups were held to investigate the post treatment experience of YA survivors. Participants completed cancer treatment and were diagnosed between 2005 and 2011. They either continued to receive follow-up care or did not. These were further subdivided based on age at diagnosis: 18-24; 25-30; 31-39 years. Participants answered predetermined questions during their session. A demographic questionnaire was given and a SCP (a treatment summary [TS] and its associated long- and late-term risks) developed based on their electronic medical records.

Results: 27 YAs participated in the focus groups. SCPs were developed for each participant and required 45 - 180 minutes to complete. 78% felt TS were accurate and 44% learned of long/late-term side effects they were previously not aware of nor receiving surveillance on. Barriers to continued follow-up were related to health insurance status, poor communication with their oncologist, and on-going adjustment challenges. Initial feedback from the SCPs indicates that YAs seek additional information on long/late-term side effects, roadmap for follow-up visit, and information on psychosocial support and YA specific resources.

Conclusion: For young adults diagnosed with cancer, there are no guidelines on follow-up care. Young adult survivors are not aware of long- and late-term side effects they may have, and many do not know how often they need to have continued follow-up. Despite great strides made in survivors of childhood cancer, the same cannot be said for young adult survivors.

P-0905 | Changes in Management of Febrile Neutropenia and Impact on Length of Hospital Stay in a Paediatric Oncology Unit

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Background/Objectives: Chemotherapy-induced febrile neutropenia (FN) is a frequent complication in cancer treatments. Various empiric antibiotic (AB) regimens are recommended worldwide to treat quickly and effectively children with fever. Since 2000s, patients were stratified into low and high risk groups for severe infection according to their underlying immunosuppression and were respectively treated with a 3rd or 4th generation cephalosporin or piperacillin-tazobactam + aminoglycosid or a broad spectrum monotherapy of beta-lactamin. This study addresses the impact of two empiric antibiotic strategies on length of hospital stay (LOS): bitherapy with ceftriaxone/amikacine for all children with FN compared to risk based stratification we introduced in 2010: meropenem monotherapy for high risk and bitherapy with ceftriaxone/amikacine for low-risk patients.

Design/Methods: Patients treated at the University Hospital of Lausanne between December 29th 2002 and December 31st 2012 were eligible for the study allowing a 10 years- retrospective analysis of the first episode of FN. The patients were distributed into 2 groups: Group 1 for patients with FN treated before August 2010 with ceftriaxone/amikacine, Group 2 for patients with FN treated after August 2010 based on a risk stratification strategy with either bitherapy or meropenem monotherapy. Various demographic, clinical and treatment-related predictors potentially influencing LOS were chosen for analysis.

Results: One hundred and fifty-six first episodes of FN were reported between December 2002 and December 2012 and were analyzed. We identified as predictors for shorter LOS the risk adapted stratification for antibiotic treatment introduced after 2010 which resulted in a significant reduction of LOS by 25% (irr=0.754, P=0.002) and diagnosis of solid tumors (irr=0.80, P=0.003). Predictors for prolonged LOS were fever duration, change of antibiotic treatment during FN, admission to continuous care, mucositis. There was no death reported.

Conclusion: Our study supports antibiotic stratification according to the underlying risk of developing severe infections among children with febrile neutropenia.

P-0906 | The Role of the Paediatric Oncologist During the Period of Bereavement: The Experience of a Single Institution

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Background/Objectives: Providing support to parents grieving over the death of their child is the concern of the physicians in our department. Grief may involve extreme emotions and behaviors. Feelings of guilt, anger, despair, and fear are common. In addition, the bereaved need reassurance that what they feel is normal. The role of the physician at this time is to talk about the loss with the persons who were involved, setting goals toward recovery and answering questions about the medical management throughout.

Design/Methods: Some 10-15 children die yearly in the Pediatric Haematology Oncology Division at Rambam Health Care Campus, the main referral center in northern Israel. For almost every child, in addition to the nurses and the psychosocial staff, the treating physician, the fellow and the head of the department visit the family the first week after the child's death.

Results: The main questions asked by the parents are about the treatments, the possibility that other experimental therapies or other chemotherapeutic protocols may have helped the child, or treatments abroad. Other concerns regard the care of staff members, or misunderstanding in the child's management or the palliative care management. In some cases, the parents are invited to come to the department to continue the discussion about the misunderstanding or some difference of opinion about the therapeutic protocol, even from the start of treatment and not necessarily at the end or at the time of the recurrence.

Conclusion: In most cases, the parents feel that the presence of the head of the department and the treating physician at that time allows them the possibility of asking all the questions they did not ask before the child's death. The second phase includes coping with the loss by retelling the story of the disease and finding an explanation for their questions.

P-0907 | Biological Therapy in Refractory Solid Tumors as Palliative Care

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Background/Objectives: In contrast to chemotherapeutic agents that disrupt cellular replication, biological agents modulate molecular pathways essential for cancer pathogenesis. Different classes of agents, including tyrosine kinase inhibitors and monoclonal antibodies, have been shown to inhibit tumour growth, improve quality of life, and prolong survival. These agents have unique side effects, and are often more tolerable than chemotherapy because of their specificity. Because of their relatively favorable efficacy and side effect profile, there is currently heated debate in the adult oncology community about whether biological therapy should be continued in some patients until death, and whether patients with poor performance status are still eligible for treatment. There is still no debate or consensus in paediatric care.

Design/Methods: We describe the use of biological agents in the last months of life in advanced paediatric cancer patients admitted to our department in the last 20 months. Next generation sequencing was performed on all the children at the time of relapse. Eleven children received biological therapy as palliative treatment, mean time 80 days (15-364 days) Diagnosis was neuroblastoma in two children, Ewing sarcoma in two, osteogenic sarcoma in two, brain tumour in one, rhabdomyosarcoma in two children, Wilms tumour one. Mean age :10.5 years (4-19 years).

Results: No complication was observed except fatigue in one child. The most common drugs were mTOR inhibitor in eight patients, anti PD1 in three, Pazopanib in one pt, anti BRAF and MEK inhibitor in one. Six children died, three are currently alive with stable disease, and two are alive without disease.

Conclusion: The degree to which biological agents are being utilized near the end of life suggests the need to re-examine the risk/benefit profile of biological therapy for this population and the decision-making process around their use.

P-0908 | Safety of Procedural Sedation and Analgesia for Bone Marrow Biopsy by Paediatric Oncologists in the Paediatric Oncology Ward and Day Care Clinic

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Background/Objectives: Procedural sedation and analgesia (PSA) for diagnostic and therapeutic painful procedures for children with cancer is widely practiced in paediatric oncology units. However, its use is mainly limited to bone marrow aspirates and lumbar punctures. We present our experience with PSA for bone marrow biopsy outside the operating/intensive care room.

Design/Methods: Data from all consecutive patients sedated for diagnostic and therapeutic procedures in our paediatric oncology ward or day care clinic were retrospectively reviewed. Sedation protocol in our Unit is based on inhalation of 50% nitrous oxide/oxygen or intravenous atropine/midazolam/ketamine given as a fixed dose of atropine (0.01 mg/kg) and midazolam (0.1 mg/kg) and incremental doses of ketamine to achieve and maintain adequate sedation level. Continues variables were compared using the Anova test. P<0.05 was considered as statistically significant. Data were analyzed using SPSS 20.0.

Results: Between April 2015 and March 2016, 342 diagnostic and therapeutic procedures were carried out in 59 patients aged 4 months to 15 years. Forty one of them had hematolymphoid malignances and 18 solid tumors. Forty-three percent of the procedures were done in the paediatric oncology ward while 57% in the day care clinic. Intravenous atropine/midazolam/ketamine and inhalation of 50% nitrous oxide/oxygen were employed in 91% and 9% of procedures, respectively. Two hundred twelve (62%) sedations were indicated for lumbar puncture, 96 (28%) for bone marrow aspirate ± lumbar puncture and 34 (10%) for bone marrow aspirate & biopsy. Median dose of ketamine was 1.2 mg/kg (range: 0.5-2.9), 1.2 mg/kg (range: 0.4-2.8) and 2.9 mg/kg (0.8-7.6), respectively ($p=0.01$). No major complications were observed.

Conclusion: Atropine/midazolam/ketamine procedural sedation and analgesia for bone marrow biopsy can be safely carried out by paediatric oncologists and nurses in the paediatric oncology ward and day care clinic.

P-0909 | Palliative Care for Children in Onco-Haematology: Role of a Specific Home-Care Team

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Background/Objectives: Our home-care unit (HCU) is specialized for paediatric cancer patients (pts) and has a strong palliative care activity. We believe that the introduction of home-care services can influence the place for palliative care, for death and the length of hospitalization. We aimed at describing characteristics and care course of pts treated in our HCU, and tried to identify some factors contributing to home care at end of life.

Design/Methods: We conducted a retrospective, observational, monocentric study about pts in paediatric onco-haematology, treated at least one day in our home-care unit, who died between July 1st 2013 and December 31st 2015. Statistical analysis was descriptive and analytical.

Results: Out of 94 pts who died during study period, 74 were known by our HCU. 2 were lost for follow-up. 43/72 pts died at home. During the last 3 months of life, oncology pts have significantly less classical hospitalization, when compared to haematology pts ($P<0.002$). Further on, oncology pts were more likely to die at home than haematology pts ($P=0.015$). The implication of general physicians (GP), as well as the number of home visits of our HCU increases the possibility for home death ($P<0.001$ both). No significant association was found between ages at death, distance between home and hospital, other life conditions and place of death.

Conclusion: Our HCU has a strong palliative care activity and a high rate of children dying at home. Good collaborations between our paediatric onco-haematology team and our HCU as well as between our HCU and GP optimize palliative care. As the implication of GP at end of life care is important, a special and individualized training for such difficult tasks by our HCU seems beneficial and should be developed.

P-0910 | Intravenous Chemotherapy at Home : A Paediatric Monocentric Experience

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Background/Objectives: Since 10 years, our home-care unit (HCU) developed the management of intravenous chemotherapy (IV CT) at home. Established criteria are: presence of a central venous line, and some characteristics of the chemotherapy itself (minor side effects, short infusion or at contrary 24-hours infusion, no hydration needed, drug stability). For Cytarabine, Vinblastine, Vincristine, Topotecan, Irinotecan and Fluorouracil, our HCU sets up a delegation leading to IV CT administration at any child's home. Home IV CT is realized by home nurses and the general physician (GP).

Design/Methods: We conducted a descriptive study, establishing synthetic figures to explain our management.

Results: We identified 2 situations for home IV CT. 1/ the 1st day is realized during daily hospitalization, and further IV CT is conducted at home. 2/ Weekly CT are realized only at home. For both situations, our HCU team meets the patient's family to explain the safety of the whole procedure and answers to all their questions. HCU nurses identify home nurses with required competencies for administration of IV CT at home. Then, our HCU coordinates care schedules, meets and trains home nurses and GP. Concerning weekly CT, HCU physicians prescribe the course and biologic monitoring. GP checks the patient's clinical exam before injection, and sends his validation to the HCU. Home nurses collect lab exams and inject IV CT. IV CT is prepared by our hospital pharmacy, and delivered at home. For both situations, HCU checks lab exams, validates IV CT, manages home material and organizes hospitalization if needed. This organization allows about 250 home IV CT per year for more than 120 patients.

Conclusion: This kind of organization allows setting up home IV CT for more and more patients. It permits to limit daily hospitalization for some patients living far from the hospital, and whose therapies lead to several hospitalizations.

P-0911 | The Psychological Needs of Haematology and Oncology Patients in a Paediatric Palliative Care Perspective: Clinical Audit and Service Development in Ireland

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Background/Objectives: Palliative care for children with life-limiting conditions is an active and total approach to care, embracing physical, emotional, social and spiritual elements. The

main focus is on enhancing quality of life for the child and supporting the family during the illness and after death. The new Psycho-Oncology Standard of Care (Kazak et al, 2015) indicates that each child diagnosed with a Life-Limiting Illness in Oncology and Haematology should be offered psychological support. This study aims to review the psychological care received by Oncology and Haematology children referred to the Specialist Paediatric Palliative Care Team (SPPCT) in 2014 and 2015.

Design/Methods: The medical notes of all children referred by the Haematology and Oncology services to the SPPCT in 2014 and 2015 were reviewed as part of a clinical audit.

Results: Of the sixty-three patients referred to the SPPCT between 2014 and 2015, sixteen (25%) had met a clinical psychologist at least once during their cancer treatment and eleven (17%) received psychological interventions before they were referred to the SPPCT. Only three (1.9%) received psychological intervention after referral to the SPPCT. At the time of this review twenty-one children were still living with their terminal diagnosis. Of these, only one is currently receiving support from the psychology service. Of the forty-three children who have died the survival after referral to SPPCT ranged from 3 days to 14 months. Significant levels of psychological distress in many children were documented by the SPPCT.

Conclusion: According to our audit, levels of psychological distress were significant. Despite clinical guidelines, not all children were referred to psychology at the same time as referral to the SPPCT due to a lack of resources. Psychological services need to be expanded to meet the current need of Haematology and Oncology children with terminal illness and the recommendations of the Psycho-Oncology Standard of Care.

P-0912 | Atypical Presentation, Diagnostic Challenges and Outcome of Dengue Infection in Children with Cancer: First Large Report on An Important Challenge in Tropical Low-Middle Income Countries

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Background/Objectives: Dengue Infection has varied manifestations from minor self limiting illness to shock and is a common cause of morbidity in children in tropical countries. There is very little knowledge about its clinical presentation and outcome in immunocompromised patients with cancer.

Design/Methods: Aim: To study the clinical profile, diagnostics and complications in children with cancer with Dengue.

Materials and methods: 78 patients with Dengue fever in children ≤ 15 years with malignancies on active chemotherapy from September 2013 to September 2015 were retrospectively analysed.

Results: 61(78%) were males with mean age of 8.53 years (range, 1-15 years). 55(71%) patients had a hematolymphoid malignancy. Fever was the most common and universal presenting complaint. Flushing was seen only in 16(21%) patients. In all the patients, only NS1 antigen was positive and both IgG and IgM were negative. Haemoglobin and hematocrit were in normal range in majority (97%) of patients. Platelets on presentation ranged between $7-384 \times 10^9/L$ which steadily decreased to a range of $4-232 \times 10^9/L$ during the illness with mean period of recovery being 7 days (range, 1-20 days). Platelet transfusions were required in 36(46%) patients; of which 25(69%) were platelet refractory. Transaminits was common with mean AST and ALT values of 337 and 156 U/L respectively. Most common complication was ascites, which was seen in 23 patients(29%). The most serious complication was Hemophagocytosis(HLH) seen in 10(13%) patients. There were 5 deaths secondary to Dengue and two died of HLH.

Conclusion: In children with cancer presenting with fever, a high suspicion has to be kept for Dengue during Dengue endemic seasons as fever may be the only manifestation without classical symptoms. NS1 antigen should be used for diagnosis as antibody response is muted. Unlike general population, Hematocrit is normal and platelet refractoriness is common. HLH is a life-threatening complication and early diagnosis and timely use of steroids may be life-saving.

P-0913 | Like Being Covered in a Wet and Dark Blanket - Parents' Lived Experiences of Losing A Child to Cancer

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Background/Objectives: Purpose: The aim of this study was to illuminate parents' lived experiences of losing a child to cancer.

Design/Methods: Method: Interviews and written narratives about parents' experiences of losing a child to cancer were gathered from six parents of children whom had participated in a longitudinal study across the child's illness trajectory. The analysis of the data was inspired by van Manen's hermeneutic phenomenological approach.

Results: Preliminary Results: One essential theme emerged; *Like being covered in a wet and dark blanket*, as well as five related themes; *Feeling powerless and distressed*, *Trying to get ready for the moment of death*, *Continuing parenting after death*, *Working through the sorrow* and *Wanting to comprehend life into a new integrated whole*.

Conclusion: Conclusion: It is important that the healthcare staff is trained in communication strategies to be able to support the parent to have an open dialogue with the child about his or her impending death. There is a need for good palliative care. If not, there is a risk that the parent will persevere and blame themselves for not being a good parent during the suffering child's last time in life. After the child has died, the parents need support from the health care staff over a long period of time. Meetings with the parents six months and two years after the child's death might facilitate healing through the grief process.

P-0914 | Improving Influenza Vaccination Rates in Paediatric Oncology Patients and their Caregivers: A Quality Improvement Initiative

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Background/Objectives: Pediatric oncology patients are vulnerable to influenza and secondary bacterial infections. The influenza vaccine protects from influenza-related morbidity and mortality. People in direct contact with the child should also be vaccinated as an adjunct strategy to limit exposure. A 2015 survey at McMaster Children's Hospital showed poor uptake of influenza vaccine in patients and their parents (13/30, 43%). In order to improve vaccination rates, an educational pamphlet was developed and distributed, and the vaccine was made available in the oncology unit to patients in 2015-16. Objectives: To determine if vaccination rates improved in 2015-16; to better understand parents' decision-making around vaccination; and, to determine the perceived barriers to vaccination.

Design/Methods: Caregivers and healthcare providers (HCPs) in the oncology unit at McMaster Children's Hospital were surveyed in February 2016. Parents were invited for in-depth semi-structured interviews. Convenience sampling occurred until data saturation was obtained. The interviews were recorded, transcribed verbatim, and coded into categories and themes.

Results: The 2016 survey response rate was 67% (72/108). Data suggested an improvement in vaccination rates overall in 2015-16 with uptake in 58% (14/24) of patients, 58% (14/24) of parents and 50% (12/24) of siblings. Although 84% (40/48) of HCPs who responded felt the vaccine was important, only 75% (36/48) were vaccinated. A total of 20 qualitative interviews were conducted with parents. Findings revealed barriers to vaccination including lack of education and difficulty vaccinating younger siblings. Most parents were unaware of the impact of influenza on their child, and were confused about the reasons for vaccination. Despite receiving educational materials, myths and misconceptions about the vaccination were uncovered.

Conclusion: With improved parent education and accessibility, influenza vaccination rates improved by 15%. Offering the influenza vaccine in the hospital setting re-enforced its importance. Additional efforts are needed to maximize vaccination rates in children with cancer and their caregivers.

P-0915 | Nasogastric Tube Feeding in Children with Cancer as a Part of Palliative Care

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Background/Objectives: Many paediatric oncology patients lose weight because of their inability to consume adequate caloric intake orally. Poor nutrition is associated with malnutrition and poor prognosis of the disease. Thus nutritional support is an important element of palliative care. Enteral nutrition (EN) is the preferred method as long as if the gastrointestinal tract is functioning. We aimed to demonstrate whether EN is feasible in daily practice of these patients.

Design/Methods: Nutritional records of children with cancer treated between May 2011- Jan 2016 at Bezmalem Vakif University Pediatric Haematology and Oncology were evaluated. Patients with poor oral intake were fed with commercial use formulas by the oral route, by the nasogastric tube (NG) and by percutaneous endoscopic gastrostomy (PEG). Patients who lost weight under the support of oral route were fed by NG. Weight of the patients were checked at every week. Children with diffuse pontine glioma after losing gag reflex, were fed by PEG. No other patients had PEG.

Results: A total of 125 (81.6%) among 153 patients required nutritional support. Forty-eight (38.4%) of them were fed by oral route, 67 (53.6%) patients were fed by NG only. Ten (8%) DPG patients initially fed by NG had PEG later. Median duration of oral supplementation was 106 (68-154) days. Median duration of NG was 23 (7-96) days. All the patients other than DPG gained or maintained their weight. No major complication occurred in the patients.

Conclusion: Weight loss is an important problem in patients with cancer. Patients who lost weight under the support of oral route should be fed by NG. Palliative enteral feeding by NG tube is safe, inexpensive, and has a low complication rate. NG feeding, rather than PEG, could be a more appropriate method of enteral feeding in children with cancer.

P-0916 | Hyperhydration Alone as Prophylaxis for Tumour Lysis Syndrome (TLS) in Children with Acute Lymphoblastic Leukemia (ALL)

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Background/Objectives: TLS is considered a potential oncologic emergency. Guidelines for the prevention and management of TLS typically involve some combination of hydration, alkalinization, and hypouricemic agents. There is however a lack of published data addressing the best management for patients with low risk of developing TLS which includes many paediatric patients diagnosed with ALL.

Design/Methods: We reviewed the records of all patients diagnosed with ALL at our institution since 2010 to identify those managed without a hypouricemic agent. Data required to establish either laboratory or clinical TLS per the 2010 Cairo-Bishop definition [Br J Haematol, 149 (2010)] were collected. We reviewed lab values from 3 days prior to 7 days following the start of systemic therapy.

Results: Of the 195 patients diagnosed with ALL, 13 were not managed with allopurinol or rasburicase. 7 were hyperhydrated and alkalinized while the other 6 received hyperhydration alone. All 13 were diagnosed with B-Lymphoblastic Leukaemia. All but 1 were considered standard risk; the 13th was assigned high risk because of age. None developed either lab or clinical TLS. In fact only 2 of the 487 labs for the key components of the TLS (potassium, phosphorus, uric acid, creatinine) were even abnormal for age.

Conclusion: These results suggest there is a proportion of children with ALL for whom hyperhydration alone is sufficient and appropriate for the prevention of TLS. Given the incidence of ALL, this potential change in management could have significant financial implications for practitioners worldwide who care for this population of patients. When we project characteristics common to our 13 patients (WBC less than 50, age between 1 and 18, without hyperuricemia at presentation) onto our most recent population of patients diagnosed with ALL, we estimate that over half of them (38 of 70) could have been successfully managed in this way.

P-0917 | Parental Decision Making and Quality of Life in Children with Cancer

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Background/Objectives: This pilot study purpose to explore the family's parental treatment decision making and quality of life of having a child diagnosed with cancer in the hospital.

Design/Methods: The institutional review board at the hospital approved all study procedures. Research design using a In depth interviews and focus group discussions approach in was parents of children diagnosed with cancer in the hospital. Using a participant observation study approach for data collection and themes were uncovered from each interview data set and rigorous methods to data analysis. Record the data with the process recording in interview and participant observation. Data analysis by authors and parent.

Results: The cancer treatment decisions made by the parents while their hospitalized children are being treated for cancer mainly include choosing the appropriate hospitals and treatment process. There are four themes of the quality of life:

(1) Physiologically: Their sleep is disturbed due to the treatments of the children; They are more prone to feeling tired or catching a cold. (2) Psychologically: They are concerned about (a) the side effects of the treatments on the children, and (b) the children's emotional changes under the invasive treatments; Feeling guilty when the other children in the family are being neglected; Feeling difficult reconciling the demands of work and caring for the sick children. (3) The changes in everyday lives: The diets are mainly composed of self-grown food; Timely isolations in the home environments; Living in one's tribe. (4) Using the support system: The mutual support among husbands, wives, siblings, and paramedical staff.

Conclusion: It was expected that findings of the study could provide family members and paramedical staff be the positive force supporting the healing of children.

P-0918 | Healthcare-Associated Infections in Paediatric Cancer Patients. Results of a Prospective Surveillance Study at a Paediatric Haematology and Oncology Unit in Morocco

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Background/Objectives: Pediatric cancer patients face an increased risk of healthcare-associated infection (HAI), complications due to their underlying illnesses and intensive anti-cancer treatment. HAI cause considerable morbidity and mortality and are associated with prolonged hospital stay and increased health care costs.

To address this problem, the department of haematology and paediatric oncology implemented an infection control program in coordination with the Infection Control Committee (ICC) and surveillance of HAS as priority of this program.

Objective: to describe the incidence of HAI in paediatric cancer patients as the first step toward improving infection control policies.

Design/Methods: A prospective surveillance study was performed in the paediatric haematology oncology unit at a university hospital in Casablanca from January 2011 to December 2014. Centers for Disease Control and Prevention adjusted criteria were used. Data including extrinsic risk factors associated with HAI were recorded. HAI rates were calculated as a density incidence rate and device-associated infections were calculated for the specific site.

Results: The incidence of HAI ranged from 28 per 1000 patient-days on 2011 to 23 per 1000 patient-days on 2014. The median age was 10 years. The most frequent diagnosis of admission was acute lymphoblastic leukaemia when most infected patients were treated from acute myeloid leukaemia. Neutropenia at diagnosis correlated significantly with risk of HAI. 55, 7% were nosocomial fever of unknown origin. Blood stream infection (23%) and respiratory infection (14%) were the most frequent HAI observed, and these were associated with use of invasive device in 20% of cases. Gram-negative bacteria were the main pathogen (55%), gram positive cocci were responsible for 30% and candida for 11% of cases.

Conclusion: Surveillance of HAS is a priority of infection control program and the basis of elaboration and evaluation of others axes us hand hygiene and training protocols.

P-0919 | Hazards of Inappropriate Use of Pentazocine; Analysis of 10-Years Use of Pentazocine for Pain Control in Children with Cancer

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Background/Objectives: Pentazocine is a narcotic analgesics used before surgery or with general anesthetic, and also used to relieve moderate pain in adults. It has been used in paediatric pain management in Japan, because most paediatricians are not familiar with strong opioids. However, its efficacy and safety for children are still unknown.

Design/Methods: Consecutive uses of pentazocine by paediatricians for cancer patients younger than 20 years old, from January 2006 to December 2015 in our hospital were analyzed retrospectively. The analytical factors included patient's age, dosage, efficacy, side effects, and switchover to strong opioids.

Results: Pentazocine was used for 157 pain episodes that could not be controlled by NSAIDs in 67 paediatric cancer patients ranging in age from 1 to 18 years (median, 10 years old). Seventy-five pain episodes were from mucositis during chemotherapy/hematopoietic stem cell transplantation, 20 from disease, 13 from paralytic ileus, 10 from neuropathy as side effects of anticancer drugs, and 39 from other conditions. Pentazocine of 0.03–0.48 mg/kg/dose was administered intramuscularly or intravenously, and was repeated according to pain. Administration periods were from 1 to 57 days. The average administration periods were 6.28 days in mucositis, 5.4 days in pain from disease, 5.1 days in paralytic ileus and 4 days in neuropathy. Although pentazocine provided pain-killing effects, they were transient, of short duration and unstable. Switchover to morphine/fentanyl was done in 36 episodes. Side effects were observed in 21 episodes. (dizziness/staggering, nausea/vomiting, respiratory depression, perspiration, headache, hypotension). The rate of side effects was unrelated to administration period, and the onset was early phase of administration.

Conclusion: Pentazocine is a powerful and easy-to-use analgesics whose application should be limited to short duration pain. Education about strong opioids is critical to reduce inappropriate use of pentazocine in paediatric pain management.

P-0920 | Febrile Neutropenia in Paediatric Oncology Patients at Chiang Mai University Hospital: Treatment Scheme, Risk Factors and Outcomes

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Background/Objectives: Febrile neutropenia (FN) is associated with morbidity and mortality in childhood cancer patients. This study aimed to determine clinical characteristics including nutritional status, therapeutic approach and outcomes of children with febrile neutropenia.

Design/Methods: This prospective study enrolled patients with a diagnosis of FN at Chiang Mai University Hospital between July 2014 – June 2015. Intravenous empirical ceftazidime and amikacin were used for fever without localizing signs. Intravenous meropenem and vancomycin were used for hypotensive patients. For patients with localizing signs of infection, additional antibiotics were selected based on the judgment of attending physicians.

