

51st CONGRESS OF THE INTERNATIONAL SOCIETY OF PAEDIATRIC ONCOLOGY (SIOP)

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ABSTRACTS

SIOP ABSTRACTS

FREE PAPER SESSION (FPS)

SIOP Award Session

AW01 SIOP19-0929 | Early Discontinuation of Antibiotics in Low Risk Pediatric Cancer Patients with Febrile Neutropenia, Before Recovery of Counts: A Phase 3 Randomized Controlled Trial (Dalfen Study)A. Kumar¹, B. Biswas¹, A. Chopra², A. Kapil³, S. Bakhshi¹¹AIIMS, Department of Medical Oncology, New Delhi, India; ²AIIMS, Department of Lab Oncology, New Delhi, India; ³AIIMS, Department of Microbiology, New Delhi, India

Background/Objectives: Stratifying pediatric cancer patients with febrile neutropenia into low and high risk groups based on various clinical and laboratory parameters has assisted in de-escalation of antimicrobials in clinics. However, there is lack of robust data for an optimal scientific approach.

Design/Methods: In an open label, non-inferiority, randomized controlled phase 3 trial at a tertiary cancer centre in India, patients aged 3-18years, with low risk febrile neutropenia were started on empirical intra-venous antibiotics in outpatient setting. Randomization was done when the patients became afebrile for at least 24 hours and remained neutropenic; standard arm consisted of oral antibiotics, while antibiotics were stopped in the experimental arm. Enrolled patients were followed for re-appearance of fever and rate of re-admission, till the resolution of neutropenia. A pilot feasibility randomized study with essentially similar design preceded this trial and the results were used for planning the primary trial.

Results: From Jan 2017-Dec 2018, 75 patients were randomized: 38 to stoppage arm while 37 patients received oral antibiotics. Baseline characteristics were equally matched. Success rates were 94.6% in the continuation arm versus 94.7% in the stoppage arm; absolute risk difference was 0.1% (95% CI: -10.0% to +10.3%). All the failure cases responded optimally to re-initiation of antibiotics and there was no re-admission in any arm. When the results of the primary trial as well as the pilot study were clubbed, in a total 139 subjects (experimental arm = 70 & standard arm = 69), the absolute risk difference

between the two arms was 0.1% (95% CI: -9.9% to + 10.2%) favoring the stoppage arm.

Conclusions: Antimicrobial therapy in low risk afebrile neutropenic patients can be managed on outpatient basis and an early de-escalation strategy is efficacious as well as safe. This approach can lead to significant cost and manpower benefits as well as help decrease antimicrobial resistance. (ClinicalTrials.gov, number NCT03003273).

AW02 SIOP19-0586 | Intra-arterial Chemotherapy (IAC) for Treatment of Intraocular Retinoblastoma: Successes and Lessons LearntS. Srinivasan¹, S. Mohd.¹, T. Vora¹, M. Prasad¹, A. Baheti², S. Qureshi³, N. Shetty⁴, S. Kembhavi², G. Chinnaswamy¹, N. Shetye⁵, S. Kulkarni⁶, B. Sd¹¹Tata Memorial Hospital, Pediatric Oncology, Mumbai, India; ²Tata Memorial Hospital, Radiodiagnosis, Mumbai, India; ³Tata Memorial Hospital, Pediatric Oncology, Mumbai, India; ⁴Tata Memorial Hospital, Interventional Radiology, Mumbai, India; ⁵Tata Memorial Oncology, Pediatric Oncology, Mumbai, India; ⁶Tata Memorial Hospital, Interventional Radiology, Mumbai, India

Background/Objectives: IAC is an effective modality for the treatment of intraocular Retinoblastoma (RB), potentially increasing globe salvage rates and avoiding toxicity of systemic chemotherapy. In LMICs, where fear of enucleation leads to high abandonment rates, IAC could be an effective strategy. We report the impact of IAC in retinoblastoma children at our centre.

Design/Methods: This is a retrospective study (2012-2018) of outcomes of RB children treated with IAC using melphalan, carboplatin and topotecan (single agent/combination). In all cases, treatment decisions were made by the multidisciplinary team which included a pediatric ophthalmologist. Study outcomes included globe salvage rates, treatment abandonment, therapy complications and analysis of risk factors for treatment failure.

Results: A total of 71 eyes in 59 children were subjected to IAC, median age:20months (2-97) and M: F=1.3:1. This included ICRB group B eyes:6 (9%), C:3 (4%), D:42 (59%) and E:20 (28%). Total IAC sessions were 223 and median sessions/eye was 4 (Range:1-8). Eighteen (25%) received

additional focal consolidative therapy. At a median follow up of 31 months, 3-year globe salvage rate is $47\pm 7\%$ and 3-year overall survival is $95\pm 3\%$. The 3-year globe salvage with primary (n=32) and secondary (n=39) IACs $29\pm 9.5\%$ and $63\pm 8\%$ ($p=0.005$) respectively and 67%, 100%, 49% and 67% for ICRB Group B, C, D and E eyes respectively. Presence of vitreous seeds was associated with increased enucleation (HR:2.73;95%CI:1.32-6.65; $p=0.007$). Two of 4 CNS relapses had tumor abutting the optic disc. Complications included transient loss of vision[4/71 (6%) eyes], retinal pigment changes[7/71 (10%) eyes], vitreous hemorrhage[6/71 (8%) eyes] and eyelid/orbital edema in 10%(23/223 sessions). Grade IV cytopenia was documented in 25%(15/59) of children and one child had a permanent loss of vision. Treatment abandonment rate reduced from 11% in 2012 to <5% post 2013.

Conclusions: IAC is an effective strategy for globe salvage in retinoblastoma and helped decreasing treatment abandonment. Presence of vitreous seeds is associated with poor globe salvage rates. Use of combination IAC is associated with significant myelosuppression.

AW03 SIOP19-1365 | The Molecular Landscape and Clinical Experience in Infant Medulloblastoma

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Background/Objectives: Infants with medulloblastoma (iMB; 0-5.0 years; ~30% of patients) are clinically distinct and commonly treated with radiation-sparing regimens aimed at minimising neuro-developmental late-effects. Outcomes remain poor (5yr OS <60%). Recent molecular advances have enabled improved biomarker-driven risk-stratification in non-infant MB clinical trials. However, in iMB, biological studies of large trials and/or retrospective cohorts have not been undertaken to support equivalent strategies.