Results: A total of 139 febrile episodes occurred in 75 neutropenic patients, with a median age of 6 years (range, 0.4–14.1 years). 56% of patients were malnourished. Bloodstream infection was documented in 12 episodes (8.6%), with 10 microorganisms isolated. *Escherichia coli* (41.7%), *Pseudomonas aeruginosa* (8.3%) and *Acinetobacter baumannii* (8.3%) were the most commonly isolated organisms. There was no multidrug-resistant nor extended-spectrum beta-lactamases producing strain in this study. Malnutrition (body mass index z-score < -2.0) was not associated with bacteremia and mortality. Infection-related mortality was 2.9%. Risk factor for bacteremia was the presence of lower respiratory tract infection (odds ratio; OR = 13.7; 95% confidence interval; CI = 7.5 – 24.9, p < 0.01). Risk factors for mortality were documented hypotension and skin infection (OR = 132.0; 95% CI = 10.5 – 1667.1, p < 0.01 and OR = 12.5; 95% CI 1.6 – 98.4, p = 0.037, respectively). In multivariate analysis, hypotension was only significant risk factor for mortality in FN (OR = 1.66; 95% CI 1.56 – 1.75, p < 0.001).

Conclusion: Hypotension was the only predictor for death in patient with FN. Our treatment scheme for empiric treatment of FN was feasible with an acceptable mortality rate. There was high prevalence of malnourished patients but not associated with bacteremia and mortality.

P-0921 | Trends of Body Composition Changes During the First Year of Treatment for Childhood Cancer

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Background/Objectives: The aim of this study was to evaluate long-term changes of body compositions in paediatric cancer patients during the first year of cancer treatment.

Design/Methods: Thirty patients (mean age 10.9 ± 3.8 yrs; 21 boys, 9 girls; 19 hematologic malignancies, 11 solid tumors) and 30 controls were recruited. Whole body dual energy X-ray absorptiometry was performed at baseline and 1, 6, and 12 months.

Results: There were no significant differences in age, sex, weight, height, body mass index, abdominal circumferences, body fats, and most lean body masses at baseline among children with hematologic malignancies, those with solid tumors, and the controls. Total lean body mass significantly decreased during the first month and between 6 and 12 months (P = 0.008 & P = 0.000), although total mass did not change significantly. In contrast, total fat mass and total body fat percentage increased significantly (P = 0.000 & P = 0.002) during the first month, but there were no significant changes between 1 and 12 months. Changes in fat percentages during the first month of cancer therapy were significant both in the extremities and in the trunk (P = 0.000 & P = 0.000). Generalized estimation equations for the analysis of trends for changes in mean body fat percentages in each paediatric cancer group revealed that there were significant upward trends between baseline and those at 12 months in children with hematologic malignancies, but not in those with solid tumors.

Conclusion: Cancer treatment significantly causes the changes in body composition during the first year, especially during the first month after initiating treatment, resulting in a significant increase in body fat and a decrease in lean body mass, particularly in children with hematologic malignancies.

P-0922 | Reversible Motor Neuropathy with Conduction Block in a Child Receiving Vincristine

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Background/Objectives: Peripheral neuropathy is commonly associated with Vincristine use. This is typically a length dependent sensory neuropathy in adult patients. In children a non-length dependent motor neuropathy has been described which can result in loss of ambulation and pain. The mechanism of the neuropathy in children is not understood.

Design/Methods: We present the case of a 4-year old girl who developed a bilateral upper and lower limb motor neuropathy following 3 doses of vincristine.

Results: Weakness was associated with marked reduction in compound muscle action potential (CMAP) amplitudes in bilateral median and peroneal motor nerves suggestive of an axonal neuropathy. Genetic testing for hereditary neuropathy was negative. Complete functional recovery was observed over 7 months with restoration of CMAP amplitudes following discontinuation of vincristine.

Conclusion: The prompt reversibility of both clinical weakness and objective neurophysiological abnormality following discontinuation of vincristine has not been described in adults or children. Recognition of this unusual iatrogenic neuropathy in children and recognition of its natural history is important for paediatric oncologists. Although the mechanism of motor neurotoxicity is unclear, our findings provide evidence that motor inexcitability or conduction block may be implicated.

P-0923 | Use of Fungal Testing in Paediatric Oncology Patients in Nottingham Children's Hospital. Could in-House Testing Reduce Unnecessary Treatment of Children with Antifungal Agents?

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Background/Objectives: In patients presenting with febrile neutropenia, who remain febrile in spite of antibiotics, negative blood cultures and negative viral test results; current practice in our department is to send b-D-Glucan (BDG) and Galactomannan (ASPG) assays to exclude invasive fungal infection. Currently both samples are sent to another hospital for processing, causing a delay in results of 7–10 days. Some of these children are commenced on empirical treatment for fungal infection pending these results. The department currently uses liposomal Amphotericin B (AmBisome®), at a dose of 3 mg/kg, costing £98.63 per vial¹. We wanted to establish the potential cost-saving that a reduced turn-around time for these tests could be.

Design/Methods: All BDG and ASPG tests performed in the two-year period between June 2013 and June 2015 for patients under the care of our department were collated. These were then divided into 'patient episodes' using the electronic admissions records. Episodes with negative fungal results were assessed to establish whether the children received anti-fungal treatment. Using the Advanced Paediatric Life Support equations, weight was estimated, to estimate AmBisome dose and hence cost.

Results: A total of 177 BDG and 98 ASPG tests were performed. Of the children with no evidence of fungal infection on testing, 8 received empirical treatment whilst awaiting results. This totalled 52 days of therapy, with an estimated total cost of £9,369.85.

Conclusion: Although the number of children receiving unnecessary empirical treatment for fungal infection is relatively low, it still represents a significant cost burden. Additional to this, it also involves giving children another potentially harmful drug, increasing their chances of side-effects. A shorter turnaround time may reduce empirical treatment pending fungal results, and such bringing the test 'in-house' could represent a significant financial saving.

P-0924 | Current Practice, Attitudes and Suggestions for Improvement for the Sickkids Fertility Preservation Program (SKFPP): Lessons Learned from Implementing This Unique Initiative in Toronto

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Background/Objectives: Fertility Preservation (FP) is a vital consideration for anyone embarking on cancer treatment. The SKFPP has been in place since 2014 and offers 1) counseling by a dedicated nurse practitioner (NP) regarding fertility risk and the processes involved in cryopreservation of sperm and oocytes (> 100 consultations completed), 2) health care provider (HCP) education, and 3) knowledge translation. The aims of the current quality improvement study are to 1) determine the self-reported practice of FP among HCP, 2) to evaluate the impact of our program on the FP practices of HCP, and 3) to review suggestions made by HCP to improve SKFPP.

Design/Methods: An interview-based questionnaire was developed and implemented by a clinician independent of SKFPP, targeting 53 HCP in March 2016. Responses were collected related to FP disclosures, procedures, resources, and HCP attitudes regarding the SKFPP. Additional comments and suggestions for the SKFPP improvement were also sought.

Results: Among staff physicians (n=12), fellows (n=21), clinic nurses (n=9), NPs (n=7), and clinical associates (n=4), 40 (76%) regularly refer to SKFPP for consultation. Forty-eight (90%) HCP agree that their awareness of FP has been increased by the presence of the SKFPP. All (100%) agree SKFPP is a useful service and that SKFPP should continue to provide a consultation service. Suggestions for improvement include: 1) create on-line education modules and resources and 2) increase capacity among other clinic NPs to also be able to offer FP counseling and procedure organization. Cost of sustaining the program was also acknowledged.

Conclusion: HCP agree that SKFPP has increased FP awareness and knowledge, however, strategies to increase capacity among HCP along with regular education is required, especially to ensure sustainability. This information suggests that creating similar programs in paediatric cancer centers around the world can be of value to patients and providers.

P-0925 | Missing Narratives in Paediatric Oncology

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Background/Objectives: Illness narratives have become a “hot” topic in various disciplines, ranging from sociology, anthropology, feminism, and philosophy to medicine. This widespread interest is the result of the fact that many diseases have become chronic rather than acute conditions. In children, chronic illnesses are a rare occurrence. Still, worldwide 250 000 minors are diagnosed with cancer each year. Stories of children however are rarely ever studied.

The study aimed to complement the results obtained from a large qualitative study on the attitudes and motives concerning end-of-life decisions in paediatric oncology in Switzerland. Progressive cancer was often cited as a reason to enhance children’s role in the decision-making process, but it was also identified as one of the main reasons to exclude them out fear that it would affect their morale. To explore this tension further, this second analysis explored those seven cases that were considered to be palliative.

Design/Methods: The presented data come from a total of 7 sets of open-ended face-to-face interviews with paediatric patients with progressive cancer, their parents and attending oncologists. Arthur Frank’s dialogical narrative analysis was chosen to analyze the data.

Results: The possibility that the child could die was integrated in either chaos or restitution narratives. This means that it was either ignored or contemplated as a possibility, but then immediately pushed away. Except for one patient, children never directly addressed the topic of death.

Conclusion: The way in which death was presented in the participants’ stories raises important questions about the larger social discourse on death as a final life project. This discourse not only constrains the way in which children and adults can relate to the minor’s death, it also constitutes an obstacle to children’s participation in decision-making.

P-0926 | Paediatric Palliative Care: Aligning Guidelines and Medical Practice

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Background/Objectives: Due to advances in the world of medicine, the number of children with life-limiting and life-threatening illnesses has increased steadily. In response to these changes within paediatrics, various guidelines have been published to direct the development and implementation of paediatric palliative care (PPC). Although the concurrent administration of curative and palliative care is the recommended approach, timely referral of paediatric patients remains problematic. The aim of the literature review was to identify studies on PPC guidelines in order to identify (1) barriers to their adherence and (2) recommendations for their adequate implementation.

Design/Methods: A systematic literature review was completed by searching the following online databases (between 1960 and 2015): Scopus, PubMed, PsycInfo, Web of Science, CINAHL and LexNexis. No restriction was placed on the type of methodology.

Results: Commonly reported barriers to PPC within the clinical practice are: cure-oriented culture, lack of training, inadequate communication skills of healthcare staff, limited financial resources, time pressure and prognostic uncertainty. More recent articles also address the problem of definitional clarity of PPC and hospice/terminal care as a major obstacle to proper implementation of PPC guidelines. Common cited recommendations include: education of healthcare staff and formation of a multidisciplinary PC team. Only a few articles focus on shortcomings in the guidelines, such as conceptual confusion, lack of clear referral models, and guidance on how to establish a multidisciplinary team.

Conclusion: The proper implementation of palliative care for paediatric patients requires a critical assessment of both research guidelines and medical practice. More empirical research is needed on the functioning of multidisciplinary research teams, on the benefits of early integration of PPC and on families’ and physicians’ perception of PPC.

P-0927 | Olanzapine for Chemotherapy-Induced Nausea and Vomiting (CINV) Prophylaxis in Children: A Multi-Centre Feasibility Study

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Background/Objectives: This study evaluated the feasibility of a single-armed trial of olanzapine to improve CINV control.

Design/Methods: Children <18yrs old receiving CINV prophylaxis with ondansetron/granisetron/palonosetron ± dexamethasone ± aprepitant were eligible to participate in this prospective, single-arm, open-label study. All patients received olanzapine (0.14mg/kg/dose; max: 10mg/dose) once daily orally starting before the first chemotherapy dose and continuing for up to 4 doses after the last chemotherapy administration. Vomiting, retching and nausea severity (assessed by children) were recorded. A future trial was considered feasible if: 15 patients were enrolled within 36 months (cumulative across 3 sites); 12 or more patients took ≥50% of the olanzapine doses and if ≤3 patients experienced significant sedation despite dose reduction. The proportion of children who experienced complete CINV control (no nausea, vomiting, or retching and no use of breakthrough antiemetic agents in the acute phase) was described. Changes in body weight and plasma glucose, AST/ALT, prolactin, and triglyceride concentrations were recorded.

Results: Fifteen patients (median age: 11.7yrs; range: 4.1-17.4) were enrolled over 38 cumulative months across 3 sites. All took ≥50% of olanzapine doses. Sedation was reported in 6 children prompting olanzapine dose reduction (N=5) or bedtime administration (N=1). Olanzapine was stopped in a child with blurry vision probably associated with olanzapine and in

another with unrelated increased GGT values. Hyperprolactinemia (N=1) and hypertriglyceridemia (N=2) were observed at the end of the olanzapine course. No changes in body weight or plasma AST/ALT concentrations were observed. Two children receiving highly emetogenic chemotherapy (HEC) experienced complete CINV control (2/10); 8 (HEC: 6/10; moderately emetogenic chemotherapy: 2/5) experienced complete vomiting control.

Conclusion: It is feasible to perform a trial of olanzapine for CINV control in children. We now will proceed to a randomized double-blinded trial. Our findings will inform the design of this future study.

P-0928 | Chemotherapy-Induced Nausea and Vomiting (CINV) in Children Receiving Intrathecal Methotrexate (IT-MTX) with or Without Vincristine

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Background/Objectives: This study describes the prevalence of anticipatory, acute and delayed phase CINV in children receiving IT-MTX during maintenance therapy of acute lymphoblastic leukaemia.

Design/Methods: Children (4-18 years) about to receive IT-MTX were eligible to participate in this prospective, observational study. Children received anti-emetic agents as prescribed by their clinical team. Nausea severity (patient-assessed), timing of emetic episodes, and administration of anti-emetics were recorded in a diary beginning immediately prior to IT-MTX administration, for the next 24 hours (acute phase), and a maximum of 7 additional days (delayed phase). Complete CINV control was defined as no emetic episodes and no nausea.

Results: 100 patients consented to participate in this study; data are available for 70 children (mean age: 8.3yrs; range: 4.1-17.6; 51 boys). 66 children (94%) received propofol-containing anesthesia for IT-MTX administration. Most (61/70; 87%) received a 5-HT3 antagonist for CINV prophylaxis prior to IT-MTX; 9 received no anti-emetic. Four children (6%) had anticipatory vomiting and 12 (17%) had anticipatory nausea. During the acute phase, 36 children (51%) experienced complete CINV control, 67 (96%) experienced complete vomiting control and 36 (51%) experienced complete nausea control. Severe acute nausea was reported by 12 children (17%). In the delayed phase, 36 children (51%) experienced complete CINV control, 60 (86%) experienced complete vomiting control and 37 (53%) experienced complete nausea control. Severe nausea was reported in the delayed phase by 26 (37%) children.

Conclusion: Although most children who receive IT-MTX and prophylaxis with a 5-HT3 antagonist experience complete acute and delayed vomiting control, nausea control is poor and severe nausea is reported by a large proportion of these children. New interventions to control nausea in children receiving maintenance chemotherapy are needed.

P-0929 | Mortality in a Paediatric Haematology Oncology Center (Rabat, Morocco)

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Background/Objectives: 72% of cancer deaths occurred in low-income and middle-income countries, where, although there is a lower incidence of cancer than in high-income countries, survival rates are also low.

The objective of this work is to study mortality and define the characteristics of patients dying in service of paediatric haematology and oncology of the child hospital in Rabat, including causes and modes of death.

Design/Methods: This prospective, descriptive, epidemiologic study was performed between July 2014 and June 2015. All patients who died in the hospital between these dates were included. were excluded patients with benign blood diseases and those who have not been treated in our center.

Results: A total of 89 children were studied. The sex ratio was 1.02. Seven percent of deaths took place in our service, six percent in intensive care and other forty Seven percent at home.

According to age groups and gender the majority of deaths (53 Children) occurred between 0 and 5 years with 28 girls and 25 boys, between 12 and 18 years, 7 deaths were recorded in girls and 13 in boys, and between 6 and 11 years 9 girls and 7 boys died. Depending on the type of tumour leukaemia accounted for 48.31%, followed by neuroblastoma with 18% and lymphoma with 11.23%, 7.86% of CNS tumors, 3.37% of Malignant germ cell tumors and 11.23% other tumors. Analysis of modes of death revealed that the most common causes of deaths were deaths followed by complications related to the disease with 28%, the death from toxicity of chemotherapy accounted 27%, the death of tumour progression accounted 24% and 21% of deaths were caused by tumour relapse.

Conclusion: The Deaths occur almost as much in hospitals and at home, the most common cause of death is complications related to the disease.

P-0930 | The Oncology Family App, An Electronic Mobile Application Providing Families with Cancer Care Information at their Fingertips

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Background/Objectives: To assist families navigate the complexities of their child’s cancer care, ‘The Oncology Family App’, an electronic mobile application (app) was released in November 2015 by the Queensland Paediatric Palliative Care, Haematology and Oncology Network (QPPHN). The app is freely available on mobile devices such as computer tablets and smart phones.

Design/Methods: The development of the app was informed by valuable input and suggestions from consumers as to features most useful for families.

6 family caregivers of a child with cancer tested the app during development before it was refined and formally rolled out.

The app was designed to provide key information for families, including:

- an emergency management plan (what to do in response to clinical signs and symptoms.)
- a state-wide directory of 24 hour contact phone numbers; non-emergency contacts; hospital address details and maps to the nearest QPPHON hospital.
- table to record blood counts.
- the ability to record appointments and allied health contacts.
- free text allowing a personal medical 'diary'.
- resources list.
- ability for consumer feedback.

Results: During the first 3 months after the release, 306 downloads were recorded with feedback obtained using a survey in the app. Statements from families include: "The app is a must-have for all paediatric oncology families" and "I hope my teenager will take more responsibility in their care and use it too".

Conclusion: The app will continue to be refined and developed, with a second phase planned to include: evidence based resources in a 'book shelf' format; the improved ability to set appointment reminders and the ability to synchronise multiple devices in the same household.

The app has the potential to improve the experiences of oncology families through easy and immediate accessibility to clinical information on their mobile device.

The app can be customised for other health facilities, leading and informing future technology for oncology families internationally.

P-0931 | Bridging the Gap between Treatment and End of Life for Paediatric Patients with Cancer

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Background/Objectives: Nationwide Children's Hospital is the largest children's hospital in the United States. Our Psychosocial Oncology Team developed a model of care to significantly enhance care for dying children. The model embodies a collaborative approach with integration of medical, psychosocial, and palliative care services that allows for comprehensive, coordinated, and integrated programming. This model seeks to assess and treat emotional and symptom burden, facilitate communication, and provide anticipatory guidance and support to patients/families, while also facilitating staff communication and support.

Design/Methods: Our program addresses specialized needs of dying children in a collaborative team approach. Patients are assessed and treated via a comprehensive psychosocial team of providers that include: psychologists, social workers, child life specialists, pastoral care, art, music, massage, and therapeutic recreation therapists. Anticipatory grief support is facilitated by ongoing relationships focused on continuity of care, medical decision-making, care conferences, and end-of-life conversations. We assist with patient/family communication with family-centered rounds, advanced care planning, and legacy building. Palliative/Oncology Rounds, team huddles, documentation, and death notification protocols were developed to improve staff communication. Additionally, we provide support for staff following patient deaths through debriefings/remembrances.

Results: In large programs with multiple providers, it is often challenging to know who is providing specific services, while ensuring that families are receiving the care they need during a time of increased stress, sadness, and overwhelm. By increasing communication between and within teams, we are better able to: ensure support, enhance/streamline services, and delineate which staff are providing services.

Conclusion: The Psychosocial Oncology Team at NCH has improved communication among medical, psychosocial, and palliative team members to enhance opportunities and provide support around a child's death. In a field with a high level of burnout and stress, open communication and support among team members can serve to enhance the well-being and service provided to patients, and also reduce staff distress.

P-0932 | Financial Burden for Caregivers of Paediatric Oncology Patients in Kumasi, Ghana

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Background/Objectives: More than 80% of children with cancer live in low and middle-income countries (LMIC) where cure rates are significantly lower compared to high-income countries (HIC). Less than one-third of children with cancer in developing countries receive treatment and almost half of children diagnosed with cancer in Sub-Saharan Africa abandon care. The financial burden for caregivers may contribute to treatment delays and abandonment in developing countries. This study aims to evaluate the financial burden of care and identify specific barriers to care for paediatric cancer patients in Kumasi, Ghana.

Design/Methods: We administered a survey to 51 caregivers of paediatric oncology patients at Komfo Anokye Teaching Hospital (KATH) in Kumasi, Ghana. Measures included average annual income, distance from the family's residence to KATH, cost of travel to KATH, number of missed work days due to their child's illness and perceived burdens of having a child with cancer.

Results: The average household income among the participants was \$3,106 with 72% supporting five or more people. Half of caregivers had to quit work or change jobs because of

their child's illness. In the first 6 months following the diagnosis, 33% missed 15 or more days of work due to their child's illness. Approximately 50% of participants live >2 hours from KATH such that 22% of participants missed two or more days of work for each clinic visit. The majority (93%) reported a lack of money as the biggest challenge to getting their child to the hospital and 95% reported 'financial burden' as the single greatest difficulty to having a child with cancer.

Conclusion: Financial burden is a major obstacle to seeking and continuing care for a child with cancer in Kumasi, Ghana.

P-0933 | Parents' Perceptions on the Participation and Capacity of the Adolescent with Cancer to Make Decisions in End of Life

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Background/Objectives: The diagnosis of incurable cancer in an adolescent has a disruptive effect on the entire family dynamic with fear and uncertainty dominating the lives of those who have to accompany the adolescent toward the end of life: the parents. In the face of the inevitability of death decisions need to be made revealing a complex and disturbing process. Given the paucity of studies on this phenomenon it became pertinent to do this study, having as starting point the research question: *How do parents of adolescents with cancer view their participation and capacity to make decisions at the end of life?*

Design/Methods: This investigation was conducted in Lisbon, Portugal, using the methodology of *Grounded Theory*. Participants were selected by theoretical sampling and included 12 parents of adolescents who had been detected as having progression of disease without the possibility of curative treatment; it also included parents whose child had already died due to cancer. A semi-structured in-depth interview was used and the data was analysed following the steps of the methodology stated. The computer program for qualitative data NVivo10 was also mobilized.

Results: "Deciding on behalf of my son" was the core category that emerged from the data. This category consists of three major categories intertwined in the *continuum* that is the end of life and were identified as **containing the news, integrating the news in their lives and awareness of the inevitability of death.**

Conclusion: Behavioural patterns common to parents of adolescents with cancer at end of life were observed and most parents were unanimous in not addressing the incurability of the disease or the inevitability of death with their sons/daughters, thus deciding for them and to them what they consider to be the best decision.

P-0934 | Improving Time to Antibiotics for Paediatric Oncology Patients with Febrile Neutropenia by Applying Lean Process Improvement Methodology

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Background/Objectives: The standard time to administration of antibiotics (TTA) at presentation with febrile neutropenia(FN) is 60 minutes. A retrospective study by the Atlantic Provinces Pediatric Haematology and Oncology Network (APPHON) reported this standard was not always met in our tertiary care emergency department (ED). Median TTA was 99 minutes (interquartile range [IQR] 72-132).

To analyze the process for patients with FN presenting to the ED using lean methodology.

Design/Methods: Lean methodology identifies "process wastes" and defines value and non-value added steps based on 5 phases: Define, Measure, Analyze, Improve, and Control. The then current FN process was mapped with stakeholders (physicians, nurses, lab personnel, ward clerks, pharmacists), led by a lean methods expert, to create a current state value stream map (VSM). This was analyzed to identify "process wastes" and root causes. A future state VSM was implemented based on these identified wastes. One year later, stakeholders reassessed the future state VSM.

Results: Types of wastes identified were categorized as over-processing, defects, skills, and waiting. Changes implemented included patient education regarding FN management in the ED, adding patient specific FN information to the electronic medical record, 1 nurse to access central venous access device immediately, and administering antibiotics after 45 minutes if the absolute neutrophil count (ANC) was still pending. After implementation, 49 patients presented with fever and 20 of them were diagnosed with FN. The median TTA improved to 59.0 minutes (IQR 38.3-78.8). Five patients received a dose of unnecessary antibiotics because the ANC was not available 45 minutes after presentation.

Conclusion: Lean methodology successfully identified root causes and improvement solutions to facilitate rapid administration of antibiotics to patients with FN improving the median TTA to less than 60 minutes. We plan an annual reassessment of the process to ensure this quality outcome measure is met.

P-0935 | Anti-Mullerian Hormone Levels Prior to Ovarian Tissue Cryopreservation are Lower in Girls Who Have Received Chemotherapy

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Background/Objectives: Anti-mullerian Hormone (AMH), a hormone produced by the granulosa cells, is an indirect marker of antral follicle counts and thus ovarian reserve. Levels

rise in childhood and adolescence, then peak in a woman's early 20s before declining to menopause. Interest in its use as a measure of ovarian reserve to measure the gonadotoxic effect of chemotherapy/radiotherapy is growing, especially for children in whom follicle stimulating hormone and inhibin B are not useful. We aimed to examine pre-procedural AMH levels in a female pre- to post-pubertal paediatric oncology population proceeding with oophorectomy for the purpose of ovarian tissue crypreservation (OTC).

Design/Methods: We reviewed our data on AMH in girls undergoing OTC at Ann & Robert H. Lurie Children's Hospital of Chicago from March 2011-March 2016. The OTC protocols were approved by the Institutional Review Board.

Results: 34 females aged 1.9-20.5 years (mean 11.4 years, median 12.2 years) underwent OTC. Four had non-malignant diagnoses while 33 had malignancies. Three did not have AMH levels checked. Data from 1 patient with Turner syndrome (45XO/46XY) was suppressed. Mean AMH in the remaining 30 patients, was 1.19 ng/mL (median 0.61, range <0.03-5.68). For the 10 subjects who had no prior therapy (mean age 9.8 years, range 3.7-16.8 years), mean AMH was 2.32 (median 1.76; range 0.2-5.68). For the 19 subjects who had received chemotherapy prior to OTC (mean age 11.6 years, range 1.9-20.5), mean AMH was 0.34 ng/mL (median 0.19; range <0.03-1.25). Of these, only 1 had previously received therapy that was considered highly gonadotoxic, although 14 received alkylating agents.

Conclusion: AMH was lower in girls who had prior chemotherapy, despite being slightly older than those who had no prior treatment, suggesting that chemotherapy, regardless of gonadotoxicity, may have some effect on ovarian reserve.

P-0936 | Indication of Enteral Nutritional Therapy for Paediatric Oncologic Patients: Single Center Experience

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Background/Objectives: Anorexia and weight loss are among the most common symptoms and signs in cancer patients. In cases of low oral intake, there is indication of enteral Nutritional Therapy (ENT). The aim of the study is to evaluate the indications of ENT in a specialized Oncology Nutrition outpatient clinic.

Design/Methods: Retrospective observational trial. Data charts of all patients attending our outpatient Oncologic Nutrition clinic over one month period were retrospectively reviewed.

Results: Twenty five patients and adolescents aging 1 to 15 years and under ENT were included. Their main oncological diagnoses were: Central Nervous System (CNS) tumors (72%), neuroblastomas (8%), leukaemia (8%), rhabdomyosarcoma (8%) and retinoblastoma (4%). Indications for ENT were: deglutition disturbances (48%) and moderate or severe nutritional impairment (36%), weight loss (8%) and inappetence (8%). All patients with deglutition disturbances carried CNS tumors.

Conclusion: CNS tumors were the main underlying neoplasms in patients undergoing ENT, possibly due to the fact that these patients receive concomitant chemo and radiotherapy, which may lead to inappetence and deglutition disturbances, depending on the irradiated area. The main indication for ENT was deglutition disturbances, which only occurred in patients with CNS tumors.

P-0937 | Period of Fasting by Paediatric Oncologic Patients Submitted to Radiotherapy Under Sedation and Complaints Related to Irritability and Sense of Hunger

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Background/Objectives: Radiotherapy is usually a short procedure, but the patient has to lie still and cannot be accompanied. Some children have difficulty in being still, and the use of sedation is necessary. To sedate these patients in our hospital, it was established an eight-hour fast before the procedure. The aim of the study is to find out the period of fasting done by the paediatric patients, submitted to radiotherapy under sedation and their main complaints related to humor and sense of hunger during this period.

Design/Methods: Restrospective analysis of patients attending the outpatient Nutrition Clinic of a Specialized Oncology Center.

Results: Twenty-three patients, ranging from 3 to 13 years old, were evaluated. Among the main diagnoses there were the tumors of the central nervous system, rhabdomyosarcomas and Wilms Tumour, and the head/neuroaxis and abdomen were the most relevant irradiated places. The average number of sessions were 20.5 ranging between 8 and 33 sessions. Regarding the nutritional diagnosis based on body mass index during the radiotherapy, 56.5% of patients presented eutrophy, 35% thinness and 8.5% obesity. The real period of fasting was an average of 14 hours, considering the time of the last meal before the procedure until the patient was released to eat. The most frequent complaints were irritability (69.5%) and irritability with sense of hunger (17.4%).

Conclusion: Despite all the new recommendations, the shortening of the period of fasting is still challenge as it entails breaking paradigms. The described complications related to a long period of fasting are based on the need to set specific protocols to shorten the period of fasting in paediatric oncologic patients. The use of the strategy to shorten the period of fasting can provide benefits to these patients with regard to nutritional status, resulting in a relief from the complications and an improvement in the quality of life.

P-0938 | Working Without Words: Where Music, Teather, Meditation, Laughter and Magic Can Reach

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Background/Objectives: In health education, particularly in the paediatric oncology setting, there are few multidisciplinary courses from other disciplines such as music or theater that may be used to contribute to improving communication among professionals, patients and families.

We present the training program of workshops of "Communication and negotiation skills with paediatric patients", developed by a multidisciplinary cooperation in which the following have participated: paediatricians, actors, musicians, and hospital clowns.

Design/Methods: The courses have been carried out for paediatricians in training (residents) and "clowns-residents" in training, psychologists, nurses or social workers. These courses use different resources (theater, cinema, music, and clown performance and magic) as conductive elements on training in the skills of communication among patients, families and medical staff.

Results: We will show videos with material from the workshops.

- Theater: works of stage presence, space, diction, modulation

- Film: viewing and discussion of ethical issues and communication

- Videos made by patients-actors

- Clown: work body language. Games with children as a communication for the paediatrician

- Magic: learning example of magic tricks for paediatric residents by paediatric age groups

- Music: musical repertoires with a focus not only on musical training but also music therapy and suitability of the material at different ages. Working improvising songs, working with special groups of children in palliative care

- Meditation: introduction of mindfulness

Conclusion: This multidisciplinary approach enriches the possibilities of mutual cooperation and training among medical staff and other art professionals working with paediatric oncology patients. This program is included as part of the training of paediatric oncology staff.

P-0939 | Micafungin Every 48 Hours as Antifungal Prophylaxis in Paediatric Patients. Measurement of Plasma Levels

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Background/Objectives: To evaluate the effectiveness of micafungin administered a 3-4mg/kg every 48 hours in children who are at high risk for developing infection fungal disease (IFD).

Design/Methods: Prospective unicenter study including children undergoing allogeneic hematopoietic stem cell transplantation (HSCT) in whom antifungal prophylaxis was indicated. Micafungin was administered once daily by intravenous infusion over at least 60 minutes at a dose of 3-4mg/kg/48h. The concentration of micafungin in plasma was determined by a modified validated high-performance liquid chromatography (HPLC) assay. Blood samples for trough concentrations were drawn immediately prior to micafungin infusion. Children were excluded if they had a history of previous fungal infection. Liver and renal function were monitored every week.

Results: A total of five children aged 1.4 to 9 years with a median age of 4.8 years were included. During the study period, 23 trough concentrations of micafungin were measured. Overall, 17/23 of the trough concentrations were > 150 ng/mL. Only 6/23 plasma concentrations were <150 ng/mL, all of them determined in two patients who had a body weight of 14.7 and 14.3 kg respectively. Proven, probable or possible breakthrough IFD did not occur in any of the patient. No adverse drug reactions were observed.

Conclusion: Micafungin administered every 48 hours at dosages of 3-4 mg per kg could be a convenient, safe and efficient alternative for antifungal prophylaxis in children at high risk for IFD.

P-0940 | Risk Factors for Psychosomatic Symptoms in Patients with Paediatric Cancers

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Background/Objectives: With increasing survival rates in paediatric malignancies, the quality of life of children during hospitalization should be given more attention. Previous studies showed more than one-third of children with malignancies develop psychosomatic symptoms (PSS) during treatment, but there are few reports evaluating the risk factors for PSS. We aimed to identify factors associated with PSS that required pharmacological intervention among children hospitalized for treatment of malignancies.

Design/Methods: We conducted a retrospective cohort study comprising 190 patients aged 2 to 18 years old. They were diagnosed with malignant diseases and admitted for treatment at St. Luke's International Hospital between July 2003 and July 2013. Patients were considered as having PSS if they were prescribed psychotropic agents during hospitalization. Demographic and clinical characteristics were evaluated with respect to development of PSS.

Results: Of the 190 patients, 56 (30%) were prescribed psychotropic agents for PSS. Types of PSS included insomnia in 21 (38%), anxiety in 11 (20%), psychogenic nausea in 9 (16%), agitation in 6 (11%), delirium in 5 (9%), and depression in 4 (7%). The most prescribed psychotropic agents were etizolam for 34 cases (61%), followed by diazepam for 9 cases (16%) and risperidone for 6 cases (11%). Bivariate analysis showed PSS to be associated with informing patients about their disease, hematopoietic stem cell transplantation (HSCT), older age at the first admission and opioid use. The multivariable analyses confirmed statistically significant independent associations for HSCT [OR, 2.76; 95% CI, 1.07-7.12], older age [OR, 1.13; 95% CI, 1.04-1.23], and opioid use [OR, 3.76; 95% CI, 1.33-10.6].

Conclusion: Older age at the first admission, undergoing HSCT, and those given opioids were found to be risk factors for PSS among children with malignancies. This study suggests

appropriate preventive measures against PSS are warranted for these patients. To confirm our results, prospective studies may be informative.

P-0941 | Challenges in Inter-Professional Care Coordination

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Background/Objectives: Advances in medicine have led to life-sustaining treatments for diseases sustaining life for extended periods even when cure is not possible. It is often difficult to maintain clarity and alignment among teams of providers in the context of critical illness. This session will present inter-professional challenges that can arise when Haematology/Oncology and Critical Care Medicine providers collaborate in the care of seriously ill children and a collaborative clinical conference to address underlying factors.

Identify three key challenges to inter-professional collaboration.

Evaluate the effect of difficulties in collaboration on delivery of care.

Examine threats to quality and safety when collaboration fails.

Design/Methods: Multiple focus groups comprised of physicians and nursing staff from both sections identified prototypical challenges of coordinating care for medically complex children with cancer across care settings in a hospital. Sessions were recorded, transcribed and reviewed for pertinent themes which informed the development of a structured collaborative care conference intervention. Three collaborative conferences using mock clinical cases were conducted to refine the intervention.

Results: Challenges identified display obvious commonalities centered around communication, professional roles and managing end of life issues. The shared reasons and strategies form the basis for a collaborative conference design as well as systemic changes in the operations of the two sections to improve shared care of patients. Results of three mock clinical cases using our collaborative conference intervention provided validation of the focus group findings and offered further insight into factors that contribute to challenges in collaborative care.

Conclusion: Providers seem to operate with understandable but divergent group ideologies that condition their views of illness trajectories, technologies, and relationships with patients and families. Initial outcomes from mock clinical cases demonstrate that a facilitated collaborative approach to communication and care planning has the potential to address inter-professional challenges in care planning for critically ill children.

P-0942 | Aprepitant used for Prophylaxis of Nausea and Vomiting Duo to High Dose Cisplatin Treatment in Adolescence Period

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Background/Objectives: Chemotherapy-induced nausea and vomiting significantly impairs patients' nutrition status, daily activities, briefly quality of life. Although is a neurokinin-1 receptor antagonist. Although it has been replaced in the adult guidelines its use in children is not yet widespread. In this study, patients administered aprepitant were analyzed retrospectively for the impact-side effect profile, performance status before and after the chemotherapy.

Design/Methods: From August 2011, 67 cycles of chemotherapy including high-dose cisplatin and aprepitant were applied to 31 patients over 10 years of age. These patients were compared with the patients over 10 years of age, treated with the same chemotherapy protocols between January 2009 and July 2011 without aprepitant, in terms of number of vomiting. Aprepitant was applied 125 mg on day 1 and 80 mg on day 2-3, one hour before chemotherapy in addition to granisetron and dexamethasone. Granisetron and dexamethasone were given 30minutes before chemotherapy in the control group. Lack of nausea and vomiting was accepted as "complete response", vomiting number 1-2 as "major response" and 3-5 as "minor response". Symptoms and activities before and after chemotherapy was investigated by using "symptom-distress scale" and "play performance scale".

Results: In the control of acute emesis 39% complete response, 54% major response, 4% minor response and in the control of delayed emesis 27% complete response, 52% major response, 13% minor response was obtained. Control of both acute and delayed emesis in aprepitant group was statistically better than control group ($p1 \leq 0.001$, $p2 \leq 0.001$). The most common side effects were rash (37%), hiccups (34%) and dry mouth (33%) respectively. It was observed that feeling good condition and appetite distorted, fatigue increased, performance status decreased according to symptom-distress scale and play performance scale before and after treatment.

Conclusion: Aprepitant significantly reduces chemotherapy-induced nausea and vomiting when high-dose cisplatin administered during adolescent period. Side effects are minimal and can be controlled.

P-0943 | Antibiotic Lock and Systemic Infusion of Linezolid for the Salvage Treatment of Persistent Catheter-Related Infection in Children with Cancer

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Background/Objectives: Initial colonization of central venous catheter (CVC) by *Staphylococcus aureus* and coagulase-negative staphylococci is followed by development of a biofilm structure, where the organisms are encased and protected in a polysaccharide matrix. This protection results in failure of intravenous antibiotic treatment and removal of CVC. Antibiotic lock therapy (ALT) is an alternative to catheter removal. Linezolid is a protein synthesis inhibitor and is active against gram-positive microorganisms. In vitro studies showed that linezolid has greater efficacy and speed in eradicating microorganisms from biomedical devices.

In this study we documented our treatment results of ALT with linezolid in paediatric cancer patients.

Design/Methods: In 2015, seven patients were treated with 10 courses of systemic and ALT with linezolid as a second line therapy after failure of systemic and ALT with vancomycin or teicoplanin. In patients with ongoing fever after 48-72 hours of first line treatment and in patients with positive blood cultures of 3rd day, second line therapy with linezolid was started. Linezolid treatment was administered both, systemic (IV, 10mg/kg t.i.d.) and catheter-lock (2mg/ml every 24 hours) for ten days. Blood cultures on 3rd day and 48 hours after completion of treatment were taken.

Results: The median age of the patients was 4,3 years (2,5-17) with the diagnosis of acute lymphoblastic leukaemia(n:4), rhabdomyosarcoma(n:2), Ewing sarcoma(n:1) and Wilms tumour(n:1). Before treatment, blood culture results revealed *S. epidermidis* in six patients and *S. hominis* in four patients. Microbiological eradication was achieved in all cases and CVCs were preserved in all cases after therapy was discontinued with a median time of follow up of 11 months (7-15). No side effects and no resistant organisms were recorded with the use of linezolid ALT.

Conclusion: Linezolid appears to be a safe and effective ALT, preventing catheter-related bloodstream infections and prolonging the survival of the CVC in paediatric cancer patients.

P-0944 | Logistical Plan for Deploying Healthcare Providers Abroad – Texas Children's Cancer and Haematology Centers's Experience

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Background/Objectives: Eighty percent of annual paediatric cancer incidence occurs in resource-limited setting with only ten to forty percent survival. Since 2007, in order to alleviate the shortage of paediatric hematologists and oncologists in Africa, Texas Children's Cancer and Haematology Centers (TXCH) has placed full and part time experts in Africa. These experts provide care and treatment to children affected by cancer and blood disorders and build local healthcare professional capacity. Our experience demonstrates that a structured onboarding process and ongoing programmatic support has been key to the success of this program.

Design/Methods: All expatriates were recruited through careful review of their qualifications and credentials, and structured multi-disciplinary interviews with hospital leadership, psychologist, medical professionals, and program managers.

The onboarding process was coordinated with local in-country NGO's to obtain work visa, medical licensing, and housing. Expatriates received two- to four-week orientation in Houston prior to their assignment in Africa to clarify their roles and mission, reinforce program ownership, and align expectations with the global program leadership team. Physicians received benefits specifically designed to meet their expatriate needs.

Finally, ongoing communication with expatriates was maintained during their placement in Africa through weekly teleconferencing with U.S. team for programmatic follow-up and for emotional support.

Results: The number of expatriate physicians increased by 11 fold over 8 years. We managed a total of 47 full time equivalent between 2007 and 2015. To date, TXCH coordinates the expatriation of 11 physicians annually to Botswana, Malawi, Uganda and Angola. The length of stay varies between 1 to 3 years.

Conclusion: A solid recruitment and orientation program combined with ongoing support during placement abroad are key components to retain expatriate physicians. TXCH needs additional resources to manage its fast growing global program. We plan to recruit additional administrative coordinators in the US and in Africa to maintain and enhance our successful outcomes.

P-0945 | Complementary and Alternative Medicine Use in Canadian Paediatric Oncology Patients

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Background/Objectives: Complementary and alternative medicine (CAM) includes therapies and remedies that are not part of conventional medicine. CAM use is common in many countries with use ranging from 31-84%. The use of CAM is increasing among the Canadian paediatric population, but the incidence within paediatric oncology is not known.

The objective of this study was to determine the incidence of CAM use within a Canadian paediatric oncology population and compare it to other countries.

Design/Methods: A questionnaire was developed and completed by parents/guardians of paediatric patients (aged 0 to 18 years old) with an oncology diagnosis at the Children's Hospital of Eastern Ontario in Ottawa, Ontario from January 2015 to July 2015. The questionnaire included reasons for CAM use or non-use, types practiced, the frequency of use, unwanted side effects, the satisfaction of CAM therapy, the amount spent on CAM and the supervision of CAM. Demographic characteristics were also collected.

Results: Of the 62 respondents, 61% of patients reported the use of CAM during their cancer treatment. The most common reasons to not use CAM were that it may interfere with their child's medical treatment and that CAM is not scientifically based (n=25%). Of those that used CAM therapies, the most commonly used modality was prayers/faith (n=35%). Females ($\mu=61.0\%$) and males ($\mu=61.9\%$) were equally likely to use CAM. Ethnicity influenced CAM use, as 100% of those that identified as European or Aboriginal used CAM, whereas approximately half of those that identified as Canadian ($\mu=57.4\%$), French ($\mu=50.0\%$), Asian ($\mu=60.0\%$) and African ($\mu=50.0\%$) used CAM. Only 57% of patients discussed their CAM use with a physician.

Conclusion: Sixty-one percent of paediatric oncology patients at our institution are using CAM therapies. This is similar to the use in other countries such as the USA, Australia, Finland and the Netherlands, where the use ranges from 31 to 84%.

P-0946 | Frequency of Radiological Pneumonia in Children with Chemotherapy Induced Febrile Neutropenia in a Tertiary Care Hospital

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Background/Objectives: Febrile neutropenia is common complication in patients on chemotherapy and a major cause of mortality in developing countries. Pneumonia has been found to be the most common cause of febrile neutropenia and mortality among neutropenic paediatric oncology patients. The objective of this study was to determine the frequency of radiological pneumonia in children with chemotherapy induced febrile neutropenia at the time of presentation to a tertiary care hospital.

Design/Methods: It is a descriptive case series conducted over a period of 6 months. All the children of 1-14 years, of either sex, diagnosed as chemotherapy induced febrile neutropenia were included. One hundred patients were included. The Chest X-ray was done within 2 days of onset of febrile neutropenia. The complete data regarding clinical features, type of malignancies, absolute neutrophil count (ANC) and CXR findings were recorded on predesigned proforma. Result was analyzed statistically with the help of SPSS version 11.

Results: Seventy five percent of the patients (N=72) presented between 1 to 5 years of age. The male to female ratio was 1.7:1. Fever was present in all patients (N=100) and cough was present in 78% of patients. Forty one percent (N=41) of patients had absolute neutrophil count (ANC) <500 cells/ μ L, 33% (N=33) of patients with ANC of 500-1000/ μ L while remaining 26% (N=26) of patients were having ANC of 1000-1500 cells/ μ L at the time of presentation. Acute lymphoblastic leukaemia was primary disease in 53% (N=53) of these patients, followed by solid malignancies and lymphoma in 16% (N=16) and 31% (N=31) of the patients respectively. Radiological pneumonia was present in 18% (n=18) of patients with chemotherapy induced febrile neutropenia, at the time of presentation.

Conclusion: Plain chest radiography is an easy and effective tool to detect pneumonia earlier as the focus of infection in patients with febrile neutropenia and may improve prognosis.

P-0947 | A Study of the Effect of Hypotonic Hyper-Hydration Fluids on Sodium Balance in Paediatric Haematology/Oncology Patients Receiving Chemotherapy

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Background/Objectives: To determine the effect, if any, that IV hyper-hydration with hypotonic fluids has on sodium balance in paediatric haematology/oncology patients receiving cytotoxic chemotherapy.

Design/Methods: A literature review was carried out. A snapshot of current practice across paediatric haematology/oncology centres in the UK was obtained. A prospective study was carried out in a tertiary paediatric haematology/oncology centre. A total of 98 patient episodes involved hyper-hydration with isotonic fluids (0.9% NaCl or 0.45% NaCl + 2.5% glucose with added sodium bicarbonate) or with hypotonic fluids (0.45% NaCl + 2.5% glucose). Serum sodium was monitored before and during hyper-hydration. Results were analysed according to whether children experienced a drop in serum sodium. A student t-test was carried out using SPSS to compare the two groups.

Results: A concrete evidence base on which clinicians may base a decision about choice of IV fluids as concurrent hyper-hydration with chemotherapy was not found in the published literature. Variation in practice regarding hyper-hydration was found between different centres in the UK and Ireland. The mean drop in serum sodium was greatest in the hypotonic fluid group (2.11 mmol/L) compared to the isotonic fluid group (0.47 mmol/L). The p-value of 0.1% is approaching significance. Five (of 98) patients hyper-hydrated with hypotonic fluids experienced a drop in serum sodium to \leq 130 mmol/L during the study. No patient's serum sodium dropped to 130 mmol/L or less in the isotonic group. During the course of the study no patient experienced clinical manifestations of hyponatraemia. No patient became hypernatraemic.

Conclusion: In paediatric haematology/oncology patients receiving hyper-hydration with concurrent chemotherapy isotonic fluids are preferable. There are many confounding factors affecting serum sodium levels in paediatric haematology/oncology patients. This study shows that hypotonic hydration fluids may be a precipitating factor of hyponatraemia and switching to isotonic fluids removes this factor. However frequent monitoring of serum electrolytes is still necessary throughout chemotherapy.

P-0948 | Bereavement and End of Life Care Issues of Children with Cancer and their Families

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Background/Objectives: The Indus Children Cancer Hospital sees children from underprivileged homes, from the ages of 0-16 years, with 500 new cases every year from all over Pakistan and Afghanistan. Half of these cases will get treated successfully but there is a chance the some patients may die due to infection or progressive disease.

Design/Methods: A bereavement support program was started in August 2014 to cater to the bereavement support required for the families of children who have died of cancer and to identify the areas of further improvement in services being offered. Fifty bereaved families were contacted, over the telephone, by the counselors from the department of psychosocial oncology, since it was not logistically possible to physically go to their homes.

Results: The factors reported by parents, associated with end of life, were of excruciating pain that the children were in, the trauma of the parents to see their child in pain and the post traumatic stress experiences. Relying on divine will as the reason for the end of suffering through death, and relief at child's death and end of suffering were also factors that came up. Some parents wanted there to be a way to ease the death of the child further as morphine would stop working after a while. The more supportive the families felt health professionals were, the better their coping mechanisms were during bereavement. Prior rapport with families was also essential in grief counseling.

Conclusion: Condolence calls made by the counselors yielded the result that these calls were beneficial for the families as they were provided with continued support, as well as the need to make home visits as families were not ready to come to the hospital. However the counselors themselves reported distress at having to deal with the families' distress, for which in house counseling was provided.

P-0949 | Creating A Legacy: Scrapbooking for Children with Cancer and their Families as an End of Life Aid

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Background/Objectives: End of life is an experience that is traumatizing not only for children with cancer but also their families and loved ones. It is a conundrum, that end of life counselors face, as they try to ease the process and prepare all concerned for the end of life of their child. Parents don't want their child to know that he or she is dying. It had been observed that parents carried only unpleasant memories of the last days of their child which would cause their distress to be more intense. The scrapbooking project was started in Indus Children Cancer Hospital in Pakistan to ease the end of life process in which the children created a legacy of fond memories.

Design/Methods: Twenty children, from the Indus Children Cancer Hospital, who were on supportive care due to their illness being untreatable, were enrolled in this study to gauge the effect of creating a legacy through scrapbooking. Counselors took art and craft material and gave the children the freedom to choose what they wanted to draw or write on each page of these books. Families were also encouraged to become involved.

Results: It was observed by the counselor that there was a reduction in distress in not only the child but also the parents or family members who were with the child at the time of the activity. This was later corroborated by the participants themselves also. There was laughter and easing of anxiety as children would become engrossed in the activity. Parents reported that they considered those last days as not only holding pain but also times of happiness.

Conclusion: The scrapbooks left behind by children who died of cancer became a tangible way to look back at with fondness, memories that were created during the process; and to rejoice over in times of remembrance.

P-0950 | Pattern of Nutritional Deficiencies in Childhood Cancer Patients- Experience from a Large Cancer Hospital in Pakistan

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Background/Objectives: Malnourished children with cancer are not only more prone to develop infections and other treatment related complications, but also they have relatively poor survival outcomes as compared to well nourished children. Proper evaluation of nutritional status is very important for intervention of nutritional issues during cancer therapy. Main objectives of this study were to evaluate the diet and identify the pattern of nutrients' deficiencies in children with cancer being treated at Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore, Pakistan.

Design/Methods: This prospective cross-sectional observational study was carried out after formal IRB approval. A trained clinical nutritionist conducted semi-structured interviews of childhood cancer patients and their caregivers in outpatient clinic. Twenty four hours dietary recalls of those patients were collected. Anonymized data were sent to St. Jude Children's Research Hospital, Memphis, USA for assessment by the software Nutritionist Pro[®]. The dietary intakes of individual patients were then compared with the age and gender based recommended dietary allowances (RDA) for macro and micronutrients.

Results: Of 29 patients, 20 were males. Median age was 57 months. Carbohydrates, proteins and fats content of the food of all the patient was more than 90% of their RDA, and were optimal for provision of calories. However proportion of potassium, fluoride, calcium and iron were less than 70% of RDA in 69%, 62%, 52% and 14% cases respectively. Food of 41%, 48%, 79% and 69% patients contained less than 70% RDA for Vitamin A (RAE), Vitamin D, Vitamin E and Vitamin K, respectively. Among water soluble vitamins, deficiencies of Vitamin C and Vitamin B12 were noted in 21% cases each.

Conclusion: Diet of most of our patients had good macronutrients composition but had inappropriate micro-nutrients contents. Inclusion of locally available food items having better micronutrients' composition can prevent potentially harmful nutritional deficiencies in childhood cancer patients.

P-0951 | Incidence of Chicken Pox or Herpes Zoster and Seroprevalence of Varicella-Zoster Virus Immunoglobulin G Antibodies before and after Chemotherapy

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Background/Objectives: Varicella-zoster virus infection may cause significant morbidity and mortality in immunocompromised patients receiving chemotherapy and make chemotherapy delayed. Few studies have measured the levels of antibodies specific for varicella zoster/chickenpox viruses in childhood cancer patients undergoing chemotherapy. We assessed the change of varicella-zoster virus immunoglobulin G antibodies (VZV-IgG) before and after chemotherapy schedules and prevalence of chicken pox (CP) or herpes zoster (HZ) during chemotherapy period to find the relationship between them.

Design/Methods: Commercial ELISA for VZV-IgG was performed at diagnosis and completing of chemotherapy. We retrospectively reviewed the transition of VZV-IgG and prevalence of CP or HZ through medical records of childhood cancer patients from 1998 to 2014 in Kyung-pook National University Hospital, Daegu, South Korea.

Results: Total 99 patients' data was analyzed (54 VZV-IgG positive patients and 45 VZV-IgG negative patients at diagnosis). Among VZV-IgG positive group at diagnosis, 40 patients showed sustained positive IgG during chemotherapy, and 8 patients underwent the disease (CP:HZ=2:6). On the other hand, 14 patients showed transition to negative IgG after chemotherapy and 8 patients experienced the disease (CP:HZ=4:4). In the case of negative group at diagnosis, 11 patients presented seroconversion to positive IgG and they had no disease of VZV. Among 34 patients who showed still negative IgG developed disease in 5 patients (CP:HZ=2:3). The seronegative group after chemotherapy showed higher morbidity of CP or HZ compare to seropositive group.

Conclusion: Although there are several issues about VZV-IgG and vaccination, higher frequency of CP or HZ in VZV-IgG negative group during chemotherapy suggest that we should monitor viral disease and carry out immunization during chemotherapy through regular VZV-IgG checking.

P-0952 | Management of Germinoma-Induced Diabetes Insipidus with Desmopressin Acetate (DDAVP) During Hydration for Chemotherapy

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Background/Objectives: Majority of children who have suprasellar germinoma present with central diabetes insipidus (CDI). Although germinoma has high sensitivity to chemotherapy including nephrotoxic agents such as cisplatin, it requires hyperhydration during its administration, which makes the management of fluid and electrolyte balance difficult. While vigilant monitoring is fundamental for continuous infusion of arginine vasopressin, there is limited literature referring to the use of desmopressin acetate (DDAVP) during chemotherapy. We examined the efficacy of DDAVP during chemotherapy with hyperhydration, and evaluated the relationship between serum creatinine concentration and DDAVP dosage.