Design/Methods: We undertook comprehensive characterisation of the molecular pathology and associated historical clinical experience in iMB, encompassing discovery and validation in cohorts totalling 387 patients.

Results: iMB displayed distinct clinico-molecular features; iMBSHH (40%) and iMBGrp3 (42%) predominated,

each harbouring clinically-significant biological heterogeneity. Within iMBGrp3, *MYC* amplification and large-cell/anaplastic pathology (LCA; 54%) strongly associated and defined a very-high-risk group which commonly progressed on therapy (0% 10yr OS vs 73% in non-LCA/*MYC* iMB-Grp3). iMBSHH was strongly associated with DN/MBEN pathology (75% of iMBSHH; $p<0.0001$). To identify heterogeneity within iMBSHH, class discovery methods were applied to DNA methylation array data from our primary discovery cohort. Two robust subgroups with characteristic clinicomolecular features were identified (iMBSHH-I-II) and validated in a larger cohort (n=154) that included published MBSHH cohorts not previously used for iMB-specific assessment ($p<0.0001$). iMBSHH-II DN/MBEN patients had better PFS, offering opportunities for stratification of radiation-sparing treatments. However, DN/MBEN and extent of resection were the only significant independent risk-factors for OS, discriminating favourable- (60% of iMB-SHH) and very-high-risk (40%) disease groups in survival modelling (93% vs 23% 10yr OS). DN/MBEN iMBSHH tumours had greatest potential for rescue post-relapse (56% survival). Survival relationships were reproducible in large validation cohorts and not influenced by treatment type (e.g. upfront radiotherapy), strongly supporting their adoption as independent risk-factors.

Conclusions: Our models outperform current risk-stratification schemes, enabling risk-status re-classification for >50% of iMB and personalisation of therapy. Routine molecular diagnostic sub-classification will be essential for the future management of iMB.

AW04 SIOP19-0383 | DNA Methylation and Mutational Analysis of Pediatric Germ Cell Tumors

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Background/Objectives: Germ cell tumors (GCTs) arise from primordial germ cells (PGCs), which migrate during embryogenesis from the yolk sac through the mesentery to the gonads. Through this migration, PGCs underwent DNA methylation erasure and reestablish their DNA methylation.

These facts could suggest aberrations of DNA methylation are associated with development of GCTs. The several genomic alterations had been frequently found in adult testicular GCTs. However, genetic basis of pediatric GCTs is still to be elucidated due to its rarity.

Design/Methods: We applied DNA methylation analysis and targeted capture sequencing (TCS) to 51 pediatric GCT samples, which included seven teratomas (four immature teratomas and three mature teratomas), six dysgerminomas, two embryonal carcinomas (EC), six mixed germ cell tumors (MGCT), and 30 yolk sac tumors (YST).

Results: Based on the unsupervised consensus clustering of the DNA methylation status, pediatric GCTs were divided into four clusters. Each cluster showed a distinctive pattern of DNA methylation and was well correlated with histological subtypes. We identified differentially methylated regions (DMRs) between subtypes of GCTs by comparing the beta values. Dysgerminomas revealed lower methylation across the DMRs compared the other subtypes. Pathway analysis based on the DMRs showed the activation of MAPK pathway was detected in YST samples. TCS revealed four out of six DG samples had activating *KIT* mutations. Teratoma and EC samples had no mutation in the regions covered by our bait. In YST, two samples had *KRAS* mutations, and *NRAS* as well as *TP53* mutations were detected in one sample, respectively. *TP53* mutation was also detected in one MGCT sample.

Conclusions: Pediatric GCTs revealed characteristic DNA methylation profiles and DMRs according to their subtypes. *KIT* and *RAS* pathways were essential drivers for DG and YST, respectively. These kinases may be targetable for refractory/relapsed DG and YST.

AW05 SIOP19-1143 | Nelarabine Abrogates Relapse Rates in CNS3 T-ALL: A Report from Children's Oncology Group Study AALL0434

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Background/Objectives: AALL0434 included a 2 x 2 randomization using an augmented BFM regimen. Patients were randomized to escalating dose Capizzi methotrexate (CMTX) or High Dose MTX (HDMTX) and intermediate (IR) and high-risk (HR) patients were randomized to +/- six 5-day nelarabine (Nel) courses. IR/HR CNS1/CNS2 patients received 1200 cGy cranial radiation (CRT). Low-risk patients received no CRT and were not randomized to +/- Nel. CNS3 patients received 1800 cGy CRT, were assigned to HDMTX and took part in the Nel randomization.

Objective: To assess AALL0434 T-ALL patient outcomes based on diagnostic CNS status.

Design/Methods: We reviewed outcomes on AALL0434.

Results: From 2007-2014, 1550 evaluable patients were enrolled, including 1128 (72.8%) CNS1, 306 (19.7%) CNS2 and 116 (7.5%) CNS3. Five-year EFS and OS rates for CNS1, 2, and 3 were 85.2%, 83.1%, and 71.4% ($p=0.0007$) and 90.4%, 89.2%, and 83.1% ($p=0.0438$), respectively. Five-year disease-free survival (DFS) rates for Arm C (HDMTX without Nel) differed by CNS status: CNS1 87.2%, CNS2 80.0%, and CNS3 70.2% ($p=0.0006$), but 5-year DFS for Arm D (HDMTX+Nel) showed no statistically significant outcome differences based on CNS status ($p=0.35$): CNS1 85.1%, CNS2 80.0%, and CNS3 93.1%. Nelarabine significantly improved DFS of CNS3 patients who received HDMTX ($p=0.02$): 93.1% with Nel ($n=29$) vs. 70.2% without ($n=71$). The 5-year cumulative incidence of isolated CNS relapse was associated with CNS status: CNS1 1.0%, CNS2 4.2%, and CNS3 11.0%; $p<0.0001$.

Conclusions: Adding nelarabine to CNS3 patients receiving HDMTX and CRT produced outcomes similar to CNS1/CNS2. CNS3 patients who did not receive nelarabine had poor EFS and high isolated CNS relapse rates. For AALL0434 patients receiving CMTX, with or without Nel, outcomes were similar for CNS1 and CNS2. This is in contrast to B-ALL where CNS2 outcomes are inferior to CNS1. It is unclear if similar results would be seen without CRT.