Design/Methods: Five children (age 7-12 years) with newly diagnosed germinoma, whom all had complication of CDI, were treated at our hospital between 2010-2014 and retrospectively reviewed. All patients were treated with the risk stratified protocol including cisplatin. Half dose of DDAVP (oral n=1, intranasal n=4) prior to chemotherapy was administered as a single dose during chemotherapy and hyperhydration. The following four indexes were considered: (1) urine volume, (2) daily fluid balance, (3) thirstiness, and (4) serum sodium concentration.

Results: Fluid balance was well controlled during chemotherapy and hyperhydration with concurrent use of DDAVP, and no relationship was found between serum creatinine concentration and DDAVP dosage. However, transient elevation of serum creatinine concentration observed after hyperhydration was associated with decrease of daily DDAVP usage. Marked variations in serum sodium levels were also observed during chemotherapy (119-148 mEq/L). Significant complications that occurred among total of 21 treatment courses were acute kidney injury (n=1) and severe hyponatremia (n=2). All patients recovered with conservative treatment.

Conclusion: The use of DDAVP referring to the indexes we proposed may be one therapeutic option for treatment of germinoma-induced CDI. However, the management should be performed with careful attention to balance of fluid and electrolyte, since optimal DDAVP dosage may vary among each patients depending on their renal function.

P-0953 | Antibiotic Susceptibility of Bloodstream Isolates in a Paediatric Oncology Population, 2013-2015

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Background/Objectives: The rapid initiation of effective empiric antibiotics is imperative in patients with febrile neutropenia. At our institution, meropenem is the empiric antibiotic of choice for gram negatives; vancomycin is added empirically to cover gram positive organisms when specific indications exist.

Our objectives were therefore to: (1) review susceptibility patterns for bacterial isolates from blood stream infections, and (2) assess efficacy of our current empiric antibiotic regimen.

Design/Methods: All blood cultures and antibiotic susceptibilities were reviewed from 01/01/2013-12/31/2015. Unique isolates were: (a) obtained on separate admissions, (b) individual species obtained from the same patient at the same time, (c) identical species showing disparate susceptibility patterns. Susceptibility patterns were reported for all isolates, and percentage susceptible to each antibiotic was calculated.

Results: Gram Negative: 38 isolates were identified, with *Escherichia coli* (n=10) and *Pseudomonas aeruginosa* (n=10) being most common. 84% of isolates were meropenem-susceptible; all resistant organisms were *Pseudomonas*, with 50% meropenem-susceptibility. 91% of gram negative isolates were ceftazidime-susceptible, including 90% of *Pseudomonas* and 80% of *E. coli*. Amikacin covered all isolates, and both gentamicin and tobramycin covered 97% of isolates.

Gram Positive: 31 unique isolates were identified, with *Streptococcus mitis/oralis* (n=9) and coagulase-negative *Staphylococcus* (n=9) being most common. 96% of gram positive isolates were vancomycin-susceptible; 50% of *Enterococcus* were vancomycin-resistant (VRE). 81%

of gram positive isolates were gentamicin-susceptible including 100% of *Enterococcus*; all gentamicin-resistant isolates were vancomycin-susceptible.

Conclusion: Weaknesses within the current empiric antibiotic regimen include (1) meropenem no longer covers all *Pseudomonas*, and (2) vancomycin no longer covers all gram positives. Substituting ceftazidime would improve *Pseudomonas* coverage at the expense of *E. coli* coverage. The addition of an aminoglycoside would provide secondary coverage for cephalosporin-resistant organisms, meropenem-resistant *Pseudomonas*, and VRE that a single antibiotic may miss.

P-0954 | Central Venous Catheter (CVC) Dysfunction Requiring Use of Tissue Plasminogen Activator is Associated with Significantly Increased Need of Subsequent Cvc in Paediatric Oncology Patients

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Background/Objectives: Dysfunction (defined as inability to flush and/or draw blood) is commonly observed in central venous catheters (CVCs). Tissue plasminogen activator (tPA) is well demonstrated to reverse CVC dysfunction but its impact on the subsequent need for a replacement of CVC is unknown. We hypothesized that use of ≥ 1 dose of tPA for 1 or more episodes of CVC dysfunction is associated with significantly increased requirement for a new CVC in paediatric oncology patients.

Design/Methods: After ethics approval, data was abstracted for all paediatric oncology patients from the Maritime Provinces managed by the IWK Health Center from January 2000 to December 2015. Patients who required ≥ 1 CVC (n=741) were included in the study. Data were combined from: (i) paediatric oncology hospital database, (iii) Electronic medical records, (iv) Pharmacy database and (v) IWK central line database.

Results: The mean number of CVCs per individual study patient was 1.6 ± 1 (range: 1-9). Twenty six percent (n=195) received ≥ 1 dose of tPA. The mean number of doses required per individual patient were 2.3 ± 2.0 (median: 2, range: 1-16).

A significantly higher proportion (55.4%, n=108 of 195) of patients who received ≥ 1 dose of tPA required > 1 CVCs as compared to those patients who did not receive tPA (32.4%, n=177 of 546) [p=0.001, odds ratio: 2.6 (95% confidence interval: 1.85-3.6)].

The mean number of CVCs (2.05 ± 1.29 per individual patient) required by patients who received ≥ 1 dose of tPA was significantly higher than the mean number of CVCs (1.52 ± 0.95 per individual patient) required by patients who did not receive tPA (p=0.0001).

Conclusion: The present study demonstrates that patients with CVC dysfunction who require tPA have significantly increased odds of requiring more than 1 CVC compared to those who do not require tPA. Enhanced strategies to mitigate risks for and treatment of CVC dysfunction are needed.

P-0955 | Use of Abandonment and Related Terms in Siop Annual Meeting Abstracts: Analysis of Group Impact by Siop Podc Abandonment of Treatment Group

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Background/Objectives: Abandonment of treatment is being recognized as the most common cause of treatment failure and inferior survival outcome in resource-limited settings. The SIOP PODC abandonment of treatment group was conceived in SIOP 2010. One of the key aims of the group is to increase awareness, recognition and reporting of abandonment. The group published standardized abandonment terminology in its position statement published in 2011. To better define future directions and areas of need, the group is presently analysing the impact of its activities. The present study was designed to study the reporting of abandonment in abstracts presented at the SIOP annual meeting over the last 9 years.

Design/Methods: All the abstracts published in the annual proceedings of SIOP meetings from 2007 to 2015 were retrieved and were hand-searched for terms abandon*, default, refusal and loss/lost to follow up. Annual data was pooled and analyzed. Era 1, 2 and 3 were defined as 2007-2009, 2010-2012, and 2013-2015 respectively.

Results: Over Era 1, 2, and 3 respectively, the mean number of times abandonment and related terms was reported were 63, 89, 193 times respectively (p=0.002 for trend, R²=0.87). Over the 3 time Eras, there was a significant increase in preferential use of the term abandonment (used 47%, 63% and 85% times respectively) over the other similar meaning terms (default, refusal and loss/lost to follow up) in the 3 eras. Reporting of "refusal" (p=0.011) increased significantly while the increase in reporting of "default" was not statistically significant. "Loss/lost to follow" was reported 25 \pm 11 times over the study period (R² of trend line: 0.022, p=0.664).

Conclusion: This study provides evidence for positive impact of SIOP PODC abandonment of treatment group in increasing awareness and reporting of abandonment in SIOP annual meeting abstracts after adopting standardized terminology for abandonment. Additional supportive evidence will guide the groups' efforts in future.

P-0956 | Solid Tumors in Infancy- Challenges and Unique Features Experience of a Paediatric Oncology Centre from a Developing Country

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Background/Objectives: Solid tumors in infants have different behavioural patterns, response to therapy and outcomes as compared to the older children. The difficulty in initiation and

sustaining chemotherapy, administration of drugs, premature abandonment of the treatment pose a big challenge for successful treatment of these children.

Design/Methods: Retrospective analysis of all the cases of infants who were diagnosed with solid tumors from 2010-2015 was done. Demography, type of the tumour, mode of diagnosis, treatment protocols used, practical difficulties and the outcomes were reviewed.

Results: A total of 22 cases of solid tumors in the infantile age group (<1year) were diagnosed in our institution from 2010-2015. Male preponderance was noted with M:F sex ratio being 2.6:1. Cases included neonates to late infants with mean age of 6.7 months. The mode of diagnosis was from biopsy and tumour markers in 20(90%) and 2(10%) cases respectively. Neuroblastoma was the most common solid tumour (36%) followed by brain tumour(18%), Hepatoblastoma(13%), yolk sac tumour(9%), benign teratoma(9%), Wilms tumour(4%), Rhabdomyosarcoma(4%) and Malignant melanoma(4%). 17(77%) cases received chemotherapy and surgery, 4(18%) cases underwent only surgical excision and 1(5%) case was sent on palliation. A total of 16(72%) cases survived, 5(22%) cases died and 1(5%) case was sent on palliation. Of all the tumors, brain tumors in infancy showed a very poor survival rate. The main challenges encountered in the treatment were difficult IV access, parental counselling, compliance to the treatment and chemotherapy related complications though most of the children tolerated the chemotherapy well and there were no drop outs.

Conclusion: Solid tumors in infancy have been increasingly recognised due to better diagnostic modalities with good survival rates except for brain tumors. Multidisciplinary approach is a key for their management. However practical difficulties pose a big challenge which needs to be addressed for a better outcome.

P-0957 | Vitamin B12 and Folic Acid Levels in Childhood Cancers

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Background/Objectives: Cancer is among the most common causes of death in children. Earlier diagnosis and more effective treatment of malignant diseases can be possible with a better understanding of the pathogenesis of cancer. This study examined the relationship between childhood cancers and vitamin B12 and folic acid levels.

Design/Methods: In a 2-year-period newly diagnosed 125 patients with solid tumour and 113 patients with lymphoproliferative / myeloproliferative malignant disease (a total of 238 patients) and 63 controls were enrolled into the study. Vitamin B12, folic acid and homocysteine levels were measured before the treatment in patient group. The children in control group were without a malignant or chronic disease.

Results: Vitamin B12 and folic acid levels were significantly lower compared to the control group (p=0.002 and 0.007). Homocysteine levels however were statistically higher than those of the control group (p=0.002). Only folic acid levels were significantly lower in lymphoproliferative / myeloproliferative malignant disease group compared to the solid tumour group (p=0.002).

Conclusion: Lower vitamin B12 and folic acid levels can be used as supportive markers in the diagnosis of cancer. Appropriate treatment of deficiencies in vitamins may contribute to cure the malignant disease. This relationship needs to be shown in studies with larger series.

P-0958 | Experience Concerning Paediatric Palliative Care in Hemato-Oncology: Lessons from the Past for the Future

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Background/Objectives: Research in paediatric palliative care is a difficult topic, as prognosis is not always easy and symptom control can be very challenging. Cases from the past can have serious impact in treating children in the future.

Design/Methods: Description of three cases of difficult palliative care in paediatric hemato-oncology.

Results: Case 1

Difficult end of life decisions and difficult symptom control in 7 year old boy with oligoastrocytoma grade III in the conus medullaris. The main problems were severe back pain, very difficult to handle because of the neuralgic character, and different coping strategies between the parents, the patient and the medical team. Because all attempts to alleviate pain by analgesics failed, at last continued sedation was installed.

Case 2

Palliative care lasting for 4 years in a boy with pilocytic astrocytoma and diffuse pial metastases. The big challenge was to obtain symptom control and to continue to offer enough quality of life, which included extensive pain therapy and repetitive palliative irradiation.

Case 3

A baby girl born with a huge supratentorial glioblastoma grade IV, taking in the whole left hemisphere. Surgery was discontinued due to severe hemorrhage and in shared decision with the parents, palliative care was started. After seven months, the girl had a head circumference of 63 cm, with the tumour growing through the skull, making even daily care very difficult.

Conclusion: Pediatric palliative care can be very challenging and learning from the past is important to treat children and families in the future. Sharing our experience concerning this holistic care, which must be very nuanced, is thus very important.

P-0959 | Physiotherapy Assistance for Paediatric Cancer Patients in Terminal Care

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Background/Objectives: Physiotherapy (PT) is part of the multidisciplinary team, improving quality of life and relieving unpleasant symptoms of terminal cancer patients. The aim of the study was to describe PT assistance to paediatric patients that evolved to death in an oncologic ward.

Design/Methods: A retrospective descriptive study, analyzing the PT care records from January 2012 to June 2014. The variables analyzed included: characterization of patients, amount of time spent in hospital, diagnosis, and type of PT care and techniques used. The nominal data was described in terms of percentage and proportions.

Results: Fifty patients died due disease progression in this period, 72% received PT treatment, of these 53% were female. The most frequent diagnosis was Leukaemia (33%), Osteosarcoma (14%), Brain tumors (11%) and other types of neoplasia (42%). The average time spent in hospital was 23.75 days, and the average time before PT treatment started was 3.36 days after that. Oxygen therapy was used in 94% of cases, 19.5% needed noninvasive ventilation support and 8% invasive in tracheostomized patients. All patients needed chest therapy, and the techniques and resources used were: 36% inhalation therapy, 33% secretion removal techniques, 19.5% nasal cleaning, 14% respiratory kinesiotherapy, 11% incentive spirometry, 11% intermittent positive pressure breathing (IPPB), 8% pulmonary re-expansion maneuvers, 5.5% positive airway pressure system exercises (Ezppap) and 5.5% blowing toys. To remove secretion, 25% of patients needed endotracheal suction, being 14% of superior airway and others of tracheostomy. Motor PT was needed in 25% of patients, with the techniques: 78% stretching, 78% passive mobilization, 33% active-passive movement, 22% active movement, 22% march and balance training, 11% resisted movement and 11% Transcutaneous Electrical Nerve Stimulation (TENS).

Conclusion: Terminal cancer care requires a multidisciplinary approach that includes the PT, relieving the negative symptoms that impact the comfort of the patient,

P-0960 | The Impact of Cancer and its Treatment on the Fatigue, Depressive Symptoms, and Quality of Life in Childhood Cancer Survivors

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Background/Objectives: Cancer-related fatigue is the most common concern reported by childhood cancer survivors. Assessing its occurrence and severity is a prerequisite for planning and evaluating appropriate interventions. Nevertheless, there is a lack of large-scale datasets or population-based surveys which examine the impact of fatigue on survivors' quality of life. The objectives of the study were to assess the occurrence and severity of cancer-related fatigue manifested by Chinese childhood cancer survivors. Additionally, the relationships among cancer-related fatigue, physical activity, depressive symptoms, and quality of life in childhood cancer survivors were examined.

Design/Methods: A cross-sectional study was used. A total of 400 childhood cancer survivors (7- to 18-year olds) who underwent medical follow-up in the outpatient clinic were invited to participate in the study. The cancer-related fatigue, depressive symptoms, physical activity level, and quality of life of participants were assessed.

Results: Results indicated that a considerable number of childhood cancer survivors were found to display symptoms of cancer-related fatigue. Besides, results showed that greater occurrence and severity of cancer-related fatigue in childhood cancer survivors were associated with more self-reported depressive symptoms, lower level of physical activity and quality of life. In addition, the study revealed that physical activity level is a strong predictor of the cancer-related fatigue.

Conclusion: The findings provide further support that cancer and its treatment have adverse effects on survivors' fatigue, which can manifest months or even years after the completion of treatment. Most importantly, this study reveals that physical activity is a strong predictor of the level of fatigue in children and adolescents. It is crucial for healthcare professionals to identify strategies that can help children and adolescents surviving cancer increase their adoption and maintenance of regular activity throughout their life.

P-0961 | Evidence-Based Supportive Care Clinical Practice Guidelines in Childhood Cancer – Current Developments

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Background/Objectives: As cure rates in paediatric oncology have improved substantially over the last decades, supportive care has become increasingly important to reduce morbidity and mortality, and to improve quality of life in children with cancer. Currently, large variations exist in paediatric oncology supportive care practice, which may negatively influence care. One of the factors contributing to practice variations is the scarcity of high-quality, evidence-based supportive care clinical practice guidelines (CPGs). To address this we have initiated a project in four phases: 1) prioritization of paediatric CPG topics in the Netherlands, 2) CPG development, 3) CPG implementation and 4) defining a research agenda to meet evidence gaps and to optimize CPG implementation.

Design/Methods: In phase 1, CPGs on pain and fertility preservation were identified as priorities for healthcare providers. In phase 2, we created CPG panels that included international experts in the specific topic. The panels identified the scope and purpose of each CPG and created working groups to address each aspect of the CPG.

Results: The pain CPG will cover pain assessment and evaluation, as well as the pharmacological and non-pharmacological management of tumour-, toxicity- and procedure related pain.

The fertility preservation CPGs will cover selection of patients and methods, aspects of discussing fertility preservation, and ethical and logistical aspects. To take maximum advantage of international /shared effort and expertise, we have joined the recently established international Pediatric Oncology Guidelines in Supportive Care Network (iPOG); a voluntary international collaboration of organizations which are actively developing or endorsing CPGs for the supportive care of children with cancer.

Conclusion: We believe CPGs are the essential next step towards better supportive care practice and, thus, a higher quality of care. Our project aims to develop transparent and trustworthy supportive care CPGs in an international collaboration. Currently, we focus on pain and fertility preservation in children with cancer.

P-0962 | Experiences and Preferences in Supportive Care in Childhood Cancer and Shared Decision Making – A Focus Group Study among Dutch Patients and Parents

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Background/Objectives: Supportive care in childhood cancer is an extremely broad field, for which we are currently developing new high-quality evidence-based guidelines. To be able to prioritize the wide variety of topics that supportive care covers, we want to learn from experiences and preferences of patients and parents. It is also important to learn in what way, and for which topics, patients and parents would like to be involved in decision making.

Design/Methods: We included childhood cancer patients, and parents of childhood cancer patients, who were under treatment for a minimum of 6 months at the time of selection or within 6 months after finalizing treatment. This study consisted of two phases: in phase one we conducted two traditional (face-to-face) focus groups to identify parents' experiences and preferences. In phase two, we investigated adolescent patients' experiences and preferences by use of an online (forum-style) focus group.

Results: A total of 19 parents and 11 patients participated in this study. Regarding supportive care topics, both patient and parents considered communication between physician and patient, provision of information and care at the paediatric oncology ward among the most important topics. Regarding shared decision making, patients and parents stated that they wanted to be actively involved in making decisions about their (child's) treatment, in particular regarding relatively easily understood medication to diminish side effects (e.g. analgesics and anti-emetics, but not antibiotics).

Conclusion: These outcomes yield important implications towards the development of high-quality evidence-based supportive care guidelines, as 1) these guidelines can now be developed in areas where patients' and parents' demand is the highest, and 2) these guidelines can focus on topic-specific recommendations for shared decision making.

P-0963 | Influence of Maternal Perception on Adherence to Nasogastric Tube Feeding in Paediatric Patients Undergoing Oncologic Treatment

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Background/Objectives: The impact of enteral nutritional therapy in parents, especially in mothers of children with cancer diagnosis, is heterogeneous and poorly studied. This study aimed to investigate the maternal perception about the use of nasogastric tube feeding in children with malignancies undergoing oncologic treatment; as well as the influence of maternal perception on the adherence to nutritional therapy.

Design/Methods: This prospective qualitative study was carried out from August 2014 to February 2015 in the Outpatient Nutrition Clinic of the Pediatric Oncology Institute - GRAACC / UNIFESP. Study participants were mothers of nine patients who used nasogastric tube feeding at home due to low food intake and/or progressive weight loss. Socio-demographic and nutritional aspects data were analyzed as well as the responses to a semi-structured interview.

Results: The main factors associated with adherence of mothers were patients' age, weight loss, sense of discomfort caused by the feeding tube in mothers' perception, esthetics, exercise of motherhood in the act of feeding, medication and immunity.

Conclusion: Careful explanation and clarification about tube feeding brings comfort to the caregiver, which is able to deal with the tube as a tool that assists her in childcare, thus increasing adherence. The creation of groups with parents and patients may provide a space for sharing experiences and stigma deconstruction related to the use of feeding tubes.

P-0964 | Improving Timeliness of Antibiotic Delivery in Paediatric Patients with Cancer and Suspected Febrile Neutropenia: A Joint Physician & Nurse Prospective Interventional Study

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Background/Objectives: Outcome of febrile neutropenia in children with cancer is improved by prompt antibiotic administration (≤ 60 minutes from admission). In a previous quality audit in our unit, delayed antibiotic administration was displayed in 72% of febrile neutropenia episodes, mainly due to wait time for blood test results at admission.

Design/Methods: A prospective interventional study to test the feasibility of prompt administration of a first dose of antibiotics in children admitted with fever and suspected neutropenia is here presented. Data from all consecutive patients hospitalized in our Unit for fever from November 2015 to February 2016 were analyzed. Patients who had received HSCT were excluded. Continuous variables were compared using Student t test or Mann-Whitney U test when applicable. Categorical variables were compared using chi-square or Fisher's exact test when applicable. $P < 0.05$ was considered as statistically significant. Data were analyzed using SPSS 20.0.

Results: We analyzed data from 25 hospitalizations of 18 paediatric patients admitted for fever and suspected neutropenia. Median age at admission was 4.3 years (range: 1.8-15.1). Patients had leukaemia/lymphoma and solid tumors in 11 and 7 cases, respectively. Febrile neutropenia was actually displayed in 23/25 episodes. In 18/23 episodes (78%), neutropenia was correctly suspected and antibiotics were administered without waiting for blood test results. Two patients received antibiotics without being neutropenic. Median time to antibiotic administration (TAA) was 60 minutes (range: 10-265) and TAA ≤ 60 minutes was achieved in 15/23 episodes (65%), thus significantly better than the same variables analyzed during the previous audit ($p = 0.047$ and $p = 0.007$, respectively). At least two blood cultures were performed in all patients, compared to 52% of the cases analyzed during the audit ($p = 0.001$).

Conclusion: A regular evaluation of the clinical practice is of major importance to guarantee a high quality of the assistance. In this process, multidisciplinary collaboration is indispensable.

P-0965 | Invasive Fungal Infections in Hemato-Oncology Paediatric Patients: A Ten Year Review

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Background/Objectives: Invasive fungal infections (IFI) are a significant cause of morbidity and mortality in children with hematologic and malignant diseases.

Aim: To describe the epidemiology and outcome of IFIs in our hemato-oncology unit during a ten-year period.

Design/Methods: The medical records of paediatric patients admitted to our hemato-oncology unit between 2006-2015 with an IFI were reviewed. Clinical characteristics of mold and yeast infections, and their proportion over time were analyzed.

Results: Twenty two patients were included (59.1% males, median age 6.2 [2.3-10.8] years) in the study. Hematological malignancies were 40.9%, solid tumors 27.3%, and benign hematological conditions 27.3%. Overall, 36.4% of patients had undergone haematological stem cell transplant (HSCT), (87.5% allogeneic), 18.2% had suffered graft versus host disease (GVHD), (75% acute), 45% of them were on antifungal prophylaxis (50% micafungin, 40% fluconazole).

Regarding outcomes, 31.8% needed PICU admission and 18.2% died.

Molds were the most common cause of IFI (59.1%, all bronchopulmonary disease), including 2 confirmed *Aspergillus*. Yeasts infections included 44.4% fungemias and 44.4% urinary infections, and were mostly caused by *Candida albicans* and *Candida parapsilosis*. Patients with mold infections were older (9.6 vs 3.8 years; $p = 0.010$), had higher initial PCR (10.9 vs 4.7 mg/dl; $p = 0.016$), higher incidence of HSCT (61.5% vs 0%; $p = 0.003$) and GVHD (30.8% vs 0%; $p = 0.066$), antifungal prophylaxis (76.9% vs 0%; $p < 0.001$), PICU admission (46.2% vs 11.1%; $p = 0.083$) and mortality (30.8% vs 0%; $p = 0.066$).

Comparing the first (2006-2010, 12/22 patients) and second period (2011-2015, 10/22 patients), the latter had an increased proportion of mold infections (33.3% vs 90%; $p = 0.007$), which coincided with higher incidence of HSCT (25% vs 50%; $p = 0.225$), GVHD (8% vs 30%; $p = 0.190$), and antifungal prophylaxis (25% vs 70%; $p = 0.035$).

Conclusion: During the second period of time (2011-2015) there has been an increased proportion of mold infections over yeast infections, with higher severity parameters, along with more intensive myeloablative chemotherapy regimens and an increased survival of these diseases in the last decades.

P-0966 | Bk Virus Infection in Paediatric Recipients of Solid Organ Transplant Recipients and Patients with Acute Lymphoblastic Leukaemia

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Background/Objectives: BK virus is a member of the polyomavirus family. Whilst infection with the BK virus is not uncommon, infections will likely pass unnoticed in the immunocompetent.

Following primary infection the virus lies latent at a variety of sites, most commonly in the urinary tract³. In the immunocompromised, the virus can become reactivated and replicate.

This review will compare and contrast the presentation of BK virus reactivation in Paediatric solid organ transplant recipients and Haem-Oncology patients.

Design/Methods: Detailed case reviews of eight patients with BK virus. Five having received a solid organ transplant and three with a haematological malignancy.

Results: All five cases in the organ transplant group developed Bk-associated-nephropathy (BKN) post transplant, which responded to medication adjustment. The three cases in the haem-oncology group developed BK virus associated haemorrhagic cystitis. One child in the transplant group, post liver transplant for hepatoblastoma, developed haemorrhagic cystitis in addition to BKNV.

Conclusion: Both patient groups had documented reactivation of BK virus and significant viraemia/viruria. Identical symptomatology following reactivation was not observed. None of

the haem-oncology group developed BKNV. Four of the five organ transplant recipients did not develop haemorrhagic cystitis. Interestingly, our organ transplant cohort included a child post liver transplant, her presentation showed similarities to both patient groups.

P-0967 | Role of the Community Play Specialist in Preparing Children with Cancer for Mri Scans and Radiotherapy

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Background/Objectives: Radiotherapy and MRI scanning are regarded as a frightening experience. General anaesthesia is often an essential component of care for such patients. The Hospital play specialist has a unique role to play in preparing children for these procedures, but often with, as opposed to, instead of general anaesthesia. In Northern Ireland the role of the play specialist has been extended to the community, where they are able to visit young children in the comfort and safety of their own homes. In these environments the children are prepared for scans and radiotherapy. With the additional support from the Community Play Specialist it was envisaged that there would be a reduction in the number of general anaesthetics required.

Design/Methods: All young patients who require elective MRI scanning or Radiotherapy are referred by the Paediatric Oncology team to the Community Play Specialist. Children are seen at home where the play specialist uses a variety of Specific Preparation Tools to prepare children and empower them with knowledge of the procedure. Detailed age appropriate photographs of the MRI scanner and Radiotherapy suite are used in play to ease any sense of foreboding. A specific Biofeedback tool (TakeTen™) is utilised to reduce stress and encourage patients to take control of their situation. Siblings and parents are encouraged to participate.

Results: Over a 15 year period, 100 patients aged 2.5 to 19 years were prepared for radiotherapy. 80% of those patients did so without the need for a general anaesthetic. All children requiring elective MRI scanning lay appropriately and successfully underwent that procedure.

Conclusion: The ability of the community play specialist to visit children in their home environment enhances their success rate in preparing children to procedures which are known to be frightening. Children and young people cope best when they know what to expect.

P-0968 | Surgical Procedures Outside the Operating Room among Paediatric Oncology Patients

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Background/Objectives: Health care costs are on the rise. The primary reason for this significant rise between 2000 and 2011 was due to an increase price of drugs, medical devices, and hospital care.⁽¹⁾ The increasing number of paediatric surgeries and the limited operating room availability necessitates health care providers to deliver care in alternative venues other than the traditional hospital setting. Pediatric oncology patients treated at the Dana-Farber/Boston Children's Hospital (DF/BCH) are offered a unique opportunity that reduces cost and provides time efficient care without compromising patient safety or enhancing anxiety levels. In an effort to accommodate the needs of our patients, the outpatient Jimmy Fund Clinic (JFC) extended its services to include removal of implantable central venous access devices (Portacaths) and central venous lines (CVLs) under general anesthesia in 2013.

Design/Methods: We identified patients who met eligibility criteria for the surgical procedure in our JFC procedure suite. Training and competency based learning of nursing staff in surgical procedures under anesthesia consisted of observations, didactic, and practical education in the operating room. Reconstruction of the physical environment included nursing input and consisted of one procedure room and two recovery beds. Scheduling of procedures has evolved to hourly time slots of five per day twice monthly.

Results: Researchers compared Portacath removals in the BCH Main OR, BCH Satellite Campus OR and the JFC Procedure Room found that overall cost of care outpatient was decreased by 16%.⁽²⁾ Parents and patients reported that their preference is that procedures are done in the familiar setting of the JFC versus the Main Operating room.

Conclusion: Portacaths and CVLs can be safely and efficiently removed in the outpatient setting. There is no increased risk with properly trained staff. Decreased length of time of the procedure and a calm environment contributes to increased patient and family satisfaction.

P-0969 | Patients and Physicians as Partners. Effectiveness of Multi-Faceted Educational Modules on Management of Patients Presenting to Emergency Department with Fever-Neutropenia

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Background/Objectives: Fever-Neutropenia (FN) is the leading cause of Emergency Department (ED) visits and hospitalization among patients receiving chemotherapy and is also associated with significant morbidity and mortality. We hypothesize that multi-faceted and focused FN education of patient/caregiver decreases their time to FN recognition, which leads to early ED presentation. Standardized FN/sepsis education for ED physician shortens their time-to-assessment and time-to-antibiotics for FN patients. The cumulative effect of these interventions improves clinical outcomes.

Design/Methods: Eligibility criteria included oncology patients receiving chemotherapy and presenting to ED at a large academic tertiary care hospital. Patient's/caregiver's educational modules included printed 2 page information, 8 minute FN video (available DVD/YouTube), and a standardized "Hem-One bag" which carried all treatment relevant information, medications and central line supplies. ED physician's education included standardized FN/Sepsis simulation modules and standardized "FN clinical order set". "Controls" (n=200) are defined

as FN patients presenting *before* introduction of educational modules and "intervention group" (n=150) is defined as FN patients presenting *after* completion of all educational modules. Effectiveness of these educational modules was analyzed by comparing patient's caregivers' baseline understanding of FN (tested by standardized 10 questioner pre/post-test), differences in ED management times (assessment/antibiotics) between patients in control and intervention groups. Power to detect difference among these variable was at least 80% ($\beta=0.8$, $\alpha=0.05$).

Results: Education of patient's caregiver improved their FN understanding by 84% and significantly decreased their time for FN recognition and ED presentation. Educational modules of ED physician led to further shortened time-to-assessment by 65% and the "FN clinical order set" shortened time-to-antibiotics administration by almost 40 minutes in 85% of events.

Conclusion: Standardized multifaceted educational modules for patients/caregivers leads to early FN recognition and prompt ED presentation. ED physician's focused education results in shorter times-to-assessment and antibiotics administration. Heme-One bag with medications and central-lines supplies likely contributes to decrease central-line bloodstream infections.

P-0970 | Early Discharge in Paediatric Febrile Neutropenia: Experiences and Perceptions of Healthcare Professionals

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Background/Objectives: Patients at low risk of septic complications of febrile neutropenia can be safely treated as outpatients using oral antibiotics, with low rates of treatment failure. Introducing these treatment regimens may improve quality of life; reduce hospital acquired infection; save costs and reduce pressures on healthcare services. However, our recent work has raised concerns that early discharge may not be acceptable to patients, parents and healthcare professionals.

Design/Methods: This multi-centre focus group study explored the experiences and perceptions of key stakeholders about early discharge and considers potential barriers and facilitators to acceptance. This abstract presents the findings of healthcare professional groups at three sites purposively selected for their service structure and management of febrile neutropenia.

Results: Doctors and nurses of varying degrees of professional experience participated (3-7 participants in each group). Their perspectives were best encapsulated by the concept of *understanding and managing risk*, where personal experience often held greater value than statistical findings and occasionally self-acknowledged illogicality enabled emotional reactions to risk to be balanced with the evidence. The challenges posed by following strict protocols and professionals' recognition of the individuality of febrile neutropenic episodes, on the background of these risks, led professionals to express a *need for discretion* within their practice. Finally, the multiplicity of parties involved in low risk febrile neutropenia services led to challenging relationships. *Negotiation of roles* and deliberations about individuals' responsibilities, as a consequence of systematic change, were particularly testing for professionals.

Conclusion: Helping professionals through the process of negotiating roles to a position where they feel most able to understand and accept the risks involved and have discretion to work within clearly defined guidelines would be beneficial. Ongoing parent and teenager focus groups will allow triangulation with these findings to inform the rational design of services to be most acceptable to all.

P-0971 | Evaluation of An Impact of a Clinical Fellowship for International Dietitians

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Background/Objectives: Medical Nutrition Therapy (MNT) in paediatric cancer treatment is very important. While there are training opportunities for medical doctors from countries with limited resources, few exist for dietitians.

Design/Methods: The Nutrition Department and the International Outreach Program at St. Jude Children's Research Hospital, Memphis, Tennessee have worked together from 2005 to 2013 to develop and implement a training program for international dietitians working with paediatric oncology patients. During that time, St. Jude has hosted 15 dietitians from various countries like Mexico, Brazil, the Czech Republic, Turkey, Russia, United Kingdom, and Guatemala. In this 3-week long program, fellows observed dietitians working in clinical and food service settings. The curriculum provided experience in nutrition risk screening, nutrition care process, nutrition for cancer prevention, palliative care, and exposure to nutrition support. Monthly online meetings were established through the cure4kids website to continue collaboration and training.

Results: The impact of the fellowship was measured by survey containing 23 general questions and 22 questions measuring impact. We evaluated the impact of the program based on changes made by formal fellows in the clinical practice, research, management and food service. We also evaluate the program based on recognition by the medical team, professional growth/networking and personal growth. The survey return rate was 100%; responses revealed that 80% of participants continued working in paediatric oncology, 67% participated in monthly meetings organized as part of this fellowship, 47% collaborated on research, 100% advanced their competency in clinical practice, 93% broadened their competency in research, 67% became increasingly competent in management, 60% implemented changes in food service, 100% were recognized by their hospitals for participating in the program, and 100% and 93% answered that participation in the fellowship aspect of the program helped their professional and personal growth, respectively.

Conclusion: International collaboration is feasible and enriches the professional life of participants.

P-0972 | End of Life Care Experience at the Paediatric Oncology unit at the Uganda Cancer Institute: What Role can Oncology Nurses Play?

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Background/Objectives: Although the majority of childhood cancers are curable, this is not yet true for low resource countries. In Uganda, there are 4,321 new cancer cases annually and about 8% occurs among children. The mortality rate is 70% annually, that is every 3 in 5 children diagnosed with cancer will not survive past one year after cancer diagnosis. Here, we review the factors contributing to poor outcomes and potential solutions.

Objectives: To describe the role of oncology nurses at the end of life care in children with cancer in Uganda.

Design/Methods: We conducted an observational prospective study, at Paediatric Oncology Unit, at Uganda Cancer Institute (UCI) between January and December 2015. Twenty five children assented to participate. A structured questionnaire was administered to the participants; data was collected on social demographic variables, diagnosis, outcomes.

Results: Majority 60% of the children presented with advanced stage of cancer at diagnosis. The majority had acute leukaemia, wilms tumour, burkitts lymphoma and neuroblastoma respectively. Among the participants, over half 60% were girls, median age 5 years. All the children had been undergoing chemotherapy, less than a third of them had received surgery or radiotherapy with palliative intent. Family involvement in decisions regarding the role of palliative chemotherapy at end of life is low (20%). The concept of quality of life for cancer patients with advanced cancer is not well perceived among caretakers and some clinicians at UCI.

Conclusion: Nurses play an integral role, identifying symptoms, providing care coordination, and ensuring clear communication. Educational initiatives for patients, families and health-care providers, are essential. Therefore oncology nurses play a key role in the multidisciplinary team approach to paediatric patients at end of life care.

P-0973 | Lived Experiences of Children with Life Threatening Illnesses Participating in 'Dream' Realization Projects

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Background/Objectives: Life threatening illnesses (LTIs) cause not only physical pain but also deep emotional side effects. The relationship between quality of life, morbidity and mortality when children have a LTI has been brought into question. Psychosocial intervention strategies are aimed at decreasing anxiety and depression symptomatology and have been linked to promoting mental, emotional and social well-being, resilience, respite and coping abilities. One such psychosocial intervention strategy is provided by the Reach For A Dream (RFAD) Foundation[®].

This study aimed to explore the psychosocial experiences of the recipients of RFAD 'dream-come-true' projects.

Design/Methods: In 2012 a narrative inquiry design was used to explore the psychosocial experiences of recipients of RFAD projects with children/adolescents and their parents from Gauteng, South Africa. Semi-structured individual in-depth interviews were conducted with randomly selected participants who are or have been clients of RFAD.

Results: The pre-dream contextual narrative constructed by children/adolescents and parents covered fear, anger, sadness, loneliness, helplessness, and lack of normality and family support. Lived experiences during the 'dream' projects indicated happiness, excitement, magical feelings, family inclusion, relaxation, feelings of normality and connection with other sick children. Post-dream findings suggested various forms of improved mental and emotional states in participants, and unique opportunities to connect with their family in a positive, normal way.

Conclusion: As a psychosocial intervention strategy to meet some challenges of LTIs in children, a 'dream-come-true' experience appears to ameliorate distress, offer respite, decrease isolation, increase a sense of empowerment and self-confidence, and decrease anxiety and fear in children and their families.

P-0974 | Experienced Chronic Sorrow in Mothers of Children with Cancer: A Phenomenological Study

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Background/Objectives: Chronic sorrow is experienced by mothers of children with cancer. It is a multidimensional concept and is experienced by mothers in different ways depends on their various contexts. Little is known about the concept of chronic sorrow in mothers of children with cancer living in Iran.

This study aimed to clarify the concept and explain lived experiences of chronic sorrow in Iranian mothers of children with cancer.

Design/Methods: In this hermeneutic phenomenological study, 8 mothers of children with cancer participated in semi structured in-depth interviews about their experiences of chronic sorrow. Interviews continued until data saturation was reached. All interviews were recorded, transcribed, analyzed, and interpreted using 7 steps of the Dickelman et al's phenomenological approach.

Results: Three main themes emerged from mothers' experiences of chronic sorrow related to child's cancer. These main themes were "climbing up shaky rocks," "Religious fear and hope," and "continuous role changing." Each of these themes consisted of several sub themes.

Conclusion: There are similarities in experiencing chronic sorrow by mothers of children with chronic diseases in different societies. However some experiences are unique in Iranian mothers of children with cancer.

P-0975 | Potential Causes of Treatment Default among Paediatric Oncology Patients in a Teaching Hospital, Ghana

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Background/Objectives: Numerous challenges negatively affect paediatric cancer chemotherapy in Africa. These challenges have contributed significantly to treatment default. Friedreich *et al.* in their analysis of treatment default of cancer in 101 countries estimated that 15% of paediatric cancer patients default treatment out of which 99% are found in low and middle income countries particularly Africa. The major cause of poor treatment outcome is treatment default. The objective of this study was to generate a baseline data for the causes of treatment default in patients in the paediatric oncology setting in Ghana in order to improve treatment outcomes.

Design/Methods: The study was cross sectional prospective conducted at the Paediatric Oncology Unit (POU) of Komfo Anokye Teaching Hospital (KATH), Ghana from May to July 2015. The POU serves about 30 patients weekly. Fifteen patients aged 12 years and below were recruited weekly for 10 weeks. A sample size of 150 was used for the study. Data on the reasons for default were obtained from the caregivers of the children after informed consent. Ethical approval was sought before the study was commenced.

Results: Ninety (60%) of the caregivers responded to the questionnaire. Thirty seven (41.1%) attributed treatment default to high cost of medicines, 29 (32.2%) sought alternative/herbal treatment and 26 (28.9%) had transportation difficulties. Defaults due to financial resource constraints (20%), side effects of the medicines (17.8%), shortage of medicines (12.2), poor tolerance (9%) and inability to attend clinic (7.8%) were also identified.

Conclusion: High cost of medicines, alternative treatment seeking, transportation difficulties and financial resource constraints were identified as major reasons for treatment default. A further study on the factors associated with these reasons will inform outcome improvement interventions.

P-0976 | The State of Health Education and Physical Activity (PA) During Treatment of Child Cancer

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Background/Objectives: Most cancer children are hospitalized over six months for infection prevention. Their range of activities is significantly restricted. This research aimed to clear the state of health education and PA during cancer treatments.

Design/Methods: Mailed questionnaires to nurses of 182 hospitals where cancer children are treated.

Results: Ninety-five questionnaires returned. Forty-five (47.4%) nurses have carried out health education to cancer children and families, and 22 (23.2%) haven't. Over 50% of nurses who answered "YES" provide opportunity of understanding of infection prevention, mouth care, chemotherapy and medicine. On the other hand, about PA, only 30% of nurses have carried out, although about 90% of nurses think these care are significant. Nurses, doctors, pharmacists, children's nurses, dental hygienists, dieticians and physical therapists are involved in these educational cares.

PA are rehabilitation by therapists (63.2%) and taking a walk going out of the ward (25.3%), regular group activities (18.9%) and exercising with video games (12.6%). Furthermore, nurses encouraged children to increase PA by clearing dishes by themselves after meals, using wash rooms out of their room but not in their room's, and increasing activity time by playing.

Nurses think reasons for necessity of these care are: many children often feel that walking is tiring and difficult, especially going school after discharge is very difficult, they are often constipated and the developmental delay risk is possibly increased. But nurses also think that it was difficult to encourage children to PA while their condition is not good or they have to stay in their own room because of infection prevention, nevertheless PAs are essential.

Conclusion: There was little implementation of health education on PA for hospitalized cancer children, but most nurses recognized its necessity. And though they felt difficulty to continue the PA in daily care, they have been trying encourage children for activities.

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P-0977 | Quality of Pain Control in a Home Based Paediatric Palliative Care Model in Nicaragua, Using Subcutaneous Elastomeric Pumps: A Qualitative Case Series

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Background/Objectives: More than 80% of children with cancer experience pain and suffering during the course of their disease; adequate pain control in a low-income country (LIC) where

oral morphine is not available represents a major challenge. One of the scopes of the paediatric palliative care program is to guarantee adequate symptom control particularly in patients with progressive disease in a home based model centered in patients and families' needs. The aim of the study was to identify the quality of pain control using subcutaneous continuous morphine infusion through elastomeric disposable analgesia pumps.

Design/Methods: A retrospective, qualitative case series including 10 patients ages one to fifteen years who presented with disease progression between January 1st 2014 and December 31st 2015 treated with subcutaneous morphine supplied by continuous infusion by elastomeric pumps. Pain control was assessed evaluating patients and parents during treatment using, Baker-Wong, Faces and Numeric Scales according to patients ages. Satisfaction of parents with pain management and symptom control were assessed using a telephonic questionnaire and graded using the Linkert scale.

Results: From January 1st 2014 to December 31st 2015 ten patients with progressive disease with Osteosarcoma(2), Soft Tissue Sarcoma (4), Retinoblastoma(1), Bilateral Wilms Tumour(1), Medulloblastoma(1) and Hodgkin Lymphoma(1) received home based patient centered palliative care. Pain control was adequate in 70%. Three patients were admitted due to poor dyspnea control at the end of life.

According to parent's perception using Likert scale, pain was adequately controlled in 80% of cases. Distressing symptoms like dyspnea and agitation were moderately control at home.

Conclusion: Continuous subcutaneous morphine infusion through elastomeric pumps in the absence of oral morphine guarantees adequate pain control in a LIC home based palliative care program. Evaluation of parent's perception of symptom management provides a good indicator of quality of Pediatric Palliative Care.

P-0978 | Chemotherapy Standardisation in Paediatric Oncology: The Our Lady's Children's Hospital (OLCH) Dublin Experience

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Background/Objectives: Several paediatric hospitals (Children's Hospital Philadelphia, Sick Kids Toronto) and organisations (COG) have developed chemotherapy standardisation programmes to reduce risk, increase efficiency and decrease cost associated with the prescription, preparation and administration of chemotherapy in children.

There is huge variety in European paediatric chemotherapy protocols using many chemotherapy doses, infusion times, hydration and supportive medicines for the same drugs. This introduces significant, unnecessary risks and complexity. Our aim is that all children at our institution should have chemotherapy administered according to a standard institutional protocol.

Design/Methods: We established a multi-disciplinary chemotherapy standardisation group. The project was developed in association with a hospital quality improvement initiative.

We reviewed all treatment protocols in use at OLCH and assessed the variation in chemotherapy administration. We performed staff and parental questionnaires regarding their perceptions of the variability in administration, supportive medicines and discharge times. We held a meeting of all senior departmental management to review and critique the project followed by multiple staff education sessions to implement the recommended changes.

Results: There is huge variation in methods of chemotherapy administration in European paediatric oncology protocols particularly in those using doxorubicin, cisplatin, ifosfamide and cyclophosphamide. For example doxorubicin is routinely given in 11 different dose schedules and 5 different infusion times.

We have developed a standard institutional document which determines how chemotherapy and supportive medicines are administered. This limits variation and risk, increases staff efficiency and decreases lengths of stay for hospital admissions.

Conclusion: There is unnecessary variation in the way chemotherapy is administered to paediatric patients in Europe. Standardising doses, length of chemotherapy infusions and the use of associated hydration/supportive medicines should be considered. There is little evidence to say that standardisation would be detrimental in terms of patient outcomes. Chemotherapy protocols can be standardised, reducing potential risk and increasing staff and ward efficiencies.

P-0979 | The Impact of Improving Nutrition During Induction Chemotherapy in Children with High-Risk Neuroblastoma

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Background/Objectives: High-Risk Neuroblastoma (HR NBL) treatment advocates intensive induction chemotherapy combining chemotherapeutic agents. These combinations are profoundly emetogenic, resulting in anorexia and poor nutrition, requiring supplementary enteral feeding.

Our institution introduced a new anti-emetic guideline in 2010 incorporating regular use of dexamethasone in addition to ondansetron for all highly emetogenic chemotherapy protocols.

Design/Methods: We performed a review of all paediatric patients with HR NBL diagnosed between 2005 and 2015 and treated according to the HR-SIOPEX NBL trial. We collected demographics, disease-related and nutritional data.

Results: 58 patients were diagnosed with HR-NBL between 2005 and 2015. Median age was 2.67 years (range of 0.16-7.41 years). The cohort was divided into group A (2005-2010) and group B (2010-2016).

Complete nutritional data were available for 28 patients in group A and 26 patients in group B. There was a statistically significant difference in weight (diagnostic v end induction) at D80 of induction (rapid COJEC), with a median of -4% (range -16 to +8%) in Group A and median of +3% (range -7 to +28%) in Group B (p=0.0002).

Group A had a greater negative weight-for-age z score change than those in Group B. More patients in Group A required nutritional support, with a greater proportion of their estimated

calorie requirements being provided by supplements during induction compared to patients in Group B.

Patients in group A were admitted with fever/infection a median of 4 times (range 1-8) during induction compared to a median of 3 times (range 0-8) for Group B.

Conclusion: Dexamethasone reduced nausea and vomiting, improving oral intake with less weight loss. Patients needed a smaller volume of enteral feed to meet their calorie requirements. Day 0-40 is a key period when more aggressive dietetic input may lead to improved nutrition. There was a trend towards fewer infection-related admissions in the group with improved nutrition.

P-0980 | Initial Assessment for Prediction of Adverse Outcomes in Children with Febrile Neutropenia at Emergency Department

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Background/Objectives: Febrile neutropenia (FN) is the most common cause of children with cancer presenting to emergency department (ED). Previous studies showed several clinical and laboratory markers for prediction of adverse outcomes in these patients. This study aimed to identify initial presenting characteristics at the ED correlated with adverse outcomes of children with FN.

Design/Methods: We analyzed the data of children with cancer presenting with FN at ED between 2010 and 2013. The patients were classified into stable and unstable groups according to our institutional guideline. The initial data included clinical characteristics, time to door (TTD), time to antibiotic (TTA), and CBC. Severe infectious outcomes were bacteremia and sepsis. Adverse outcomes consisted of receiving inotropic drugs, ICU admission, and death. Significant risk factors for predicting these adverse outcomes were statistically analyzed.

Results: There were 235 FN episodes classified into stable (43.8%) and unstable (56.2%) conditions. The median age of the patients was 6 years (IQR; 3.9-11.1 years). Acute leukaemia was the most common underlying disease. Bacteremia and sepsis occurred in 19 (8.1%) and 17 (7.2%), respectively. Adverse outcomes including inotropic drugs, ICU admission, and death were found in 10 (4.3%), 11 (4.7%), and 2 (0.9%), respectively. Using multivariate analysis, the risk factors for bacteremia were high-risk cancer (relapsed ALL and ANLL) and unstable condition. The temperature (T) > 39°C at ED was significantly associated with sepsis and adverse outcomes. The factors associated with prolonged length of stay were high-risk cancer, T > 39°C, and ANC < 500/mm³.

Conclusion: In this study, the initial risk characteristics of FN were high-risk cancer, unstable condition, T > 39°C, and ANC < 500/mm³.

P-0981 | Fertility Preservation Methods for Young Adolescent Patients Following Cancer Diagnosis

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Background/Objectives: Cancer treatment can affect the gonads. Thus, we have established practices for securing future reproductive potential.

Design/Methods: Since 1997 (males) and 2016 (females) sperm and ovarian tissue cryopreservation has been proposed to newly-diagnosed patients. As we are allowed admission to patients <16 years old (<14 until 2007), our patient pool was limited. Patients in good general condition (excluding leukaemias), demonstrating Tanner stage≥III and adequate testicular volume (males) or regular menses (females) were eligible, if few days delay in initiating treatment was not jeopardizing their cure prospective. Sperm collection and diagnostic spermogram were performed simultaneously. Pelvic ultrasound and sex hormone measurements were necessary for girls.

Results: Sperm cryopreservation was proposed to 21 boys, median age 14.7 years (range, 12.2-17.1) diagnosed with: Hodgkin Lymphoma (12), Non-Hodgkin Lymphoma (2), Sarcomas (7). Four families denied to proceed due to religious conflicts and 1 patient did not produce sperm due to paternal attitude. For the remaining 16 patients, successful sperm donation was obtained 1 to 3 times. One Hodgkin Lymphoma patient was azoospermic and the remaining 15 patients had normal spermogram (10) or oligospermia (5). Ovarian tissue cryopreservation without prior stimulation has been proposed to 2 families (Hodgkin Lymphomas) and 1 has successfully completed the process. None of the preserved products has been requested for fertilization so far. The young patients understood and complied with the procedure readily. Facing fertility preservation issues strengthened patients' expectations for long-term survival.

Conclusion: With proper approach and explanations, with older siblings support, our young patients proved mature and competent in handling complex issues, like future fertility preservation, while facing the diagnosis of malignancy. The procedure was fast and effective. In parallel, fertility preservation attempts imposed to the young patients our strong expectation for their long-term survival and our manifold approach to their malignancy treatment.

P-0982 | Optimizing Vap Scars after Childhood Cancer Treatment

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Background/Objectives: Majority of the paediatric cancer patients are treated with chemotherapy using Venous Access Ports (VAP). However, after surgical removal of the VAP often prominent scars remain, which can be quite debilitating for patients. Due to lack of standardized care for VAP-scars, the aim of this study was to determine the efficacy of two different treatments for optimal healing of VAP-scars.

Design/Methods: Pediatric cancer patients (n=20) were included prior to surgical VAP-removal. Patients had the option to either choose from Meridian Color therapy (MCT), Silicone cream (Dermatix®) or no additional treatment after VAP-removal. Assessment of scars was done prior to and 3, 6 and 12 months after surgical VAP-removal. High quality photos of scars were made and patients were asked to evaluate their scars, using POSAS-patient questionnaire (parents filled out questionnaire if patients were < 8 years). Two independent dermatologists also assessed the scars, using photos and POSAS-observer questionnaires. To identify whether Dermatix® or MCT is associated with better scar healing than without additional treatment, Mann-Whitney-U-tests were used.

Results: Data were collected from March 2014 till March 2016. A total of 21 scars were evaluated, 8 were treated with Dermatix®, 7 with MCT and 6 without additional treatment. After 12 months of follow-up both patients and dermatologists noted VAP-scars had healed better after MCT compared to those without treatment (P=0.010 for both POSAS-patient and POSAS-observer). Interestingly, prior to VAP-removal, scar tissue assessed in the MCT group was significantly worse compared to scars with no treatment (P=0.007). No significant differences were observed between VAP-scars after Dermatix® use and those with no treatment (both POSAS-patients (P=0.055) or POSAS-observer (P=0.240) scales).

Conclusion: Meridian Color Therapy showed better results and could be used for optimizing the healing of scars after surgical VAP-removal in paediatric cancer patients.

P-0983 | Cancer Rehabilitation of Children with Solid Malignant Tumours

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Background/Objectives: Cancer rehabilitation is becoming more of a focus for the field of physiatry due to increased longevity and the side effects of treatment.

Design/Methods: Chart analysis was conducted on 88 children at the mean age of 10,11 ± 0,55 years (aged 9 month - 19 years), 46 (51,7%) males, 42 (47,2%) females treated for primary solid malignant tumors by chemotherapy, radiotherapy, oncologic surgery, included limb-sparing procedures. Histologically, 29 (33,0%) patients had ESFT, 20 (22,7%) - OS, 6 (6,8%) STS, 13 (14,8%) - CNS, 5 (5,7%) neuroblastoma, 4 (4,5%) neuroblastoma, other - 11 (12,5%). The most often affected area was lower extremity - 33 (37,5%) cases, abdomen - 15 (17,0%), CNS - 13 (15,9%), 41 (46,6%) patients had distant metastases. This study evaluated the short and long-term changes in physical fitness of a child with a childhood malignancy; using an individual rehabilitation program, consist with combined physical exercise, kinesiotherapy, aquatic rehabilitation, laser therapy, massage, gait training, and orthopaedic correction implemented during and shortly after treatment. Training is performed individually, under the supervision of an experienced paediatric physical therapist.