AW06 SIOP19-0245 | Randomized Phase 2 Trial of the Combination of Vincristine and Irinotecan With or Without Temozolomide, in Children and Adults with Refractory or Relapsed Rhabdomyosarcoma (RMS)

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Background/Objectives: Vincristine with Irinotecan (VI) is effective in patients with relapsed RMS but outcomes remain poor. The addition of temozolomide to VI (VIT) is attractive owing to different resistance mechanisms and distinct toxicity profiles.

Design/Methods: The VIT-0910 trial, an EpSSG-ITCC randomized phase 2 trial, evaluated efficacy and safety of VI and VIT in patients (pts) aged 0.5-50 years with relapsed/refractory RMS. Pts received Vincristine 1.5 mg/m² d1, d8, Irinotecan 50mg/m² d1-d5 +/- Temozolomide 125 mg/m² d1-d5 (150 mg/m² from cycle 2 if no toxicity > grade 2); 21-day cycles were given until progression/unacceptable toxicity. The primary endpoint was centrally reviewed objective response rate (ORR) after 2 cycles (primary lesion, WHO response criteria: metastatic sites, RECIST 1.1). Secondary endpoints included progression-free survival (PFS), overall survival (OS) and adverse events (NCI-CTCAE v4). Initially a Simon 2-stage design was used to analyse separately 40 pts/arm. After amendment, the trial sample size was increased to 120, and a comparison between arms, adjusted for confounding factors, was added to the statistical plan.

Results: 120 pts (60 VIT, 60 VI) were recruited in 37 European centers from 03/2012-04/2018. Median age was 11 years (0.75-46), 89% pts relapsed RMS. ORR was 24/55 (44%) for VIT vs 18/58 (31%) for VI; adjusted odds ratio =0.50, 95%CI, 0.22-1.12, p=0.09. The VIT arm achieved significantly better PFS (adjusted Hazard Ratio (HR)=0.65, 95%CI, 0.43-0.97, p=0.036) and OS (HR=0.53, 95%CI, 0.33-0.83, p=0.005) compared to VI. PFS and OS results were similar when only relapsed patients were included. Adverse events > grade 3 were more frequent in VIT compared to VI, but only hematological toxicity was significantly increased (81% for VIT, 59% for VI, odds ratio=1.36, 95%CI, 1.06-1.76, P=0.02).

Conclusions: The addition of temozolomide to VI improves PFS and OS of pts with relapsed/refractory RMS. VIT is now standard treatment for relapsed RMS in Europe.

FPS 01: ALL - Clinical

FP001 SIOP19-1096 | COG AALL0434: Randomized Trial of Escalating Dose Versus High Dose Methotrexate and Nelarabine for Adolescents and Young Adults with Newly Diagnosed T-Cell Acute Lymphoblastic Leukemia

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Background/Objectives: Background: Previous clinical trials have reported that adolescent and adult (AYA) patients treated for T-cell acute lymphoblastic leukemia (T-ALL) have lower event-free survival (EFS) and overall survival (OS) and increased toxicity as compared to younger patients. Results for the AYA cohort on AALL0434 are reported here.

Design/Methods: Methods: AALL0434 enrolled 1562 T-ALL patients (2007-2014) and included a 2 x 2 pseudo-factorial randomization using the COG augmented BFM (ABFM) regimen. AYA were defined as age greater than or equal to 16 years of age n=226 with 1336 participants <16 years old. Participants were randomized to receive escalating dose methotrexate without leucovorin rescue + pegaspargase (CMTX) or high dose MTX (HDMTX) + leucovorin rescue. Intermediate and high-risk patients were randomized to receive or not receive six 5-day courses of nelarabine (Nel) 650 mg/m²/day. The intermediate and high risk patients received prophylactic (1200 cGy) or therapeutic (1800 cGy for CNS3) cranial irradiation. Those with induction failure were non-randomly assigned to HDMTX+Nel.

Results: The 5-year EFS for AYA is 81% compared to 84% for those <16 years old (P=.5965), and OS was similar at 88% and 90% respectively (P=.3478). AYA patients randomized to CMTX n=70 had a superior DFS/OS compared to those

randomized to HDMTX $n=72$ with 5-year DFS 96% versus 78% ($P=0.0038$) and OS 97% vs 88% ($P=0.0296$). No advantage was seen in AYA receiving Nel with 5-year DFS 85% for + Nel ($N=56$) and 89% for -Nel ($N=54$) ($P=0.8116$). AYA patients did not have higher induction failures or induction deaths compared to younger patients but were higher risk group category ($P=0.0002$).

Conclusions: COG AALL0434 shows outstanding overall outcomes for AYA patients which are similar to younger aged T-ALL patients despite AYA patients having higher risk group categories. CMTX holds a survival advantage for AYA T-ALL patients.

FP002 SIOP19-0460 | ZUMA-4 Phase 1: KTE-X19, an Anti-CD19 Chimeric Antigen Receptor (CAR) T Cell Therapy, in Children and Adolescents with Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia (R/R B-ALL)

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Background/Objectives: KTE-X19, formerly KTE-C19, has shown promising early results in children and adolescents with R/R B-ALL. Presented here are end of Phase 1 results from ZUMA-4.

Design/Methods: In this dose-finding study, patients aged 2–21 years with R/R B-ALL (Ph+ allowed) and >5% bone marrow (BM) blasts received 2 or 1×10^6 CAR T cells/kg after conditioning chemotherapy. The primary endpoint was incidence of dose-limiting toxicities (DLTs). Secondary endpoints included complete remission (CR) rate (CR and CR with incomplete hematologic recovery [CR+CRi]) and overall survival (OS). KTE-X19 formulation was optimized in two 1×10^6 dose groups: 40-mL versus 68-mL.

Results: As of 10/11/2018, 24 patients received KTE-X19 (median age 13 years; 42% ≥ 3 prior regimens; 29% primary refractory disease; 25% R/R post-alloSCT; 37% median pre-conditioning BM blast count). Median follow-up was 13.2 months. Four patients received 2×10^6 cells/kg (with no DLTs in evaluable patients [$n=3$]); 11 received 1×10^6 cells/kg (68-mL), and 9 received 1×10^6 cells/kg (40-mL). The most common Grade ≥ 3 AEs were hypotension (50%) and anemia (33%). Rates of Grade ≥ 3 neurologic events were 25%, 36%, and 11% in the 2×10^6 , 1×10^6 (68-mL), and 1×10^6 (40-mL) groups, respectively, and rates of Grade ≥ 3 CRS were 75%, 18%, and 22%. There were 3 Grade 5 AEs, all unrelated to KTE-X19. All but 2 patients in the 1×10^6 (40-mL) group were evaluable for efficacy with ≥ 2 months of follow-up. The CR+CRi rate was 100%, 64%, and 71% in the 2×10^6 , 1×10^6 (68-mL), and 1×10^6 (40-mL) groups. Median OS was not reached for either 1×10^6 group and was 8 months for the 2×10^6 group. CAR T cell expansion was observed at all doses/formulations.

Conclusions: Children and adolescents with R/R B-ALL treated with KTE-X19 achieved high remission rates, with a manageable safety profile. Phase 2 of ZUMA-4 is ongoing at the 1×10^6 cells/kg (40-mL) dose.

FP003 SIOP19-0249 | Impact of Asparaginase Discontinuation on Outcome in Childhood Acute Lymphoblastic Leukemia: A Report from the Children's Oncology Group (COG)

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Background/Objectives: Asparaginase (ASP) is an important component of acute lymphoblastic leukemia (ALL) treatment, but is often discontinued for toxicity. For allergic reactions, but not other toxicities, Erwinia Asparaginase (EA) is often substituted. Most treatment protocols use discrete, discontinuous periods of asparagine depletion. In the context of such protocols, the impact of EA substitution or complete ASP discontinuation is unknown.

Design/Methods: Patients age 1-30.99 years enrolled on frontline COG trials for B-ALL [standard risk (NCI SR):

AALL0331; high risk (NCI HR) AALL0232] were included. The number of prescribed pegaspargase (PEG) doses varied from 2-11, depending on trial, risk strata, and randomization. Maintenance therapy did not contain ASP. Landmark analyses starting at Maintenance compared event free survival (EFS) between those receiving all prescribed doses of PEG vs. those switched to EA but receiving all doses vs. those not receiving all ASP doses.

Results: This study included 5,195 AALL0331 and 3,001 AALL0232 patients. The cumulative incidence of PEG discontinuation was $12.2 \pm 4.6\%$ on AALL0331 and $25.4\% \pm 0.8\%$ on AALL0232. In multivariable analyses adjusted for patient and disease variables, NCI HR patients who did not receive all prescribed ASP doses had inferior EFS [hazard ratio (HR) 1.5, 95% confidence interval (95CI) 1.2-1.9; $p=0.002$] compared to those receiving all prescribed PEG doses. Patients with EA substitution who completed their courses were not at increased risk (HR 1.1, 95CI 0.7-1.6; $p=0.69$). Sensitivity analyses excluding patients discontinuing ASP due to pancreatitis or thrombosis yielded similar results. NCI SR patients who discontinued ASP were not at elevated risk (HR 1.2, 95CI 0.9-1.6; $p=0.23$), except when analyses were restricted to NCI SR patients with slow early response (HR 1.7, 95CI 1.1-2.7; $p=0.03$).

Conclusions: Discontinuation of ASP doses is associated with significantly inferior EFS and must be balanced against the risks of ASP re-challenge. Our results also illustrate the potentially severe consequences of EA shortages.

FP004 SIOP19-0635 | Determinants of Survival After First Relapse of Childhood Acute Lymphoblastic Leukemia (ALL): A Children's Oncology Group (COG) Study

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Background/Objectives: Patients with relapsed ALL have a historically poor outcome.

Design/Methods: We examined overall survival (OS) after first relapse, defined as duration from first relapse to death,

for patients treated on 10 COG frontline trials between 1996 and 2014.

Results: Of 15,874 patients enrolled on frontline trials, 1,967 (12%) relapsed. Rates were similar for T and B-ALL, 11% vs. 12%. Relapse patterns differed by phenotype: 47% of B-ALL relapses occurred late (≥ 36 months), and bone marrow (BM) relapse predominated at all times. Conversely 65% of T-ALL relapses were early (< 18 months) with similar numbers of isolated CNS (iCNS) and isolated BM (iBM) relapses.

Five-year OS ($\pm$ SE) after relapse for patients with B (N=1623), T (N=221), and infant (N=123) ALL were $52 \pm 1\%$, $33 \pm 3\%$ and $19 \pm 4\%$. Five-year OS rates for early BM relapse were similar for both B and T-ALL (28%), but differed for late relapses: B-ALL $65 \pm 2\%$ and T-ALL $50 \pm 12\%$. Cytogenetic subtype was significantly associated with 5-year OS post-relapse: *ETV6-RUNX1* $76 \pm 4\%$, double trisomy $70 \pm 4\%$, *E2A-PBX1* $32 \pm 7\%$, *KMT2A*-rearrangement $28 \pm 10\%$ and hypodiploidy $16 \pm 6\%$.

In multivariable Cox regression analysis, time to relapse, site of relapse, age < 1 or ≥ 10 years at diagnosis, initial WBC $\geq 100K$, T-cell phenotype and unfavorable cytogenetic subtype (within B-ALL) were associated with worse outcomes post-relapse.

Compared to the prior COG report (Nguyen, Leukemia 2008), 5-year OS has improved over time for relapsed B-ALL from $37 \pm 2\%$ to $52 \pm 1\%$ ($p<0.001$) and T-ALL from $23 \pm 4\%$ to $33 \pm 3\%$ ($p<0.05$). Five-year OS improved significantly for iBM relapse from $24 \pm 2\%$ to $45 \pm 2\%$ ($p<0.001$), but was similar for iCNS relapse ($59 \pm 3\%$ vs. $65 \pm 3\%$, $p=0.15$).

Conclusions: Relapse rates for ALL have decreased over time with relapse sites and outcomes differing by phenotype and genotype. Similar to initial diagnosis, outcomes for relapsed B-ALL track with cytogenetic subtype. Compared to prior analyses, survival after relapse improved significantly, especially for iBM relapse.