Results: 49 patients (from 88) were alive without disease, died - 14, relapse occurred in 7 cases (5 patients are alive), 10 patients with died from progression, 2 patient died from fatal toxicity. The individual rehabilitation programs are well tolerated. We suggest that the usage of an individual rehabilitation program can decrease pain, improve muscle strength and range of motion in joints, an increased supply of blood to the muscles, higher muscle metabolism, and more circulation in the limbs, improves tissue nutrition and helps the healing process.

Conclusion: Childhood cancer patients undergoing long-term cancer therapy may benefit from an individual rehabilitation program since it may maintain or enhance their physical fitness and increase their quality of life.

P-0984 | A Systematic Review of the Lived Experience of Young People with Cancer, Specifically Bone Tumours

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Background/Objectives: Aim:

Systematic review on the lived experiences of young people cancer

Based on patients' experiences, to identify factors that could be incorporated into an adolescent cancer care pathway with a specific focus on the needs of these adolescents.

Design/Methods: A modified qualitative systematic review with a descriptive qualitative research methodology. Using two critical appraisal tools 6 studies met the inclusion/exclusion criteria.

Results: Thematic analysis was used to systematically organise the findings into four themes: social functioning; school; resilience; self-perception and loss of normality and education; and communication. Results showed persistently lower scores and reduced coping strategies in maintaining physical, emotional and social resilience, reduced quality of life and loss of normality and social functioning, compared to healthy peers.

Conclusion: Physical, emotional, psychological and social resilience is greatly reduced, resulting in a sense of loss of control and normality leading to social isolation and a change in their sense of self perception and inability to maintain their basic needs and activities of daily living. The deficits in the literature highlights the need for further qualitative studies on the actual lived experience of the adolescents in order that achievements, social interaction, social acceptance, emotional and social resilience is comparable to their healthy peer group. Further research will assist health care professionals in providing a more comprehensive approach to care and lead to reintegration post treatment from a place of illness to health through on going parallel care planning from the outset of treatment throughout care and into long term follow up robust care pathways.

P-0985 | Study of Nutrition Related Myths and Practices in Families with Childhood Cancer

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Background/Objectives: Malnutrition is associated with inferior survival and increased chemotherapy toxicity. The present study was conducted to evaluate the level of knowledge of nutrition and hygiene and assess the impact of nutritional education in families with childhood cancer.

Design/Methods: Mothers of children < 18 years of age undergoing treatment for cancer at Cancer Institute, Chennai, during January 2016 were included in the study. All parents participate in a nutrition and hygiene orientation program conducted our hospital. A structured questionnaire on diet and hygiene in native language was administered by a physician to the parents.

Results: The study enrolled mothers of 72 patients. The median age of patients was 8 years and 51/72 (71%) were males. Maternal literacy level was less than secondary school level in 50% of mothers. Malnutrition, normal nutrition status and obesity was seen in 32%, 62% and 6% of patients respectively. However, only 21%, 62% and 0% of mothers of malnourished, normal and obese patients respectively concurred with their child's objective nutritional assessment. Diet was linked to cancer was perceived by 20% of mothers and 37% of mothers had changed their child's diet after diagnosis. Inclusion of meat in child's diet was avoided by 37% of mothers after diagnosis. 36% of mothers felt that specific foods could increase white blood cell counts. Only 4% of mothers believed that milk products should be avoided. Street food and tap water was safe to consume was reported by 6% and 10% of mothers respectively. Junk food, meat and raw food were perceived as harmful, while eggs, fish, nuts and protein powder were perceived to be beneficial.

Conclusion: Diet counselling had a positive impact on parents nutrition and hygiene awareness. Intake of meat products was restricted during treatment. Parents perception of child's nutritional status is different from objective assessment.

P-0986 | Complications of Percutaneous Endoscopic Gastrostomies in a Regional Paediatric Oncology Centre

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Background/Objectives: Percutaneous Endoscopic Gastrostomies (PEGs) are often highly beneficial to the nutritional wellbeing of children with cancer but have been associated with substantial complications, including significant infection. We undertook a comprehensive service evaluation to explore the use of PEGs with focus on complications and particularly infection rate.

Design/Methods: The medical records of all paediatric oncology patients who had a PEG placed between January 2009 and December 2015 at Alder Hey Children's hospital, Liverpool, were retrospectively reviewed. A numerical grading was used to assess infection severity, ranging from 1 (Erythema at PEG site) to 4 (Surgical Removal of PEG).

Results: Seventy-two patients were identified (38 male, 34 female), with a median age of 6.5 years (range 0.083-19.25). Diagnoses were categorised into CNS tumours (n=18), solid tumours outside the CNS (n=35) and leukaemia & blood disorders (n=19). Treatment protocols were categorised into high risk (n=49) and low/average risk groups (n=22), principally based on recent guidelines from the Royal College of Nursing. One hundred and eighty complications occurred in 60 patients, including 131 episodes of infection in 55 patients. Minor infections (Grade 1 and 2) accounted for 78.6% of episodes while the remainder were major infections (Grade 3 and 4). Fifteen patients had infections within 7 days of PEG placement. The median neutrophil count at the time of infective episodes was $0.18 \times 10^9/L$. There was a statistically higher number of infections in patients undergoing high-risk treatment regimens (p=0.03) as well as higher infection rates in patients with tumours outside the CNS and the youngest patients in the study (0-4 years), although this was not statistically significant.

Conclusion: Further studies are needed to confirm whether specific diagnoses and treatment regimens has an impact on local PEG site infection and which interventions may reduce the risk of complications.

P-0987 | Outcome of Empiric Therapy for Febrile Neutropenic Patients at Paediatric Oncology Department at South Egypt Cancer Institute

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Background/Objectives: The goal of initial empirical antibiotic therapy is to prevent serious morbidity and mortality due to bacterial pathogens until the results of blood cultures are available to guide more precise antibiotic choices.

Purpose: Assessment of the outcome of empiric therapy in febrile and neutropenic patients at Pediatric Oncology Department In South Egypt Cancer Institute.

Design/Methods: Prospective study included all patients admitted to Pediatric Oncology Department, South Egypt Cancer Institute with fever and neutropenia who are subjected to empiric antibiotic therapy either high risk or low risk, piperacillin/tazobactam + amikacin were given to high risk patients and cefotaxime + amikacin were given to low risk patients as initial therapy, antifungal therapy was added on day 5 fever neutropenia for high risk patients, vancomycin, antiviral and antianerobe were added when needed.

Results: Low risk patients had a better outcome with short periods of neutropenia and less complications. Patients with haematological malignancies were mostly high risk patients with worse outcome and prolonged neutropenia, Gram positive bacteria and fungal infection were

common factors in patients with severe morbidity and mortality, using prophylactic antifungal agents had a less value in patients' outcome during fever neutropenia.

Conclusion: Modified empirical therapy in management of fever neutropenia according to the environment and microbial colonization is mandatory, better methods for diagnosis and management of fungal infection are also required.

P-0988 | Tracking Children with Acute Lymphoblastic Leukemia Who Abandoned Therapy: Experience, Challenges, Parental Perspectives and Impact of Treatment Subsidies and Intensified Counselling

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Background/Objectives: Refusal for treatment and therapy abandonment are important contributors of poor outcome of childhood ALL in resource-poor countries. However, few studies have addressed therapy abandonment, the reasons behind it and parental perspectives in Indian children with ALL.

Design/Methods: The present study, conducted in a tertiary care teaching hospital in North India from January 2007 through September 2013, has attempted to track all children with ALL who refused/abandoned therapy, to ascertain the causes and the outcome of therapy abandonment/refusal. Parental perspectives were assessed using a pre-structured telephonic/mail interview. Measures to prevent abandonment were introduced in the form of treatment subsidies and intensified multistage counselling.

Results: Of the 77 (of 418) children who abandoned therapy, 17 (22%) refused upfront while the rest abandoned during various phases of chemotherapy. Only 39 (50.6%) of these 77 families could be subsequently tracked. Financial problems, too many dependents at home, wrong perceptions about cancer led to abandonment in majority of children. Children who abandoned treatment before completion of induction had a significantly shorter survival than who abandoned post-induction ($p < 0.0001$). Intensified pre-abandonment counselling and subsidised treatment led to significant reduction in abandonment rates ($p < 0.0001$).

Conclusion: Abandonment and refusal of therapy was common and led to poor outcome in children with ALL. Financial problems and wrong beliefs were the important contributors behind abandonment. Treatment subsidies and intensified counselling helped in improving compliance. Similar targeted interventions tailored to the care setting may help in improvement of outcome of childhood ALL in the developing countries.

P-0989 | Time to Antibiotic Administration in Febrile Neutropenia in Children with Cancer: A Joint Physician & Nurse Quality Improvement Audit

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Background/Objectives: Prompt antibiotic administration, defined as ≤ 60 minutes from patient admission, is associated with improved outcome in febrile neutropenia in children with cancer. In this context, an audit was performed in the Paediatric Oncology Department at La Fe Hospital in order to verify the quality of the assistance.

Design/Methods: Data from all consecutive patients hospitalized for febrile neutropenia in our Unit from October 2014 through September 2015 were analyzed by paediatric oncology nurses. Patients who had received HSCT were excluded. Time to antibiotic administration (TAA), age, sex, type of diagnosis, risk factors for febrile neutropenia according to IDSA guidelines, place of initial admission (urgency room vs day care clinic), persistent fever, blood test at admission and number of blood cultures were analyzed. Continuous variables were compared using Student's *t* test; categorical variables were compared using chi-square or Fisher's exact test when applicable. $P < 0.05$ was considered statistically significant. Data were analyzed using SPSS 20.0.

Results: Twenty-nine hospitalizations for 22 patients met the inclusion criteria. Median age at admission was 5.4 years (range: 0.6–14.0) with male/female ratio of 1:1. Diagnosis was mainly leukaemia and lymphoma (18/22, 82%). Median TAA was 135 minutes (range: 30–360). TAA ≤ 60 minutes was achieved in 8/29 episodes (28%). An antibiotic administration based on blood test results was significantly correlated to delayed TAA ($p = 0.00$). In spite of current institutional guidelines which recommended at least two blood cultures at admission, only one blood culture was performed in 15/29 episodes (52%). All episodes had a favorable evolution under antibiotics.

Conclusion: In our Unit, time to antibiotic administration in patients with febrile neutropenia is longer than recommended. The feasibility of the administration of a first dose of antibiotics in patients with suspected neutropenia without waiting for blood test results will be prospectively evaluated.

P-0990 | Selective Use of Implantable Venous Access Devices for Paediatric Oncology Patients in Botswana

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Background/Objectives: Implantable central venous access devices (ports) are an integral part of the safe and efficient delivery of chemotherapy to children in high-income countries. However, the use of ports in low and middle-income countries (LMICs) is limited by lack of surgical expertise, equipment, and resources to manage the presumed increase in the risk of port-related complications, such as infection and thrombosis.

Design/Methods: This retrospective case series reviewed the paediatric oncology patients treated with ports at Princess Marina Hospital (PMH) between January 2013 and December 2015. Variables of interest included patient diagnosis, age, indications for port placement, and frequency of port access, number of documented infections, and reason for port removal.

Results: Between January 2013 and December 2015, twenty ports were placed by a skilled paediatric surgeon in South Africa. The most common diagnosis associated with port placement was Acute Lymphoblastic Leukaemia ($N = 15$), while the remainder were placed for a variety of solid tumours. Indications for port placement included a diagnosis necessitating chemotherapy and difficult peripheral venous access. There were 100 port access events at PMH over this 3-year period, all of which were either performed by or under the direct supervision of a paediatric hematologist/oncologist. There were no documented port infections or episodes of thrombosis associated with the access events in Botswana. One patient required revision of the port due to an ineffective location of the catheter tip.

Conclusion: This experience of port utilization in Botswana reveals a low level of complications. Limiting the number of health care professionals accessing the ports may have been a factor in decreasing the risk of infection in this population. With appropriate surgical expertise and a standardized approach to maintenance, ports have the potential to be a safe and effective alternative for delivery of chemotherapy in LMICs.

P-0991 | Hepatitis C Viral Infections among Families of Children with Cancer in Egypt

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Background/Objectives: Egypt has the highest worldwide prevalence of Hepatitis C virus infection. It is estimated that about 15 million Egyptians currently suffer from Hepatitis C. Every year there are 170,000 to 200,000 new HCV cases. Horizontal interfamilial transmission of the virus has been demonstrated previously in the general population; however, available data in families of children with cancer are limited. The present work aimed to study the prevalence of hepatitis C viruses among families of known HCV-positive children with cancer and to identify risk factors for this infection.

Design/Methods: Three hundred and five household contacts of paediatric cancer patients diagnosed with HCV infection were included in this study. They were invited for face-to-face questionnaire including socio-demographic data, medical routes of infection, previous surgery, hospitalization and blood transfusions, invasive procedures such as urinary catheterization, sutures, abscess drainage, biopsy and hemodialysis, history of tattooing, and common use of nail clippers, scissors and razors at home. For all household contacts, HCV serology using the enzyme-linked immunosorbent assay (ELISA) and polymerase chain reaction (PCR) were checked. In seropositive children, HCV-RNA were measured. The relationships with study parameters were statistically analyzed.

Results: Thirty-six of 305 household contacts were proved to have HCV by PCR (11.8%). Mothers had higher risk of HCV than fathers, brothers and sisters ($P < 0.001$). The risk of infection increased with aging and illiteracy. Those who had contact with HCV index bleeding, did not wear gloves during handling them, and had needle-prick injuries had significant higher HCV prevalence. Moreover, sharing nail clipper at home had significant higher risk to infect the household contact ($P < 0.005$).

Conclusion: There is a relatively higher prevalence of HCV infection among families of HCV-positive children with cancer. Health education programs are essential to reduce the HCV burden, and to increase the awareness of HCV transmission of the general population.

P-0992 | Vancomycin Dosage in Paediatric Cancer: Variability, Age Effects, and Toxicity

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Background/Objectives: Children with cancer require higher doses of vancomycin to achieve minimum inhibitory concentrations. Target trough levels are 10–20 mg/l. Previously, our regional policy was to start immediate empirical treatment with vancomycin and piperacillin-tazobactam in children with neutropenic fever. Most children required several dose increases.

Design/Methods: A retrospective audit of 100 treatment episodes was performed using prescription charts, clinical notes and laboratory results to determine initial doses, dose changes and final doses required to achieve therapeutic blood levels. Microbiological data also were obtained. Final dosage, daily dosage schedule, and body weight were used to derive final (therapeutic) daily dose per body weight (TD/W). This figure was subjected to an analysis of covariance with predictors age and weight, and contrasted against published figures for therapeutic vancomycin dosage in children.

Results: TD/W was strongly predicted by body weight itself ($F(1, 96) = 7.41, p = 0.0077$) and by the interaction of body weight with age ($F(1, 96) = 4.33, p = 0.04$) but not by any effect of age alone given its covariation and interaction with weight. Mean TD/W was 50% greater than, and thrice as variable as, previously published figures; 10 episodes exceeded the maximum published TD/W of 70 mg/kg. This effect was driven largely by the youngest (lightest) patients; when 1–2-year-olds were eliminated, mean TD/W became comparable to published figures. Toxic (≥ 20 mg/l) trough levels were reached in 17 episodes, the greatest exceeding 50 mg/l (median 28.0 mg/l). Nineteen episodes featured vancomycin-sensitive organisms.

Conclusion: Children with cancer – especially the youngest – may require greater D/W than those with non-malignant diagnoses to achieve therapeutic vancomycin levels. Nevertheless, variability is high and toxic levels are fairly common. Furthermore, vancomycin is not often microbiologically indicated. Currently the regional policy is to start vancomycin only if a sensitive organism is isolated, or if there is high clinical suspicion.

P-0993 | Nutritional Status at Diagnosis in Paediatric MalignanciesP. Soni¹, S. Jain¹, G. Kapoor¹¹Rajiv Gandhi Cancer Institute & Research Centre, Paediatric Haematology and Oncology, Delhi, India

Background/Objectives: Nutritional status of children with cancer is clinically important. The study aimed to determine the nutritional status of children at the time of diagnosis and correlate it with early morbidity and influence on treatment.

Design/Methods: In this prospective study, 65 children underwent assessment of nutrition by measurement of body mass index (BMI), arm anthropometry (Mid upper arm circumference, MUAC), triceps skin fold (TSF), body composition by DEXA scan (wherever feasible). BMI and lean body mass (LBM) were expressed as z-scores and MUAC and TSF as percentiles and early morbidities were assessed in relation to these.

Results: Median age at diagnosis was 9 year with male to female ratio of 5:1. Diagnostic categories of the group included leukaemia 29(44.6%), bone tumors 17(26%), lymphoma 11(16.9%), sarcomas 5(7.6%), neuroblastoma 2(3%) and germ cell tumour 1(1.5%). The duration of illness was more than one month in 72% patients. There was history of weight loss in 18.4% and loss of appetite in 81.5% patients. Malnutrition was seen in 16.9% by BMI for age criteria ($z < -2$), 40% by MUAC (<5th percentile), 9.2% (<5th percentile) by TSF. DEXA scan was done in 29 patients out of which 51.7% patients had z-score < -2 for lean body mass. As per BMI criteria, the difference in well nourished and malnourished group, febrile neutropenia (FN) (63% vs 91%), interval admissions (72% vs 91%), chemotherapy delays (50% vs 27%) and nutritional support (20% vs 36.3%). LBM in well nourished and malnourished group, FN (35.7% vs 93%), interval admissions (35.7% vs 93%), chemotherapy delays (21.4% vs 46.6%) and nutritional support (21.4% vs 40%). MUAC & TSF did not reveal difference in morbidities.

Conclusion: Body composition by DEXA scan and BMI are better predictors of malnutrition and morbidities.

P-0994 | Working for Normality: The Impact of Infection Prevention and Control on Children with Invasive Devices at HomeC. Soto¹, C. Tarrant¹, M. Dixon-Woods¹¹University of Leicester, Department of Health Sciences, Leicester, United Kingdom

Background/Objectives: The lives of children with cancer have been transformed by the use of invasive devices. Devices such as tunneled central lines and gastrostomies are used to take blood samples, or to administer nutrition or medications (including chemotherapy). Such devices are a potential source of healthcare-associated infection (HCAI), with serious consequences for children, families, and health services. Strict adherence to infection prevention and control (IPC) practices can significantly reduce the incidence of HCAs in the hospital setting. Children with cancer spend much of their time at home where their daily care is carried out by families, supported by professionals. Implementing IPC practices in this environment poses unique challenges.

Design/Methods: We explored the real-life challenges faced by children, families, and professionals carrying out IPC practices in the home. Semi-structured interviews were conducted with twenty parents and children, and twenty professionals who support the home care of children with invasive devices.

Results: The safe care and maintenance of invasive devices in the home imposes a substantial burden on family life. Families and professionals work to sustain normality in their lives whilst adhering to IPC practices. The labour undertaken by families to maintain this balance adds substantially to their emotional, cognitive, and technical burden. Professionals may not fully appreciate the demands that are placed on families; thus the systems for supporting IPC practices in the home are limited.

Conclusion: The impact of IPC on children and families in the community is poorly recognised. Supporting families to manage the challenges posed would improve patient safety and relieve the burden on families.

P-0995 | Clostridium Difficile in Paediatric OncologyC. Sprinz¹, J. Ponnampalam¹, N. Elumogo², A. Soman¹¹Norfolk and Norwich University Hospital, Paediatrics, Norwich, United Kingdom; ²Norfolk and Norwich University Hospital, Microbiology, Norwich, United Kingdom

Background/Objectives: Children receiving treatment for cancer are more susceptible to Clostridium difficile infection (CDI). At present there are no evidence-based consensus guidelines on how to manage these cases.

Design/Methods: A literature review was undertaken to identify evidence-based management for CDI in children with cancer, and a collaborative audit between the paediatric oncology (UK Level 2 Shared Care Unit) and microbiology departments was performed. Clostridium difficile toxin-positive episodes in all children – with or without cancer – were identified from the Infection Control database from its inception in February 2008 to March 2016. Electronic discharge summaries were reviewed to determine presenting complaint(s), comorbidities, and antibiotic exposure, and the management of CDI was compared to Public Health England (PHE) and other guidance for adults.

Results: Twenty-five children with paediatric CDI were identified. Ten (40%) of these had cancer, but they contributed 17 (51%) of 33 toxin-positive episodes, and 4 (80%) of 5 cases of repeated toxin-positive episodes ($U=49$, one-tailed $p < 0.08$). One child had 4 episodes with 3 different ribotypes. Adequate background information was available in 29 episodes, 25 (86%) of which were associated with recent broad-spectrum antibiotics. Management details were available in 25 episodes, 19 (76%) of which were managed correctly according to adult PHE guidance. The most common deficiency was failure to institute second-line antibiotic treatment where first-line had failed.

Conclusion: In children with cancer, who receive multiple and sometimes prolonged courses of broad-spectrum antibiotics, risk of sepsis must be balanced with risk of CDI. The recent lowering of neutrophil count threshold for febrile neutropenia treatment is a step in the right

direction. Close collaboration between microbiologists and paediatric teams is essential. Development of an evidence-based guideline for treatment of CDI in children would help to reduce variations in management.

P-0996 | Evaluation of Serum Procalcitonin, Serum Interleukin-6 and Interleukin-8 in Children with Febrile Neutropenia and Cancer to Predict Risk GroupsA. Srinivasan¹, P. Balasubramanian², N. Kumar¹, S.G. Suresh¹, J.X. Scott¹¹Kanchi Kamakoti Childs Trust Hospital-The Childs Trust Medical Research Foundation, Department of Paediatric Hemato-Oncology, Chennai, India; ²Kanchi Kamakoti Childs Trust Hospital-The Childs Trust Medical Research Foundation, Department of Biochemistry, Chennai, India

Background/Objectives: Early diagnosis of sepsis in children with febrile neutropenia remains difficult due to non-specific clinical and laboratory signs of infection. There is a need to assess the utility of inflammatory markers in clinical risk assessment for their ability to discriminate between low-risk and high-risk neutropenic patients since presently there is an insufficient data to recommend their routine use.

Design/Methods: This is a prospective study of children on therapy admitted with febrile neutropenia between 2015-2016 and sampled for serum procalcitonin (PCT), interleukin-6 (IL-6), interleukin-8 (IL-8) at admission. The febrile neutropenia episodes were categorized into two groups - Group I: no focus of infection and Group II: clinically/microbiologically documented infection. Statistical analysis for comparison were performed using z-test and Receiver operating curves at various cut-off levels.

Results: A total of 46 episodes of febrile neutropenia were analysed. 76% were categorized as group I and 24% as group II. The mean value of PCT in group II was higher (28.07 ng/ml) as compared to group I (1.03ng/ml) though there was no significant statistical difference. At a cut off level of 2 ng/ml for PCT, sensitivity of 63%, specificity of 91%, PPV of 70%, NPV of 88% were observed. There was no significant difference in the IL-6 and IL-8 levels between both the groups. But at an optimal cut off value of 50 pg/ml, IL-6 had a NPV of 80% and at a cut off level of 130 pg/ml, IL-8 had a NPV of 73%, however with low sensitivity and specificity.

Conclusion: IL-6, IL-8 and PCT can be utilized to define a group of patients with a low risk of sepsis in view of their favorable NPV. The use of these biomarkers together can facilitate early discharge from the hospital, and the use of oral antimicrobial therapy in turn reducing the cost of supportive therapy in a developing country.

P-0997 | Using A Heuristic Approach to Understand the Symptom Experiences of Adolescents and Young Adults (AYAs) with CancerK. Stegenga¹, J. Erickson², C.F. Macpherson³, L. Linder⁴, S. Ameringer⁵¹Children's Mercy Hospital, Haematology/Oncology/BMT, Kansas City, USA; ²University of Wisconsin-Milwaukee, School of Nursing, Milwaukee, USA; ³Seattle Children's Hospital, Oncology Unit, Seattle, USA; ⁴University of Utah, College of Nursing, Salt Lake City, USA; ⁵Virginia Commonwealth University, School of Nursing, Richmond, USA

Background/Objectives: AYAs with cancer suffer numerous distressing symptoms. The biology of their cancers coupled with their developmental stage makes AYAs symptom experiences unique, and effective symptom management remains challenging. To better understand their symptoms and symptom management challenges, we developed the Computerized Symptom Capture Tool (C-SCAT), a heuristic-based iPad application for AYAs to communicate their symptom experience from their perspective. Heuristics are mental rules used to interpret situations, and, with regard to symptoms, are proposed to guide self-management. Four classes of heuristics are pertinent to understanding how individuals evaluate and respond to their symptoms: 1) spatial/temporal mapping; 2) patterning of symptoms based on prior experience, trajectory, control; 3) cultural beliefs and social experience; and 4) active social comparison.

Design/Methods: We conducted a secondary analysis of C-SCAT free-text data from 72 AYAs receiving chemotherapy about priority symptoms, causes, management strategies, and effects of symptoms on daily living. This qualitative data was analyzed using the four classes of heuristics to characterize their symptom experience.

Results: For spatial/temporal mapping, AYAs had less concern with symptoms if mild or time limited. Symptoms such as skin changes, hair loss, dry mouth and cough were viewed this way. For patterning, symptoms such as nausea, vomiting, lack of energy, difficulty sleeping, and lack of appetite tended to occur together and led to isolation and mood changes as AYAs withdrew from typical activities to deal with the impact. Many used self- and medical management for these symptoms (control) with mitigation of isolation/irritability. Pain and nausea were uniformly seen as managed with medication as AYAs reported few additional strategies.

Conclusion: Applying heuristics to symptom assessment is a novel but useful way to help providers understand how AYAs self-manage their symptoms and why they choose specific strategies. Future research is needed to explore application to clinical practice.

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P-0998 | The End-Of-Life Care in Paediatric Cancer Patients in a Medical Center: Chart Review between 2008 and 2015H.L. Su¹, L.M. Wu²¹Kaohsiung Medical University Chung-Ho Memorial Hospital, Paediatric Haematology/Oncology, Kaohsiung, Taiwan; ²Kaohsiung Medical University, School of Nursing, Kaohsiung, Taiwan

Background/Objectives: Despite the dramatically improved outcomes for paediatric cancer patients, cancer is the leading cause of death in Taiwan, accounting for 21.8% of death in 2014.

The paediatric end-of-life (EOF) care has not been extensively explored in the paediatric cancer patients. The study was to evaluate the trends in paediatric cancer EOF care in a medical center from 2008-2016 in Taiwan.

Design/Methods: A retrospective chart review was conducted. All participants were diagnosed with cancer, and died between 2008 and 2015 in the southern medical center in Taiwan. Fifty six participants were included.

Results: The average age at diagnosis, and death were 7.7 ± 4.9 year olds, and 11.3 ± 5.9 year olds, respectively. These patients in their last month of life spent greater than 14 days (82.1%) in the hospital, completed Do-Not-Resuscitate (DNR) (75%), dying in the intensive care unit (69.6%), received related chemotherapy (62.5%), underwent intubation (30.4%), or received cardiopulmonary resuscitation (7.1%). Only 28.6% patients received hospice care or hospice share-care in their last month of life, of these patients 25% started such service within the last 3 days. The care of the paediatric cancer EOF did not change over the study period except for significantly increasing DNR permits, and related chemotherapy in the last month of life.