FP005 SIOP19-0575 | CD9 Confers Poor Survival in Pediatric B-Precursor Acute Lymphoblastic Leukemia and can be Effectively Targeted by Antibody Blockade

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Background/Objectives: CD9 has been implicated in cancer progression but its prognostic relevance and therapeutic value in pediatric B-precursor acute lymphoblastic leukemia (B-ALL) remain largely unknown. This study aims to: (1) characterize the association of CD9 expression with long-term patient survival outcomes; (2) assess the impact of CD9

blockade on leukemia progression; and (3) evaluate the effect of anti-CD9 on normal hematopoiesis.

Design/Methods: Patients were stratified into CD9+ and CD9- subgroups for comparison of overall survival (OS) and relapse-free survival (RFS). NOD/SCID mice were infused with B-ALL cell lines, patient-derived leukemic blasts or cord blood CD34+ cells, and treated with control IgG or anti-CD9 as a single-agent or combined with standard chemotherapy. Leukemic load and stem cell engraftment were measured by flow cytometry.

Results: Among 136 pediatric B-ALL cases, blasts of 107 patients (78.7%) were CD9+. The 5-year RFS rate of CD9+ patients was significantly lower than that of CD9- patients (65.4% vs. 86.2%; $P=0.038$). Multivariate analysis revealed that CD9 positivity independently predicted inferior OS (HR=4.4; $P=0.049$) and RFS (HR=5.2; $P=0.004$). In NOD/SCID mice transplanted with B-ALL cell lines ($n=3$) and primary leukemic blasts from patients with high-risk and refractory B-ALL ($n=5$), administration of CD9 antibody substantially reduced leukemic burden by 78.4–99.9% ($P<0.01$) and prolonged animal survival by 1.6–2.1-fold ($P<0.01$). Anti-CD9 did not compromise hematopoietic stem cell engraftment ($n=3$), indicating leukemia-selective activity. Combined treatment with anti-CD9 and chemotherapy further reduced leukemic load and extended survival, when compared with animals receiving monotherapy ($P<0.001$).

Conclusions: Our study identified CD9 as a new prognostic marker in pediatric B-ALL and validated the efficacy of anti-CD9 for suppressing leukemia progression. Inclusion of CD9 into the diagnostic marker panels would potentially identify patients who might benefit from targeted therapy. In addition, anti-CD9 could be developed as an adjunct to conventional chemotherapy for combating chemoresistant B-ALL.

FP006 SIOP19-1500 | Socioeconomic Status and Physical Late Effects: Social Inequalities in Health in Long-Term Childhood Leukemia Survivors

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Background/Objectives: In a growing population of childhood leukemia survivors, issues surrounding post-cancer life are now mainly asked in terms of morbidity due to long-term side effects of treatment received. Using data of the French LEA cohort (Leucémie de l'Enfant et Adolescent [childhood and adolescent leukemia]), our goal was to explore the link between socioeconomic status and physical late effects in childhood leukemia survivors, long after treatment period.

Design/Methods: The cohort includes children treated for acute leukemia since January 1980, surviving at one year after the end of treatment. Regular assessments are based on clinical examinations during specific medical visits and laboratory exams to document the occurrence of late side effects (height and weight growth, thyroid function, second cancer, metabolic syndrome, osteonecrosis...) in association with evaluation of socioeconomic data and quality of life reported by patients themselves or their parents. To evaluate the association between socioeconomic status and late effects, a multivariate logistic regression was performed.

Results: The present study included 1,206 patients. The mean current age was 16.1 ± 7.0 years and the mean duration of follow-up from diagnosis to evaluation was 10.4 ± 6.1 years. Most of the patients have been diagnosed with ALL (85.9%) and 228 patients (18.9%) underwent a hematopoietic stem cell transplantation (HSCT). Among patients included, 843 (70.0%) have developed late side effects. Patients from a disadvantaged socioeconomic environment were more likely to develop at least one sequela than the others (406/551, 73.7% versus 437/654, 66.8% - $P=0.01$). After adjustment (sex, type of leukemia, age at diagnosis, duration of follow-up, relapse, HSCT, irradiation of central nervous system), the link was still significant (OR=1.4 [1.1–1.7]).

Conclusions: If there seems to be a potential link between socioeconomic level and late side effects, it is important to consider the role that a standardized program of long-term follow-up can play in reducing these social inequalities in health.

FPS 02: Psychosocial 1

FP007 SIOP19-0282 | Cortical Thinning and Altered Functional Coherence in Survivors of Childhood Sarcoma

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Background/Objectives: High-dose chemotherapy is increasingly evidenced to be neurotoxic and result in long-term neurocognitive sequelae. However, research on cortical development in childhood cancer patients is currently limited. As patients with childhood sarcoma receive high-dose chemotherapy, we aimed to investigate cortical brain alterations in adult survivors.

Design/Methods: We analyzed high-resolution structural (T1-weighted) MRI and resting-state functional MRI (rsfMRI), to derive structural and functional cortical information in adult survivors of childhood sarcoma, who had received high doses of intravenous chemotherapy (n=33). These scans were compared to age- and gender- matched controls (n=34). Cortical volume and thickness were investigated using voxel-based morphometry (VBM) and vertex-wise surface-based morphometry (SBM), respectively. Cortical regions showing lower volume or thickness were then further implemented as seeds of interest for rsfMRI-derived estimates of functional coherence. Then, we explored whether structural measures were associated with potential known risk factors, such as age at diagnosis, and cumulative doses of chemotherapeutic agents (methotrexate and ifosfamide). Finally, we investigated the link between functional regional strength, neurocognitive assessments and subjective daily life complaints.

Results: We observed lower grey matter volumes in cerebellar and frontal areas, as well as frontal cortical thinning. Cerebellar volume appeared dose-dependent, while orbitofrontal thickness was age-related. Furthermore, cortical thickness of the parahippocampal area appeared lower in survivors, if the group comparison was not controlled for depression. This region specifically showed lower functional coherence in survivors, which was associated with lower processing speed.

Conclusions: This study suggests cortical thinning as well as decreased functional coherence in survivors of childhood sarcoma, which could be important for both long-term attentional functioning and emotional complaints in daily life. Frontal brain areas might be specifically vulnerable during adolescence.

FP008 SIOP19-1010 | Could Single White Matter Tracts Tell Us Something about Long-Term Executive and Motor Functioning of Survivors of Childhood Posterior Fossa Tumors?

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Background/Objectives: Posterior fossa tumors (PFTs) in children are the most prevalent central nervous system tumors in pediatric patients. We investigated their long-term executive and motor outcomes and its association with the microstructure of specific white matter tracts.

Design/Methods: Diffusion-weighted MR-scans and neurocognitive assessments were acquired in 19 adult survivors of PFTs and 21 healthy controls. Mean age at diagnosis = 8.6 years; >2 years out of treatment [16-34] years, pilocytic astrocytoma (n=7), ependymoma (n=1), medulloblastoma (n=11). MR-scans (echo-planar, multi-shell b=700,1000, 2800s/mm²) were preprocessed using MRtrix3. ExploreDTI was used for manual delineations of a set of predefined white matter tracts. Mean Fractional Anisotropy (FA) was calculated as microstructural feature of each tract in each individual.

Processing speed and executive functioning were assessed using the BRIEF questionnaire, computerized Amsterdam Neuropsychological Task battery, working memory index (WMI) and processing speed index (PSI) of the WAIS-IV intelligence test. Motor functioning was clinically evaluated using the PedsQL and observed post-surgical ataxia. Kruskal-Wallis tests were performed for group comparisons between FA values of each tract in irradiated patients (n=13), non-irradiated (n=6) and healthy controls (n=21). Spearman rank correlations were calculated between FA (of significant tracts) and executive outcomes patients.

Results: The left superior longitudinal fasciculus, corpus callosum, right inferior longitudinal fasciculus and bilateral inferior occipital fasciculus appeared significantly different between the three subgroups, but only the right ILF survived correction for multiple tests. The latter tract was associated with the subscales flexibility, working memory and task evaluation of the BRIEF, WMI and PSI, baseline speed and motor complaints in daily life. The majority of tracts (7/9) showed lower FA in patients with post-surgery ataxia, albeit non-significant.

Conclusions: This study suggests that decline in executive and motor functioning in survivors of PFTs could partly be

explained by therapy-induced damage to specific tracts, which are important for visually-guided behavior.

FP009 SIOP19-0744 | Exploring the Use of Virtual Reality in an Inpatient Paediatric Oncology Environment

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Background/Objectives: To pilot the use of Virtual Reality in an inpatient paediatric oncology setting. We investigated whether immersive VR distraction has a greater positive influence on children's physical (pulse rate, nausea, pain) and emotional mood states (anxiety, anger, depression), when compared to an iPad attentional control condition. A secondary objective was to understand what factors influence the effectiveness of VR intervention.

Design/Methods: Participants were 90 oncology inpatients, aged 7-19 years, and their primary caregiver. Using a randomised controlled study design, children were allocated to VR or iPad conditions, and one of three content groups (i.e. 360° footage of animals, nature, travel). Measures included a trait anxiety scale, pre-post-intervention state measures using visual analogue scales and an objective measure of physiological arousal (pulse rate). Post intervention, patients reported on level of immersion, enjoyment and simulator sickness.

Results: Compared to iPad, patients accessing Immersive VR reported enhanced mood, and greater reductions in negative symptoms of anxiety, anger, pain and nausea. Effect sizes ranged from 0.1–0.4. Patients also benefited from novel iPad distraction, with trends in the same direction. There was no change in physiological arousal levels in either condition before, during or immediately after intervention. Moderation analysis was used to investigate the influence of immersion, enjoyment, content and patient variables on outcomes. There was evidence that patient's functional status (PedsQL), gender, age, and level of immersion were variably important in influencing the magnitude of differences between the VR and iPad conditions on mood, anxiety and pain.

Conclusions: Findings support the use of immersive VR in clinical oncology settings to improve patient care and well-being, particularly mood. Further investigation into how immersive VR can support children's adjustment to hospitalisation and coping with cancer treatment is warranted. Consideration of factors moderating the effectiveness of VR contribute knowledge to VR content development.

FP010 SIOP19-0030 | Diminished Social Attention in Pediatric Brain Tumor Survivors

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Background/Objectives: Pediatric brain tumor survivors (PBTS) experience significant social deficits, including fewer friends and greater social isolation than peers. Research is needed to understand the factors contributing to these problems. Difficulties with regulating visual social attention have been implicated in an extensive number of studies in youth with autism spectrum disorder (ASD). This study used eye tracking technology to compare the visual social attention of PBTS, youth with ASD and typically developing (TD) youth using an established social play paradigm.

Design/Methods: Three groups (PBTS, ASD, TD), each consisting of 30 age-, gender-, and IQ-matched youth (ages 6-17), participated in the study. PBTS participants were > 5 years from diagnosis and > 2 years from the completion of tumor treatments. A Tobii X120 gaze tracker recorded participant eye gaze patterns during the Social Play Task, which involved watching videos depicting siblings engaging in either interactive/joint or parallel play. Analyses compared Social Prioritization scores (higher scores indicate more face looking and less background looking) between groups.

Results: Groups significantly differed on Social Prioritization scores for the joint condition, $F(2,86) = 6.37$, $p < .01$, $\eta^2 = .13$. TD youth had higher Social Prioritization scores than youth with ASD, $p < .05$, and PBTS, $p < .01$. Groups also differed on Social Prioritization scores for the parallel condition, $F(2,86) = 7.05$, $p < .01$, $\eta^2 = .14$, with TD youth having higher Social Prioritization scores than youth with ASD, $p < .05$, and PBTS, $p < .01$. Across conditions, PBTS had Social Prioritization scores that were similar to youth with ASD.

Conclusions: This innovative study offers the first evidence for disrupted social attention in PBTS that resembles that of youth with ASD. Findings could represent a new conceptualization of the social difficulties of PBTS and guide interventions that increase gaze preference for socially relevant stimuli during social interactions.

FP011 SIOP19-0686 | Personalised Medicine in Paediatric Cancer Care: What Matters in Decision-Making?

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Background/Objectives: The clinical application of genomics in paediatric oncology is in its infancy and knowledge about healthcare provider (HCP), parent and community attitudes to this technology is limited. This study aimed to examine factors that inform decision-making related to genomic sequencing and targeted (personalised) therapy in the context of difficult-to-treat childhood cancer.