Conclusion: Overly aggressive treatment was reported in the last month of paediatric cancer patients in Taiwan. A quality of EOF care in paediatric cancer patients should be developed to meet the individuals and family's needs and preferences.

P-0999 | Nutritional Profile and Clinical Outcome of Paediatric Oncologic Patients Admitted to Intensive Care Unit

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Background/Objectives: To assess the nutritional status (NS) of paediatric oncologic patients on admission to the intensive care unit (ICU) and clinical outcome.

Design/Methods: Retrospective study with data collection in electronic record in a paediatric oncology reference center.

Results: From August to December 2015 there were 121 admissions to 97 patients to the ICU, 60 (61.85%) were male and 37 (38.15%) were female, with mean age of 9.5 years old ranging from 0 to 31 years old. The anthropometric assessment could not be done in 13 admissions, 6 (5%) due to the clinical severity of the patient and 7 (6%) due to the short stay of the patient in the ICU (less than 24 hours). In relation to the body mass index (BMI), in 77 (71.3%) assessments, patients had adequate BMI/A score, 11 (11%) assessments resulted in NS with some degree of malnutrition and in 19 (17.6%) assessments patients had BMI/A score compatible with overweight. According to Frisancho, 2008, there is no measurement of arm circumference (AC) for children under the age of 2, therefore 19 (17.6%) assessments were excluded regarding NS from AC and in 3 assessments the AC could not be measured due to the position of the patient in bed. In the other assessments adequate NS was observed in 59 (56.2%) patients, malnutrition in 6 (5.7%) and overweight in 8 (7.6%). During this period 13 (13.4%) patients died, 6 (46%) from the category that was not subject to the anthropometric assessment on admission due to clinical severity, 5 (38.5%) with BMI/A and/or AC showing signs of malnutrition and 2 (15.5%) with result compatible with adequate NS.

Conclusion: The conventional anthropometric assessment in critically ill children has limitations as a result of the clinical conditions of the patient. However, malnourished patients have a higher risk of death.

P-1000 | Complementary and Alternative Medicine: A Survey of its Use in French Paediatric Oncology Centers

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Background/Objectives: Complementary and alternative medicines (CAM) are commonly used in children with cancer despite few evidence of their efficacy. More and more paediatric oncology centers offer these treatments fully integrated to conventional care. A national survey was conducted to assess the frequency and the CAM use in centers affiliated to the SFCE (Société Française des Cancer de l'enfant) in 2015.

Design/Methods: E-Questionnaires were sent to the physicians in charge of supportive care in the 32 SFCE centers.

Results: 29 out of the 32 centers participated (90.62%). Hypnosis (n = 25centres (86.21%)), sophrology (n = 17 (58.62%)), and touch / massage therapy (TM) (n = 15 (51.72%)) are the most common CAM proposed. 52% of the centers declare allowing families to use food supplements (FS), homeopathy (62.7%) and vitamins (48.2%). The most prescribed CAM are FS (58.62%) and homeopathy (31.03%). 82.76% of responders state that over 50% of their doctors support the use of hypnosis, sophrology (65.52%) and TM (65.5%). Hypnosis, sophrology and TM are provided by caregivers of units, in respectively 82.7%, 41.3% and 55.1% of the cases. Most of them graduated in the field. Most of the time the hospital finances the MAC practitioners. Hospital management boards are often informed of these practices, but only few contracts are formalized. The reasons reported for the absence of use of CAM are the lack of training, fear of risk of interactions and conviction of inefficiency. The proportion of centers implementing evaluation process remains low.

Conclusion: This survey confirms that the majority of French paediatric oncology centers allow CAM practice within their units. These are accepted by caregivers, prescribed by doctors, financed by institutions and sometimes integrated into conventional care. These practices are underappreciated and caregivers receive limited training. Actions should be implemented in order to improve the scientific framework of these practices.

P-1001 | The High Prevalence of Functional Complement Defects Induced by Chemotherapy

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Background/Objectives: Due to intensive (chemo)-therapy bone marrow suppression oncology patients will be more dependent on the non-cellular complement system for host defense against pathogens. Since data on complement functionality in oncology patients are limited, we investigated complement function in relation to the type of malignancy and therapy in a longitudinal cohort of these patients.

Design/Methods: In a large single-center, a prospective non-intervention study was conducted, in which blood samples were taken from patients before, during and after treatment with chemotherapy and/or subsequent admittance for (febrile) neutropenia. The primary end-points of the study were: (1) the presence and prevalence of transient reduced complement functionality, (2) the effect of therapy and malignancy on reduced functionality of complement activation, (3) the association of neutropenia and reduced complement functionality.

Results: Analysis of the complement functionality of 48 patients showed a high percentage of defects in complement activity in the alternative pathway (11.5%), the classical pathway (4.6%) or both (8.8%) at different time points in these patients. Post-hoc analysis of six different treatment protocols with more than 3 patients each showed distinctive effects of specific therapies. Whereas patients treated for Ewing sarcoma, rhabdomyosarcoma or germ cell tumors showed no defects in complement functionality, patients treated for leukaemia, or osteosarcoma or medulloblastoma showed almost universal reductions in complement functionality. Although we could not explain reduced complement functionality under all conditions, a strong effect was observed following high-dose methotrexate or ifosfamide.

Conclusion: Acquired complement defects occur at high frequency in oncology patients, some of which was directly associated with certain chemotherapeutic drugs. Additional studies are needed to determine the clinical and therapeutic context of complement defects and the possible effect on both treatment or increased risk of infection.

P-1002 | Nutritional Diagnosis of the First 100 Patients in the Hospital Infantil Teleton De Oncologia (HITO)

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Background/Objectives: The American Association for Parenteral and Enteral Nutrition (ASPEN) defined malnutrition as "subacute or chronic disease of the nutritional status, in which a combination of varying degrees of overfeeding or malnutrition and inflammatory activity has led to a change in body composition and decreased function". Malnutrition has been defined but there is an indefiniteness for the nutritional diagnosis; some authors identify body reserves as a more sensitive marker to identify malnutrition especially in patients with solid tumors.

Objective: To establish nutritional status at the time of cancer diagnosis and epidemiological characteristics on the first 100 patients of the Teleton Children's Oncology Hospital.

Design/Methods: To establish nutritional status of paediatric patients at the time of cancer diagnosis. We used three measurements, two anthropometric: BMI/Waterlow body reserves and a biochemistry determination of albumin.

Results: In an initial sample of 100 paediatric cancer patients, 58% were male, average age of 94 months, range from 2 to 220 months, 63% of the sample was found with malnutrition (malnutrition, overweight and obesity), undernutrition was the greatest indicator of malnutrition with 41% paediatric cancer patients, 22% of the sample were overweight/obesity and only 37% of the patients were found to be eutrophic to the time of cancer diagnosis.

The five most common cancer diagnosis were leukaemia, neuroblastoma, TSNC, lymphoma and bone sarcomas, at all was observed higher percentage of malnutrition. The most sensitive indicator for the diagnosis of malnutrition was the measurement of body reserves, identifying the highest percentage of malnutrition by 45% vs. 30% by Waterlow and albumin.

Conclusion: The nutritional status of paediatric cancer patients must be comprehensive, taking into account more than one indicator anthropometricas Waterlow, BMI, body reserves and biochemical such as albumin and prealbumin, being this last indicate more sensitive for diagnosis of nutrition for a lifetime average.

P-1003 | The Influence of Different Fever Definitions on Diagnostics and Therapy after Diagnosis of Fever in Chemotherapy-Induced Neutropenia in Children with Cancer

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Background/Objectives: There is no uniform definition of the temperature limit defining fever (TLDF) in paediatric cancer patients. This study aimed to investigate the influence of different TLDFs on diagnostics and therapy after fever in neutropenia (FN) diagnosis.

Design/Methods: In a single paediatric cancer center using a high TLDF (39°C tympanic temperature) patients undergoing chemotherapy were observed prospectively (NCT01683370). Temperature measurements and key procedures of diagnostics and therapy during FN were recorded. The effect of applying lower TLDFs (range, 37.5°C to 38.9°C) versus 39.0°C on these procedures was simulated *in silicon*.

Results: 45 FN episodes were diagnosed in 20 of 39 study patients (maximum, 6 episodes per patient). Of 3391 temperatures measured, 193 were $\geq 39.0^\circ\text{C}$, and 937 $\geq 38.0^\circ\text{C}$.

For persisting fever ≥ 24 hours, additional blood cultures were taken after start of antibiotics in 31 (69%) episodes in reality. This number decreased to 22 (49%) by virtually applying 39.0°C, and increased to 33 for 38.0°C (73%; plus 11 episodes; plus 24% [95% CI, 13 to 40]).

For persisting fever ≥ 48 hours, intravenous antibiotics were escalated in 25 (56%) episodes in reality. This number decreased to 15 (33%) by virtually applying 39.0°C, and increased to 26 for 38.0°C (58%; plus 11 episodes; plus 24% [95% CI, 13 to 40]).

In reality, the median length of stay was 5.7 days (range, 0.8 to 43.4). In 43 episodes with hospital discharge beyond 24 hours, virtually applying 38.0°C instead of 39.0°C led to discharge delay by ≥ 12 hours in 24 episodes (56% [95% CI, 40 to 71]), with a median delay of 13 hours, and a cumulative delay of 68 days.

Conclusion: Applying lower TLDFs led to relevant increases of diagnostics, therapy, and hospitalization in children with FN. This, in turn, increases treatment-related side effects and costs, and decreases quality of life.

P-1004 | Implementation of a Telephone Triage in Paediatric Haematology Oncology

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Background/Objectives: Our Lady's Children's Hospital Crumlin (OLCHC) is the national referral centre for paediatric haematology oncology in Ireland. A 24 hour phone nursing helpline for parents and staff of 16 Shared Care Centres (National Paediatric Units) has been provided for many years. Recent challenges to the delivery of this service included nursing time required to support the service, change in skill mix such with reduced numbers of experienced nurses to support helpline, cumbersome documentation and inconsistent approach to managing telephone queries. The objective of this quality project was to develop a Haematology Oncology Triage Process to support junior nursing staff in the management of telephone calls from parents and professionals.

Design/Methods: An audit of the current helpline was carried out to identify telephone call topics, the grade of nurse answering the calls, questions asked and advice given, time of calls made to service and the documentation in use was reviewed. A questionnaire was given to junior staff about their experiences of managing the helpline. International telephone triage models were reviewed. A Telephone Triage Guide was developed, guiding staff in the assessment and management of symptoms using core questions, algorithms and advice. The documentation was revised, triage documents were co-located with telephone for ease of use and a staff education programme was delivered.

Results: Nurses were asked to evaluate the new process. They found it was easy to use, relevant, helped to get detailed information from callers and had defined algorithms to provide clear information.

Conclusion: This project has resulted in the development of a robust and consistent approach to managing telephone queries, and has empowered nursing staff to competently assess patient's needs and respond to queries. The next phase will be evaluation of the service users- healthcare professionals and parents.

P-1005 | Eating Behavior During Dexamethasone Treatment in Children with Acute Lymphoblastic Leukemia

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Background/Objectives: Dexamethasone, a highly effective drug in the treatment of paediatric acute lymphoblastic leukaemia (ALL), can induce significant changes in eating behavior and energy intake, which may contribute, together with impaired physical activity and metabolic toxicities to the higher incidence of metabolic syndrome in survivors. Since data are limited to small studies, we prospectively studied eating behavior, energy and nutrient intake during dexamethasone administration in children with ALL.

Design/Methods: Fifty patients (aged 3-16 years) treated with 5-days dexamethasone pulses in the maintenance phase of recent Dutch ALL protocols were included. Data on eating behavior were collected during one dexamethasone course, i.e. before start of dexamethasone (T1), and at day 5 (T2). During the four days of dexamethasone treatment energy intake and nutrient intake (energy percentiles = E%) were assessed using a parent-reported dietary diary and compared with the individual energy requirements.

Results: The energy intake per day (kcal) increased significantly during one dexamethasone course ($P < 0.01$), including an increase of total protein, fat, saturated fat, carbohydrate, and sodium intake. 64% of the patients had a higher energy intake on the fourth day of dexa-

methasone treatment than their energy requirements. Intake of saturated fat (12-13 E%) and salt (1.4-1.9 gram/day) exceeded the healthy range for age and gender. There was a high inter-patient variability in dexamethasone-induced eating behavior, but dexamethasone significantly decreased restraint eating in the total group ($P = 0.04$).

Conclusion: Four days of dexamethasone treatment significantly increased energy intake, including excessive saturated fat and salt intake, and changed eating behavior in the largest subset of patients with ALL. Nutritional and behavioral interventions during dexamethasone treatment are recommended to stimulate a healthy lifestyle, which could potentially reduce the risk of metabolic syndrome at the long term.

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P-1006 | Malnutrition in Paediatric Lymphoma Patients in Malawi is Best Identified Using Mid-Upper Arm Circumference

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Background/Objectives: Among all Malawian children, 22% are underweight. Malnutrition is even more prevalent among children with cancer, and contributes to worse survival compared with resource-rich settings. Acute malnutrition among paediatric cancer patients in sub-Saharan Africa is associated with increased risk for infection and chemotherapy-related adverse effects.

Design/Methods: Children with lymphoma were prospectively enrolled in Malawi between August 2015 and March 2016. Comprehensive baseline assessment included weight, height, and mid-upper arm circumference (MUAC) for all patients at initial cancer diagnosis. Children were classified with severe malnutrition if their MUAC was $< 11.5\text{cm}$ (< 6 years), $< 13.5\text{cm}$ (6-10 years), $< 16\text{cm}$ (10-18 years) as per UNICEF recommendations.

Results: Of 32 patients enrolled, 28 had Burkitt lymphoma, 3 Hodgkin lymphoma, and 1 lymphoblastic lymphoma/leukaemia. Median age was 11 years (range 1-15) and 9 (28%) were female. Most had advanced, bulky disease with 74% having stage III/IV, 86% having Lansky performance score ≤ 70 , and median tumour size being 11 cm (range 3-20). At diagnosis, median hemoglobin was 9.3 g/dL (range 5.5-12.3) and median albumin was 3.2 g/dL (range 1.9-4.9). MUAC identified 22 (68%) children as having severe acute malnutrition, 6 (18%) with moderate malnutrition, and 4 (12%) with normal nutritional status. Using body mass index (BMI) for children ≥ 5 years and WHO weight-for-height for children < 5 years, 48% children classified as malnourished based on MUAC would have been incorrectly classified as having normal nutritional status.

Conclusion: In sub-Saharan Africa, children with cancer typically present with advanced, bulky disease. As a result, MUAC is more sensitive than BMI or weight-for-height to identify children with concurrent malnutrition, as massive tumors may significantly contribute to measured weights at initial diagnosis. Our findings suggest that MUAC should be adopted as a simple bedside assessment to identify paediatric oncology patients requiring nutritional rehabilitation concurrent with cancer treatment.

P-1007 | Supporting Choice in End of Life (EOL) Care: Ten Year Analysis of Sites of Death for Patients of a UK Tertiary Paediatric Haematology/Oncology Service

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Background/Objectives: Little has been documented about the preferred place for end of life (EoL) care within the paediatric population. This study explores the sites of EoL care for patients of a regional Haematology/Oncology service.

Design/Methods: A 10-year retrospective analysis of a tertiary UK Paediatric Haematology/Oncology service was undertaken to identify place of EoL care/death. Data collected included patient demographics, tumour type, cause and site of death. Data is grouped into 2 periods, 2006-2010 and 2011-2015.

Results: One hundred and sixty nine patients died over the 10-year period, 94 patients between 2006-2010 (mean 9 deaths/year ± 3) and 75 between 2011-2015 (mean 15 deaths/year ± 2), $p = 0.08$. Causes of death were: tumour progression (143), toxicity (21), accident (1), suicide (1) and second malignancy (3). No statistically significant difference was identified in the site of death over the 2 time periods, with 25.38% ($\pm 7.86\%$) deaths occurring in hospital between 2006-2010, compared with 11.06% ($\pm 10.96\%$) in the latter period ($p = 0.11$). Out of hospital deaths occurred in 67.94% ($\pm 10.39\%$) of patients between 2006-2010 and 77.45% ($\pm 16.26\%$) between 2011-2015 ($p = 0.42$). Further analysis identified a significant reduction in numbers of patients dying on the oncology ward over the 2 time periods, 24 patients, mean 1.2 deaths/year (± 4.08), compared to 9 patients, mean 1.8 deaths/year (± 1.78), $p = 0.044$. This coincided with a non-significant two-fold increase in patients receiving EoL care in the hospice, 14 patients compared to 28 patients in the latter period ($p = 0.15$).

Conclusion: By developing close links with the local paediatric hospice, outreach nursing teams and the creation of joint hospital/hospice staff contracts during this period, we have been able to promote continuity of care and coordinated rapid hospital discharge enabling families/patients to have a real choice of where they receive EoL care and die. A limitation of this study is the small numbers involved.

P-1008 | Prevalence of Zinc Deficiency in Childhood Malignancies and its Relation to Morbidity and Mortality in Initial First Month of Treatment

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Background/Objectives: Zinc has definitive role in immunity which may be more relevant to immunocompromised cancer patients. We aimed to determine the prevalence of zinc deficiency in children with malignancies at presentation and its association with morbidity and mortality during initial phase of chemotherapy.

Design/Methods: Serum zinc levels were measured in 219 children with various malignancies (117 haematological & 102 non haematological) from July 2014 to June 2015, by inductive coupled plasma- optical emission spectrometry. The haematological, infectious complications and mortality over one month in relation to initial serum zinc levels is reported.

Results: The mean serum zinc level in 219 patients was $78.70 \pm 32.83 \mu\text{g/dl}$ and zinc deficiency was noted in 84 (38.4%) patients. More patients with haematological malignancy had a low serum zinc level as compared to those with non-haematological malignancy (47% vs 28.4%, $p=0.005$). Respiratory infections were more common in zinc deficient patients ($p=0.054$). Mean serum zinc levels were significantly lower in those who died as compared to alive patients (83.3 ± 36.4 vs. $68.8 \pm 23.53 \mu\text{g/dl}$, $p<0.01$). The risk of mortality was significantly higher in patients with zinc deficiency as compared to those with normal zinc levels (Hazard ratio=2.02, 95% CI=1.14 to 3.57).

Conclusion: Zinc deficiency was more common in haematological malignancies. Respiratory infections and mortality were significantly higher in children with low zinc levels.

P-1009 | Home-Based Palliative Care for Children with Recurrent And/OR Refractory Central Nervous System Tumour

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Background/Objectives: In response to the unprecedented increase in the elderly population demographic, the Japanese government tries to improve transitions from hospital to home health care mainly to reduce medical expenses. There are increasing number of the institutions providing home-based end-of-life care for adult patients in Japan. Objectives of this paper is to obtain a better understanding of the complications found at home and to ascertain the feasibility of terminal care at home for children with complex problems for recurrent and/or refractory central nervous system (CNS) tumours.

Design/Methods: Descriptive and retrospective study of data from both medical and home care charts and also from the written records of interviews with the parents. The palliative home care program is based in the multidisciplinary teams in two university hospitals, and in the local medical clinics whenever available. Tele-consultation is provided as a support service for parents and local professionals.

Results: Forty-three patients under the age of 15 years with recurrent/refractory CNS tumours needing specialized terminal care at home were included from April 2007 and March 2016. These included 18 patients with diffuse intrinsic pontine glioma (DIPG), 8 with supratentorial high-grade glioma, 5 with medulloblastoma, 4 with ependymoma, 4 with germ cell tumour, 2 with pineoblastoma, and 2 with malignant rhabdoid tumour. All were cared at home, with palliative chemotherapy. Five patients died at home and thirty-four died in the hospitals mainly depending on the parents' wishes, partly for inadequate local medical support. Four are alive. Parents found end-stage dyspnea the most worrisome complication to discontinue home care.

Conclusion: This study confirms the feasibility of the terminal care at home for children with recurrent CNS tumours. Various complications can be well tolerated by the parents if the medical team is readily available. All the parents considered the time at home as very meaningful even discontinued in the end.

P-1010 | Chemotherapy-Induced Neutropenia among Paediatric Cancer Patients in Egypt: Risks and Consequences

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Background/Objectives: Chemotherapy-induced neutropenia (CIN) is the major dose-limiting toxicity of systemic chemotherapy, and is associated with substantial morbidity, mortality and costs. The aim of the current work was to identify risk factors that may predispose paediatric cancer patients, treated with myelo-suppressive chemotherapy, to CIN and associated sequels.

Design/Methods: 113 neutropenia episodes were analyzed, risk factors for CIN were classified into: patient-specific, disease-specific and regimen specific while consequences associated with CIN were divided into infectious and dose modifying sequels. Both risks and consequences were analyzed to target high risk patients with appropriate preventive strategies.

Results: 28% of patients presented with single neutropenia attack while 72% experienced recurrent attacks. Mean absolute neutrophil count (ANC) was 225.5 ± 128.5 ($10^9/L$), ranged from $10-497$ ($10^9/L$) started at 14.2 ± 16.3 days (ranged 2-100) after the onset of chemotherapy and resolved within 11.2 ± 7.3 days either with (45.1%) or without (54.9%) granulocyte colony stimulating factor (G-CSF). No significant association was found between any patient character or disease stage and CIN risk. However, certain malignancies (ALL, Neuroblastoma and Burkitt lymphoma) and certain regimens (induction block for ALL, AML) had the worst myelotoxic effect. G-CSF significantly shortened the neutropenia episodes. Febrile neutropenia was the leading complication among patients (73.5%), associated with several documented infections particularly mucositis (54.9%), respiratory (45.1%), GIT (38.9%) and skin (23.9%) infections. 6% of our cases died of infection-related complications. Neutropenia was responsible for treat-

ment discontinuation (13.3%), dose delay (13.3%), and dose reduction (5.3%) in patients. The mean cost for each episode was 9386.5 ± 6688.9 Egyptian pounds.

Conclusion: Although this study is preliminary survey with relatively small number of patients, our findings are relevant to clinical care of paediatric cancer patients in our region. Special attention to CIN prevention should be directed to hematologic malignancy cases especially at early cycles. Severe and prolonged neutropenia are life-threatening events that need aggressive management.

P-1011 | Fever in Neutropenia in Children and Adolescents: Evolution of Main Characteristics Over Two Decades, 1993-2012, in a Single Center

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Background/Objectives: This study aimed to describe the long-time evolution of fever in neutropenia (FN) characteristics at presentation, its management, and its outcome, in children and adolescents treated with chemotherapy for cancer.

Design/Methods: This retrospective single center cohort study in patients <17 years presenting with FN covered two decades (1993 to 2012). FN was defined as fever in severe neutropenia (absolute neutrophil count <0.5 G/L) induced by chemotherapy for cancer. Mixed logistic regression, accounting for multiple FN episodes per patient, was used for analysis, results are given per decade.

Results: In total, 703 FN episodes were reported in 291 (50%) of 583 patients with chemotherapy (maximum per patient, 9).

Characteristics at presentation: Central venous catheters (CVC; odds ratio [OR] per decade, 21.1; 95% CI, 10.9-40.9), diagnosis of acute lymphoblastic leukaemia (ALL; OR 1.66; 1.25-2.19) clinical signs of bacterial (OR 2.39; 1.65-3.46) and of viral infections (OR 1.54; 1.11-2.13), and fever itself (plus 0.10°C per decade; $0.04-0.17$) all significantly increased over time.

Management: the empirical use of ceftriaxone/amikacin decreased over time (OR 0.56; 0.35-0.91), the duration of intravenous antibiotics remained stable (-0.4 days per decade; -1.5 to 0.7), but was more frequently escalated (OR 8.47; 4.93-14.6). Hospitalization <3 days increased (OR 2.11; 1.15-3.90).

Outcomes: microbiologically defined infections increased over time (OR 1.71; 1.25-2.33), because viral (OR 6.02; 3.26-11.1) and fungal (OR 6.77; 1.46-31.4) infections were more frequently diagnosed, while bacteremia (OR, 0.93; 0.64-1.35) remained stable.

Conclusion: Significant and clinically relevant changes over time were detected in characteristics at FN presentation, management, and outcome. Clinically, they reflect changes over time towards routine use of CVC, higher chemotherapy intensity in ALL, a more liberal definition of fever, and thus FN itself; and increased diagnostics for viral and fungal infections. Scientifically, these changes need to be accounted for in longitudinal research projects.

SURGERY (IPSO)

P-1012 | Differential Diagnosis between Wilms Tumors and Desmoplastic Tumors: An Important Surgical Issue

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Background/Objectives: Wilms tumors are much more frequent in children than desmoplastic tumors. In Wilms tumors, cure can be reached more than 90% with multidisciplinary treatment, whereas in desmoplastic tumors, literature shows that the aim of the surgical treatment is to enhance survival from 26 to 70% in 3 years. Desmine and cytoqueratine identification, as well as the chimerical transcription EWS - WT1 differentiates those tumors. Such evaluation changes the surgical strategy radically. The aim of this study is to highlight the importance of the differential diagnosis between those two conditions.

Design/Methods: Description of 2 cases that were initially diagnosed as desmoplastic tumors and turned out to be Wilms tumors.

Results: CASE 1: 13-year-old boy presented with pleural effusion and thoracoabdominal tumour. He was submitted to diagnostic thoracoscopy that revealed desmoplastic tumour. Pathology revised and confirmed the diagnosis and the patient was submitted to HIPEC of both the thorax and abdomen. The pathology of the surgical specimen revealed Wilms tumour.

CASE 2: 7-year-old boy, presented with abdominal mass. The initial biopsy revealed desmoplastic tumour. In this case, the kidney was the tumour origin and because of the previous experience, we indicated nephrectomy prior to HIPEC, which would be indicated if the desmoplastic tumour diagnosis was confirmed. Pathology revealed Wilms tumour.

Conclusion: Conclusion: Both cases were initially diagnosed as desmoplastic tumors and turned out to be Wilms tumors. The lack of significant tissue in the initial biopsy can explain this, but it is of essence that the right diagnosis is made, so that the adequate surgical treatment is indicated, for it lessens the morbidity in proven Wilms cases initially diagnosed as desmoplastic tumors.