Design/Methods: The study used a discrete choice experiment approach. Participants completed an online survey which presented scenarios and asked them to consider whether or not they would choose (parents and community) or recommend (HCP) a genomically guided approach to the child's/patient's care in each scenario. Participants responded to 8 scenarios which varied based upon 9 attributes: potential survival benefit, prognosis, likelihood of finding a target drug, quality of life (QoL), parent/HCP preference, need for a biopsy, cost and funding source. Data were analysed using a probability regression model (PROBIT) for the overall sample and examined differences between respondent groups.

Results: Participants were 130 Australian and New Zealand HCPs, 126 parents of childhood cancer survivors and 531 community members. Overall, the probability of recommending or agreeing to genomics increased significantly with improved prognosis, potential survival benefit, improvements in QoL, and where it was supported by the decision-making partner. It decreased based on increasing cost of care and if parents were the source of funds. Sample-based results showed that HCPs were more responsive to all factors, community members were least concerned regarding QoL or support for the decision, and parents were least concerned regarding costs or the likelihood of finding a target. None were influenced by whether or not a biopsy was required.

Conclusions: This study provides important insights into the factors that influence preferences for genomics and personalised medicine across 3 stakeholder groups. The results are highly relevant for the development of clinical genomics programs and guiding ethical decision-making.

FP012 SIOP19-0682 | Feasibility, Acceptability and Safety of a Novel Online Group-Based Psychological Support Program for Parents After Their Child's Cancer Treatment: A Three-Armed Randomized Trial of 'Cascade'

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Background/Objectives: Completing cancer treatment can represent a time of uncertainty and vulnerability. Online group-based psychological therapies could provide an opportunity for parents of young cancer survivors (0-18 years) to develop new coping skills and connect with others. We investigated whether 'Cascade', a 4-session, videoconferencing group-based cognitive-behavioural intervention, was feasible, acceptable and psychologically safe. Cascade aimed to improve parents' quality of life in the early stages of their child's survivorship.

Design/Methods: A randomised-controlled trial compared Cascade with an online peer-support group and waitlist control. Parents completed baseline, 1-week, 5-week and 6-month post-intervention questionnaires. We used enrolment rates, participant engagement and perceived benefit/burden to ascertain feasibility and acceptability. We monitored distress weekly to determine safety. We delivered 6 Cascade and 5 peer-support groups (2-4 parents/group).

Results: Seventy six parents opted-in to the study, 55 of whom enrolled in the program (87% mothers; 67% from major cities; mean child age: 8 years; 35% leukemia/lymphoma). Parents were randomized to Cascade (n=20), peer-support (n=17) or waitlist (n=18). Ninety percent of parents completed ≥3/4 Cascade sessions. Perceived benefit outweighed perceived burden, with 92% of parents rating participation as beneficial and 69% rating it as 'not at all' burdensome. Twenty-four percent of parents returned a clinically-concerning distress screen at some point during the study, however upon further assessment, none were at immediate mental health risk.

Conclusions: Findings suggest that Cascade is a useful model for delivering psychological support after cancer treatment completion. Further trials will be important to determine whether Cascade elicits improvements in quality of life.

FPS 03: Toxicity and Supportive Care 1

FP013 SIOP19-0160 | In Children with Chemotherapy for Cancer 39.0°C Ear Temperature is a Safe Fever Limit. The Randomized Controlled Multicenter SPOG 2015 FN Definition Study (NCT02324231)

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Background/Objectives: Fever in neutropenia (FN) is the most frequent complication of chemotherapy for cancer. In children, FN mortality is <1% thanks to emergency treatment including broad-spectrum antibiotics. The temperature limit defining fever (TLDF) used clinically varies from 37.5°C to 39.0°C. As previously published, a higher TLDF can avoid FN diagnoses in patients spontaneously recovering. This study aimed to determine if a TLDF of 39.0°C ear temperature is non-inferior to a TLDF of 38.5°C regarding safety.

Design/Methods: This controlled non-blinded multicenter study randomized pediatric patients in monthly clusters to a TLDF of 39.0°C or 38.5°C. FN diagnosis and therapy below the randomized TLDF was allowed for clinical reasons. The primary outcome was the rate of FN with any safety relevant event (SRE) per chemotherapy exposure time (CET). SREs were death, admission to intensive care unit (ICU), severe sepsis and bacteremia.

Results: Six sites of the Swiss Paediatric Oncology Group (SPOG) recruited 269 patients from 04/2016 to 08/2018. A SRE was diagnosed in 72 (20%) of 360 FN episodes (death, 0; ICU admission, 16; severe sepsis, 22; bacteremia, 56). In 92 CET years randomized to 39.0°C, 151 FN episodes were diagnosed (1.64/year), including 51 (34%) below 39.0°C and 22 (15%) with SRE (0.24/year). In 103 CET years randomized to 38.5°C, 209 FN episodes were diagnosed (2.03/year), including 28 (13%) below 38.5°C and 50 (24%) with SRE (0.49/year). The mixed Poisson regression rate ratio of FN with SRE in 39.0°C versus 38.5°C was 0.56 (95% upper confidence limit, 0.72). The predefined non-inferiority margin was 1.33.

Conclusions: In children with chemotherapy for cancer, a high TLDF of 39.0°C is efficacious and safe. For Switzerland and comparable settings, 39.0°C can be recommended as new evidence-based standard TLDF. The responsible physician will decide to diagnose and treat FN below this TLDF if clinically indicated.

FP014 SIOP19-1724 | Using the Model for Improvement to Decrease Time to Antibiotic Administration Among Pediatric Oncology Patients with Fever and Neutropenia in Two Emergency Departments in Mexico

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Background/Objectives: Reduction of treatment-related mortality by introducing quality improvement methodologies is one out of four strategic pillars of the Mexico in Alliance with St. Jude (MAS) group. Decreasing time to antibiotic administration (TTA) to less than 60 minutes in pediatric cancer patients with fever and neutropenia (The Golden Hour Project) is part of the MAS supportive therapies portfolio. We used the Institute of Healthcare Improvement (IHI) model for prototyping the implementation of "The Golden Hour Project" in two emergency departments (EDs) in Guadalajara and Culiacan, Mexico.