P-1013 | Outcome of Pulmonary Metastasectomy in Paediatric Solid TumorsV. Khanna¹, S. Agarwal¹, S.S. Panda¹, S. Bakhsh², M. Jana³, A.K. Gupta³, M. Srinivas¹, V. Bhatnagar¹¹All India Institute of Medical Sciences, Paediatric Surgery, New Delhi, India; ²All India Institute of Medical Sciences, Medical Oncology-BRAIRCH, New Delhi, India; ³All India Institute of Medical Sciences, Radiodiagnosis, New Delhi, India**Background/Objectives:** To evaluate surgical management and outcome of patients undergoing pulmonary metastasectomy.**Design/Methods:** Retrospective review of patients operated for pulmonary metastases from September 2001 till January 2015 for their presentation, surgery and outcome.**Results:** A total of 46 patients underwent 69 thoracotomies for removal of 196 lung metastases (range 1-20 metastases). Primary diagnosis was Osteosarcoma (OSA) 23; Wilms tumour (WT) 11, hepatoblastoma (HB) 5, malignant germ cell tumour (MGCT) 3 and 1 each had Ewing sarcoma (EW), malignant mesenchymal tumour (MMT), rhabdomyosarcoma (RMS) and synovial sarcoma (SS). Thirty-eight thoracotomies were done for lung metastases that were already present at the time of diagnosis while 31 thoracotomies were done when lung metastases that presented as recurrence. Sixteen patients (12 OSA, 3 HB and 1 WT) had bilateral metastases and 12 of them underwent staged metastasectomy. One patient with bilateral re-recurrence followed by surgery on one side and other whose metastases resolved with alternate chemotherapy did not undergo second metastasectomy. Three patients with bilateral disease are waiting for contralateral surgery following unilateral metastasectomy. Nine repeat thoracotomies were required in 7 patients (5 OSA, 1 WT and 1 HB). Fifteen patients underwent lobectomy (>1 lobe was removed in 4 patients), 31 patients had wedge resections, 9 had subpleural resections and 11 had both wedge and subpleural resections. Only biopsy was performed in 1 patient for an unresectable tumour. Two had negative thoracotomy. Ten patients died and 20 patients (9 OSA, 5 WT, 4 HB, 1 MMT and 1 MGCT) had re-recurrence in the lungs giving a 3-year overall survival of 77% (95 CI 58-88) and 3-year event-free survival of 43% (95CI 26-59).**Conclusion:** Pulmonary metastasectomy, even when done for bilateral and metachronous disease, is a viable option for achieving survival in patients. It leads to acceptable event-free (43%) and overall survival (77%) rates in patients who otherwise would have progressed and died.**P-1014 | Catheter Tip Position of Chemoport Devices in Children**M. Bhagat¹, S. Qureshi¹, S. Kembhavi², T. Vora³¹Tata Memorial Hospital, Paediatric Surgery Oncology, Mumbai, India; ²Tata Memorial Hospital, Radiology, Mumbai, India; ³Tata Memorial Hospital, Paediatric Oncology, Mumbai, India**Background/Objectives:** Chemoport devices are invaluable in paediatric oncology for providing long-term venous access, which ensure convenience and compliance for treatment. However, a perpetual question relating the position of the catheter tip has remained unanswered. The aim of this study was to analyze the factors influencing the incidence of complications in relation to the catheter tip position.**Design/Methods:** This study evaluated 205 consecutive cases of chemoport's inserted in 203 children. Demographic data, diagnosis, site, and method of insertion, intraoperative events, catheter tip position in the postoperative chest radiograph and early and late complications were evaluated.**Results:** Median age of the patients was 20 months with 113 males and 89 females. Most common indication for chemoport's insertion was hematological malignancies followed by neuroblastoma. Ultrasound guided localization method for vein puncture was used for 181 patients and open method was used in 22 patients. The catheter tip position was in the right atrium in 128 patients and in the superior vena cava (SVC) in 71 patients. The median catheter days in situ were 217 days. Intraoperative difficulties including failure to negotiate guide wire and localizing the vein were encountered especially in younger patients. Early catheter related complications occurred in five patients including catheter malposition, bleeding, and arrhythmias. Most common late complication was infection as seen in 10 (4.87%) patients. Other complications included catheter migration, fracture, and wound gap. The position of catheter tip had no correlation with infectious or noninfectious complications.**Conclusion:** Long-term venous access with chemoport's is safe with minimal morbidity in children. The position of catheter tip, in the SVC or right atrium, has no significant effect on incidence of complications.**P-1015 | Diagnostic Difficulties and Therapeutic Dilemmas in Patients with Colorectal Tumors**R. Dousek¹, J. Tuma¹, M. Jezova², D. Stary¹, L. Planka¹¹University Hospital Brno, Paediatric Surgery, Brno, Czech Republic; ²University Hospital Brno, Pathology, Brno, Czech Republic**Background/Objectives:** Malignant tumors of the large intestine are very rare in children. The aim of this study was to evaluate the treatment results of patients with colorectal tumors in one paediatric surgery center and to highlight related specific diagnostic and therapeutic problems.**Design/Methods:** A retrospective review of patients treated for malignant tumors of the large intestine in our paediatric surgery center between 2012 and 2015.**Results:** Five patients were included in this study. Two of them had colorectal carcinoma, located in the ascend colon, resp. sigmoid colon. One patient was diagnosed with haemangiopericytoma of the rectum and one patient Burkitt lymphoma of the cecum. One patient, followed up for tuberosus sclerosis, developed a PEComa (perivascular epithelioid cell tumour) of the cecum. In all these cases some diagnostic and therapeutic difficulties or unexpected findings occurred: delayed diagnosis, misdiagnosis, massive rectorrhagia in a newborn, a 28 mm primary tumour accompanied by a 60 mm lymphatic metastasis, bifocal colorectal carcinoma, false detection of distant metastases and problems associated with microscopic residuum of malignant tissue. All 5 patients underwent resection, 4 of them as a part of complex therapy. None of the patients died. All the patients have no digestive problems and exhibit no sign of macroscopic malignant disease.**Conclusion:** Despite the limited number of patients treated for tumors of the large intestine, authors experienced a wide range of unexpected findings and problematic issues during the diagnostic and therapeutic process.**P-1016 | Surgical Treatment of Neuroblastoma with Opsoclonus-Myoclonus Syndrome in Children**W. Han¹, H.M. Wang², H. Qin²¹Beijing Children's Hospital, Department of Surgical Oncology, Beijing, China; ²Beijing Children's Hospital Affiliated to Capital Medical University, Department of Surgical Oncology, Beijing, China**Background/Objectives:** To investigate 14 cases of neuroblastoma with opsoclonus-myoclonus syndrome in our hospital from Jan 2010 to Jan 2016.**Design/Methods:** From Jan 2010 to Jan 2016, the clinical manifestation, operation method, pathology and prognosis of 14 children with neuroblastoma and opsoclonus-myoclonus syndrome in our hospital were analyzed retrospectively.**Results:** Fourteen patients, 2 boys, 12 girls, average age was 25.3 months and mean time from the onset of such disease to the final diagnosis was 3.1 months. All cases were Han nationality. There was no obvious difference of geographical distribution. 1 case's father took heroin during mother pregnancy, in another case, her mother took medication during pregnancy to treat flu. The clinical manifestations: 3 cases mainly presented as opsoclonus, 6 cases for myoclonus, and 5 cases for ataxia. 1 case had EEG abnormal findings. All patients went to see neurologist first instead of oncology surgeon. 10 cases received immunosuppressive drugs such as hormones, gamma globulin. 3 cases were effective after these treatment, while 7 cases were ineffective. All the patients's diagnosis was confirmed by pathology after the operations, which were surgical removal of tumors, all of them got the gross resection. Pathology: 5 cases were neuroblastoma, including 3 cases of differentiated type and 2 cases of poorly differentiated type. 7 cases were ganglioneuroblastoma, including 4 cases of differentiated type and 3 cases of poorly differentiated type. 2 cases were ganglioneuroma. Symptoms of 8 cases improved significantly after surgery. There was no surgical complication. 4 cases received postoperative chemotherapy, 1 case received postoperative radiotherapy. Patients were followed up until recently and have long-term survival, 8 cases significant recovered. No recurrence cases of tumour, but 2 cases symptoms recurrence.**Conclusion:** For children with neuroblastoma combined OMS syndrome, the removal of the tumour can significantly improve symptoms.**P-1017 | Renal Cell Carcinoma in Children**R. Kebudi¹, B. Cakir², G. Omer¹¹Istanbul University - Cerrahpasa Medical Faculty and Oncology Institute, Paediatric Haematology-Oncology, Istanbul, Turkey; ²Bezmialem Vakif University, Paediatric Haematology-Oncology, Istanbul, Turkey**Background/Objectives:** Renal cell Carcinoma (RCC) occurs rarely in children, comprising 1.8 to 6.3% of all renal malignancies in children. The aim of this study is to evaluate the demographic features, treatment and outcome of RCC in a tertiary paediatric oncology center.**Design/Methods:** Medical files of children with RCC between 1990-2016 in the Istanbul University, Oncology Institute, were retrospectively evaluated.**Results:** Ten patients (5 females), eight with primary RCC with a median age of 9, 5 years (4-14 years), and 2 with RCC as a second malignancy (2 males, 9 and 24 years old) were evaluated. Primary RCC comprised 8% of renal malignancies in our series, five had stage I, two stage III, one stage IV. Five were in the right kidney. All stage I patients are alive with no evidence of disease at a median of 2 years (4months-12 years). Secondary RCC patients were diagnosed as stage 1; one 8^{3/12} years after the diagnosis of stage 4 neuroblastoma at 11 months, the other 10 years after the diagnosis of osteosarcoma at 14 years of age and both are in remission for 5 years, the latter developed thyroid papillary carcinoma as a third malignancy. Surgery was the only treatment for stage I patients. Interferon + 5-flourouracil + interleukin-2 were used for stage III and IV. The stage IV and one stage III patient progressed despite treatment and died at 2 and 12 months after diagnosis. The other stage III recurred in the contralateral kidney 5 years after diagnosis and treatment with interferon and died 9 years after diagnosis.**Conclusion:** RCC is rare in children, with excellent prognosis with nephrectomy alone at early stages. Prognosis is poor in advanced stages. RCC may occur as a second malignancy, abdominal ultrasound should be included in the regular follow up of survivors of childhood cancer.**P-1018 | Paediatric Lymph Node Biopsy - an Eleven year Single Center Experience**F.J. Murphy¹, E. Evans¹, C. Barton², J. McPartland³, B. Pizer², P.D. Losty⁴¹Alder Hey Children's Hospital, Paediatric Surgery, Liverpool, United Kingdom; ²Alder Hey Children's Hospital, Paediatric Oncology, Liverpool, United Kingdom; ³Alder Hey Children's Hospital, Paediatric Pathology, Liverpool, United Kingdom; ⁴Alder Hey Children's Hospital, Academic Paediatric Surgery, Liverpool, United Kingdom**Background/Objectives:** Lymph node biopsy is integral to the management of paediatric patients with suspected malignancy. In this study we examined referral pathways to a surgical service to critically evaluate investigations undertaken and positive yield of malignancy.**Design/Methods:** Two hundred and seventy one patients had lymph node biopsy over an 11 year time period. Data were analysed for - (1) referring physician (2) laboratory tests (3) radiology (4) anatomical site (5) pathology and (6) morbidity from surgical biopsy.**Results:** One hundred and seventy five males and ninety six females - [age range 5 months - 20 years; mean age 7.6 years] underwent biopsy. Referral patterns varied with 169 (62%) biopsies performed by the paediatric surgery service, 81 (30%) by ENT and 21 (8%) - maxillofacial, plastics, orthopedic departments. Time from patient referral to a hospital clinic visit averaged 3 months (range 0.5-8 months). Biopsy was performed at an interval of 1 day -10 months [mean

2 months]. Sixty one (23%) patients had malignant disease. Two hundred and ten cases (77%) had benign pathology - reactive hyperplasia, mycobacterial adenitis, other diagnosis. Chest x-ray was performed in 116 (43%) patients and 105 (39%) had ultrasound imaging. Sites involved were head and neck (n=216) - 80%, axilla (n=18) - 7% and groin regions (n=37) - 13%. Fifty seven percent (n=155) had blood / serology testing. Malignancy (%) and abnormality on chest x-ray was significant (p=0.0029). Morbidity from surgical biopsy included : wound infection (n=15) - 5.5% and nerve injury (n=3) - 1%.

Conclusion: This study shows wide variation in clinical management of paediatric patients with lymphadenopathy. Excluding malignancy is paramount. The high yield of benign pathology indicates a co-ordinated care pathway may better manage patients more effectively.

P-1019 | Surgical Treatment of Abdominal Compartment Syndrome in Paediatric Oncology

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Background/Objectives: Abdominal Compartment Syndrome (ACS) and Intra-Abdominal Hypertension (IAH) occurs when the pressure in the abdominal cavity increases, what leads to cascade of pathological processes.

The aim was to determine the possibility of surgical treatment of ACS in oncological patients.

Design/Methods: Since January 2012 in our hospital ACS was diagnosed in 7 children. 6 of them were suffered from neuroblastoma 4S stage with significant hepatomegaly. In 1 case IAH occurred in a child with initially germ-cell tumour after resection of the small bowel because of strangulated intestinal obstruction more than 24 hours with the postoperative development of heavy dynamic intestinal obstruction.

Results: Transversal laparotomy with installation of partially absorbable mesh device fixed to aponeurosis and muscles was performed in 3 children.

In 1 case the laparotomy was performed in a newborn of 21-day age. After complex examination N-MYC negative neuroblastoma 4S stage was determined. After repeated examination the good response was established and the plastic surgery of abdominal wall was performed at the age of 3 months.

In the second case the laparotomy was put in a child at the age of 5.5 months. The reconstructive operation was carried out at the age of 11 months. However, at the age of 2 years old the systemic relapse was diagnosed, which in addition to chemotherapy mandated the relaparotomy and removal of the primary lesion - tumour of the left adrenal.

In the third case of ACS against a background of severe dynamic intestinal obstruction we performed temporary laparotomy for 4 days.

One child with the neuroblastoma 4S stage died because of ACS accompanied with compression of the great vessels and disturbance of the liver blood supply which led to veno-occlusive hepatic disease.

Conclusion: We consider that timely accomplishment of laparotomy in oncological patients with ACS may become the key to successful treatment of severe conditions.

P-1020 | The 5-Year Oxford Experience of Paediatric Ultrasound Guided Percutaneous Biopsies

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Background/Objectives: Children with cancer require histological diagnosis to guide appropriate therapy. This can be performed by percutaneous image guided biopsy. The aim of this study was to assess the diagnostic accuracy and safety of percutaneous ultrasound guided paediatric biopsies in a tertiary referral centre.

Design/Methods: A retrospective analysis of clinical data related to percutaneous ultrasound-guided biopsies performed for histological diagnosis in patients aged 0 to 18 years old between January 2010 and December 2015 in a tertiary paediatric hospital was conducted. A total of 116 percutaneous US-guided biopsies were performed in 114 children. The median age of the children was 5.8 years. A primary diagnosis was made in 114 patients and suspected recurrence in 2. Most biopsies were performed using 18-gauge core biopsy needles with a minimum of 2 cores per examination.

Results: There were 81 malignant lesions, 34 benign lesions and 1 infectious lesion with 51% as localised, 17% locoregional and the remainder metastatic disease. In 99% of lesions the needle biopsy was diagnostic. An accurate diagnosis was achieved in 50/81 (62%) of percutaneous biopsies for suspected malignancy cases or recurrence as confirmed on subsequent surgical specimen. None of the cases underwent repeat biopsy. All were without complications. The majority of cases required an overnight stay and simple analgesia post procedurally.

Conclusion: The use of US-guided percutaneous biopsy is an accurate, safe and cost-effective method for evaluation of suspected lesions in the paediatric population. This can be performed instead of or in addition to open biopsy and help guide subsequent treatment.

P-1021 | Posterior Sagittal Anorectal Mobilization for Radical Treatment of Pelvic-Perineal Tumors in Children: A New Technique in Surgical Oncology

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Background/Objectives: Diffuse or massive tumors involving the perineal and pelvic compartments may require aggressive surgical treatment in children. In such cases, as rhabdomyosarcoma originating from the prostate or bladder neck, different surgical approaches have been suggested and performed, including radical retropubic, trans-perineal, or transpubic surgical techniques. The authors, propose and present their results using a Posterior Sagittal Anorectal Mobilization (PSAM).

Design/Methods: The oncologic patient is placed in a prone position with the pelvis elevated, without a previous colostomy. A 10 Ch bladder catheter is positioned. A midline sagittal incision is performed from the coccyx to the posterior margin of the anus. Fine electrocautery is used to obtain an accurate dissection all around the anal margin itself. The incision also involves the midline dissection into the perineal body. This approach allows to identify and respect the rectal sphincter structures (parasagittal, vertical and muscle complex fibres). At the same time it permits to obtain a wide exposure of the tumour and perineal-pelvic area. The complete exposure allows a complete tumour resection with a sharp and safe haemostasis. Reconstruction is achieved by the classical pelvic-perineal anatomical structure approximation.

Results: The authors report two cases of tumour resection performed through a PSAM approach. The first case is a 3-year old boy affected by prostatic anaplastic rhabdomyosarcoma. The second case, a 1-year old baby girl, presented with a diffuse lipoblastoma including immature elements of the perineal and pelvic compartments. No intraoperative or post-operative complications occurred. The oldest boy presented at follow-up a complete normal faecal and urinary continence (Kriekenbeck criteria).

Conclusion: The presented technical approach, defined as PSAM, is completely suitable for surgical resection of perineal-pelvic tumors, without the need of more invasive operations including transpubic dissection and/or anorectal split. Moreover, nervous and muscular sphincter structures are easily identified and preserved.

P-1022 | Uretric Stenting: A Safe Adjunct to Prevent Ureteric Injury in Retroperitoneal Tumour Excision

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Background/Objectives: In very large retroperitoneal or pelvic tumours there is a significant risk of injury to the ureters. Although preoperative imaging with CT urogram can delineate the anatomy of ureters, however, stenting makes ureter easily visible and prevention of injury is more predictable. We are presenting our experience of preemptive ureteric stenting in excision of large retroperitoneal tumours.

Design/Methods: This is a retrospective case series to study the role of preemptive ureteric stenting in patients with large retroperitoneal or pelvic tumours. All patients had radiological assessment with a CT urogram to delineate ureteric anatomy. Risk of iatrogenic ureteric injury was considered high in the presence proximal hydronephrosis, inability to trace ureter along the entire course of the mass or significant ureteric displacement. Ureteric stenting is performed before laparotomy if assessment showed high risk.

Results: Three patients underwent this type of ureteric stenting over 8-month period from July 2015 to March 2016. One patient had bilateral stents and two had only unilateral stent. Two patients had germ cell tumour and one patient had a large ganglioneuroma. Ureteric catheters were used in two patients with distal end coming out of urethral orifice, and in the third patient a double J stent was used. All three patients had uneventful complete excision of the tumour without any injury to the ureter. Ureteric catheters were pulled out at the end of procedure and stent was left in situ for six weeks and removed electively. Two patients had gross haematuria that settled in 48 hours after surgery.

Conclusion: Preemptive ureteric stenting is a safe adjunct for retroperitoneal tumour excision and helps in protecting ureter from inadvertent injury during extensive retroperitoneal dissection for excision of large retroperitoneal tumours.

P-1023 | Video-Assisted Pericardio-Peritoneal Window for Recurrent Pericardial Effusion after Bone Marrow Transplantation

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Background/Objectives: Cardiac chronic tamponade can be a complication after bone marrow transplantation. The drainage is the standard treatment. We propose the pericardio-peritoneal window for recurrent pericardial effusion.

Design/Methods: We describe a patient with chronic cardiac tamponade that was treated successfully with video-assisted pericardio-peritoneal window.

Results: An 11-year-old boy, diagnosed with T cell Acute Lymphoblastic Leukaemia. He underwent allogeneic related bone marrow transplant. The myeloablative conditioning regimen was done with total body irradiation and cyclophosphamide. The graft versus host disease prophylaxis was performed with cyclosporine and methotrexate. He presented grafting of leukocytes on D+11. The patient developed pulmonary aspergillosis treated with oral voriconazole with resolution of the clinical signs. He presented severe BK-virus-associated hemorrhagic cystitis (cidofovir, intensive intravenous hydration, insertion of a large-bore three-way catheter and normal saline continuous bladder irrigation, vesicostomy due to bladder perforation), fortunately there is satisfactory progress. He presented seizure. In brain magnetic resonance there were lesions then patient underwent a biopsy and pathology shows radionecrosis. Finally the patient developed significant pericardial effusion on echocardiography with indirect signs of cardiac tamponade of day 79. He underwent pericardiocentesis with negative culture. There was recurrence of pericardial effusion with another pericardiocentesis (negatives culture and galactomannan) and intrapericardial catheter was inserted. Laparoscopic pericardio-peritoneal window was performed. This procedure allowed visibility of the pericardial sac and a good

site to be biopsied. Pathology was inespecific but in this moment patient developed hair and eyebrow hypopigmentation thus way the pericardial effusion was assigned to chronic graft versus disease. The patient started treatment with corticosteroid. He presented resolution the clinical signs. Currently, the patient finished systemic treatment with corticosteroid without any sign by chronic graft versus disease.

Conclusion: Video-assisted pericardio-peritoneal is an alternative treatment for chronic tamponade cardiac. This technique allows evaluation of pericardium with biopsy and samples microbiology.

P-1024 | In Utero Twin-To-Twin Neuroblastoma Metastasis

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Background/Objectives: Neuroblastoma is one of the most frequent neonatal solid tumors. Some occurrences in monozygotic twins were described. Fetal-placental metastasis is extremely rare.

Design/Methods: To report a case of fetal-placental metastasis in monozygotic twins.

Results: The patients were baby girls born following a healthy pregnancy at 41 weeks gestation. At 4 months of age the first patient presented abdominal swelling. She was submitted CT scan showed adrenal mass and heterogeneous hepatomegaly. The urinary catecholamine's level was high. After that, a complete tumour resection was performed. The tumour was histologic favorable neuroblastoma without MYCN amplification. There was infiltration on hepatic biopsy and bone marrow biopsy (unless than 5% of infiltration). The diagnosis was 4S Neuroblastoma and she didn't receive chemotherapy. The other twin was screened with abdominal ultrasound that showed multiple hepatic nodules. MRI confirmed these findings. These images didn't found the primary tumour. She was submitted a laparoscopy biopsy that revealed a neuroblastoma metastasis with the same characteristic of sister's tumour. Bone marrow biopsy and level urinary catecholamines was negative. The control MRI, two months after the initial exam, revealed reduction of the number and the size of hepatic nodules. Neuroblastoma in monozygotic twins is rarely reported. We found just two cases of hepatic metastasis without a recognizable primary site.

Conclusion: From these clinical and pathologic findings we described twin-to-twin neuroblastoma metastasis.

P-1025 | Venous Access in Treating Children with Cancer: A 6-Year Experience of a Single Institution

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Background/Objectives: The treatment of any oncologic disease is impossible without a venous access. The purpose of our study was prevention of complications of intravenous chemotherapeutic agent administration.

Design/Methods: From 2010 to 2015 we were monitoring the treatment of 2286 children (3 months – 17 years) with oncologic diseases. 2099 (91.8%) patients underwent 3930 subclavian vein catheterization, 187 (8.2%) patients – 118 venous ports implantations.

Results: Complications and technical difficulties during catheter insertion were observed in 98.3% of cases, during venous port implantation – in 23% of cases. Complications of subclavian catheter and venous port use were observed in 97.3% and in only 11% of cases, respectively. Subclavian catheters compromised cancer treatment in 45.9% of patients, implantable venous ports – in 1.7% of patients. Each patient with a subclavian catheter underwent central venous catheterization 4 to 19 times (mean 6 times) during treatment. Catheter dwell time exceeded the recommended limit in all patients except for cases of catheter removal by patients. On multiple occasions all patients were discharged with a subclavian catheter in place.

Conclusion: Venous ports obviously match the criteria mentioned in the introduction. Subclavian catheter use resulted in cancer treatment protocol deviation in almost 50% of cases, thus leading to a poorer prognosis and significantly increasing the number of invasive procedures and instances where general anesthesia was needed. But in Russia, implantable venous port systems are used only in 13 clinics.

P-1026 | Venous Access in the Treatment of Children with Cancer: Results of a 10-Year Multicenter Study

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Background/Objectives: Prevention of complications of intravenous chemotherapeutic agent administration at paediatric oncology.

Design/Methods: From 2006 to 2015 we were monitoring the treatment of 463 children (aged 3 months to 17 years) with oncologic diseases. This patients underwent venous port implantations (IVPs).

Results: Normal 0 false false false RU JA X-NONE

In 463 cases during insertion of 463 IVPs the following complications and technical difficulties were present:

1. Unintended puncture of the common carotid artery (CCA) during the puncture of the IJV – 19 cases (4.3%);
2. Retrograde positioning of the distal end of the guidewire in the IJV – 67 cases (14.4%);
3. Placement of the distal end of the guidewire into the punctured SV – 35 cases (7.6%);
4. Difficulties driving the guidewire into the IJV after successful puncture – 43 cases (9.3%);
5. Retrograde port catheter positioning in the IJV during ECG-guided implantation – 8 cases (1.7%).

Despite the use of intraoperative fluoroscopy, there have been cases of the retrograde positioning of the distal end of the guidewire in the IJV due to the peculiarities of topographic anatomy of children. However, visual inspection in all cases facilitated intraoperative adjustments of these complications.

The use of 463 IVPs was complicated by the following:

1. Venous port contamination – 11 cases (2.5%);
2. Occlusion of the IVP by a thrombus – 23 cases (5%);
3. Subcutaneous fat layer thinning above the port chamber – 7 cases (1.7%).

Venous port contamination was caused by violation of rules of operation - Huber needle clinicians used more than a month without replacement. This resulted in infection of the tissues around the port chamber. This has resulted in the removal of the IVP. Subsequently, these patients were implanted port systems on the opposite side.

Conclusion: IVPs are safe, implanted only once during the treatment course and have minimal risks associated with implantation and use. Unfortunately, in the Russian port systems are used only in several hospitals.

P-1027 | Paediatric Renal Tumors with Inferior Vena Cava Involvement - Management at a Specialist Cancer Center in a Developing Country

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Background/Objectives: Pediatric renal tumors involving the Inferior vena cava (IVC) present a complex problem for the operating surgeon. Additional expertise in dissection, isolation and exploration of IVC is important in management of these tumors. We report our institutional experience in operative management of renal tumors with IVC involvement from a developing country.

Design/Methods: Records of all paediatric patients with renal tumors and IVC involvement who underwent surgery between 2014 and 2016 were retrieved through the Electronic Hospital Information System. Demographic and clinical data, type of tumour, extent of IVC involvement, and operative management strategies were recorded.

Results: Since January 2014, a total of 44 paediatric nephrectomies have been performed. There were 8 patients with renal tumors involving the IVC. Of these, 7 patients had Wilms tumour and one patient had clear cell sarcoma of the kidney. Median age was 5 years. Median tumour size was 13 cm (Range 9 – 20 cm). Median Hospital Stay was 6 days.

Three patients were managed with IVC thrombectomy. Three patients had tumour adherent to IVC which were separated using sharp dissection. One of these had bleeding that required lateral repair of IVC. One patient had the tumour densely adherent to IVC which required segmental IVC resection and end-to-end anastomosis. There was one patient with chronic obstruction and post treatment fibrosis of infrarenal IVC with good collateral flow. The IVC was ligated in this case.

Conclusion: Management of renal tumors with IVC involvement depends on type of tumour and the extent of IVC involvement but requires expertise in vascular dissection, and reconstruction. Our institutional experience suggests that a strategy depending on the extent of involvement of IVC helps in management of this complex problem.

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