Design/Methods: A multidisciplinary team was identified in each ED. Both teams received simultaneous weekly online coaching on the IHI methodology. First, a block diagram was created to understand the current processes. Then, after reviewing the published literature, the data collection plan and measures were identified. Each team identified different change ideas and prioritized them using an impact-effort matrix. Finally, several Plan-Do-Study-Act (PDSA) cycles that executed changes such as using an urgent stamp in the WBC order, creating standing orders for antibiotics, use of a cart with supplies at the point of care (golden cart), and staff training were implemented.

Results: A total of 234 FN events were included. We found a significant decrease in the median TTA in both EDs (240 vs. 103 and 356 vs. 170 minutes). The time from triage to antibiotic indication predominately decreased in the ED that implemented the urgent stamp in the WBC order (250 vs. 90 minutes) and the time from antibiotic indication to

antibiotic administration predominately decreased in the ED that used the golden cart (169 vs. 31 minutes). ICU admission ($p=0.037$) and mortality ($p=0.024$) decreased when compared with baseline data.

Conclusions: Our approach was effective to decrease TTA and improve clinical outcomes. The MAS group will scale-up this model to 20 centers in Mexico using the IHI Breakthrough Series collaborative methodology.

FP015 SIOP19-0690 | Time to Antibiotics and Clinical Outcomes in Fever and Neutropenia During Chemotherapy for Cancer, A Systematic Review

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Background/Objectives: Fever in chemotherapy-induced neutropenia (FN) is a frequent complication in patients with cancer. Prompt antibiotic therapy is standard of care; however, the association of time to antibiotics (TTA) with clinical outcomes is unclear. We systematically reviewed available data on the association between TTA and clinical outcomes in FN.

Design/Methods: The search covered seven databases, reference lists were reviewed, forward citations searched and experts contacted. Biases and study quality were assessed with the ROBINS-I tool. Safety (death, intensive care unit (ICU) admission, sepsis) and treatment adequacy (relapse of primary infection, persistence or recurrence of fever) were the primary outcomes.

Results: Of 5389 titles and abstracts screened, 142 studies were retrieved and 10 studies included. All were observational and all but one with at least moderate risk for bias, mostly due to baseline confounding. Findings regarding safety were inconsistent. Two studies at lower risk for bias and controlling for triage bias reported impaired safety for longer TTA: 28-day mortality was lower in patients with TTA ≤ 30 min (3.0%) versus 31-60min (18.1%) ($n=307$; HR, 1.18; 95%CI, 1.10-1.26); and adverse events (mortality, ICU admission, fluid-resuscitation) were less frequent in patients with TTA ≤ 60 min (5.2%) versus 61-120min (14.2%) ($n=1628$; OR, 2.88; 95%CI, 1.70-4.89). Meta-analysis was feasible on four studies at moderate risk of bias, with three studies each reporting on death (OR 0.78; 95%CI, 0.16-3.69) and on ICU admission (OR 1.43; 95%CI 0.57-3.60). No study reported data on treatment adequacy. Triage bias, i.e., faster treatment of patients in reduced general condition or with known risk for poor outcome, was identified as a relevant confounding factor.

Conclusions: There seems to be an association between longer TTA and impaired safety. More knowledge about TTA effects on safety are important to optimize treatment guidelines for FN. Controlling for triage and other biases necessary to gain further evidence.

FP016 SIOP19-0658 | Adaptation and Evaluation of the Symptom Screening in Pediatrics Tool for Use in Australia: A Child Friendly Patient Reported Outcome Measure

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Background/Objectives: Routine use of Patient Reported Outcome Measures (PROMs) to assess symptoms in childhood cancer is not common, yet children experience a significant number of symptoms.

Our aims were to adapt and evaluate the Symptom Screening in Pediatrics Tool (SSPedi), a PROM developed in Canada for use with Australian children.

Design/Methods: SSPedi wording was adapted and item relevance assessed by an expert clinical group ($N=7$) resulting in the Australian version (SSPedi-Aus). Cognitive interviewing with children ($N=10$, 8-18 years) established understanding and difficulty with completing. A second group of child-parent dyads ($N=30$) were recruited to evaluate psychometric properties (content validity, test-retest reliability, and parent-proxy) measured with Intraclass Correlation Coefficients (ICC) with 95% Confidence Intervals (CI). Acceptability and usefulness of SSPedi-Aus were also assessed.

Results: Results Children reported some difficulty with completing SSPedi-Aus, however correctly understood items and the scale. Construct validity was confirmed across all items by 30 children. Child test-retest achieved excellent concordance (ICC 0.98, 95% CI 0.91 to 0.99). Symptoms causing the most distress were related to fatigue (30%), changes in taste (30%) and appetite (20%). Although parents also identified fatigue (27%), they did not identify changes in taste or appetite. Children and parents returned a similar mean total score (13.43 vs. 13.80) with a weak overall interrater reliability (ICC 0.37, 95% CI -0.26 to 0.70, $p=0.12$). Free text responses were positive: "Answering questions about my symptoms makes me feel more secure about how I will be treated in the future." (Male patient) and "It's a good idea to have some structure to help children communicate about their symptoms" (Parent)

Conclusions: Conclusion Children are distressed by symptoms that may not be identified by parents or reported to

clinicians, yet these symptoms are amendable to intervention. The SSPedi-Aus is useful to assess the level of distress caused by symptoms in children.

FP017 SIOP19-0728 | A Qualitative Review of the Care Provided to Young UK Patients Who Received Chemotherapy up to 60 Days Prior to Death or Critical Care Admission

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Background/Objectives: The National Confidential Enquiry into Patient Outcome and Death (NCEPOD) is an independent body which aims to improve the quality of health care by reviewing clinical processes and outcomes. The aim of this study was to examine the pathway of care of patients aged 24 years and younger who died and/or had an unplanned admission to critical care within 60 days of receiving chemotherapy.

Design/Methods: UK-wide hospital data was used to identify patients with malignancy who had chemotherapy between 1.3.2014 and 31.5.2016 who were admitted to critical care or who died between 1.6.2014 and 31.5.2016. Questionnaires were sent to the clinician responsible for chemotherapy prescription, to the clinician responsible for the last admission and data was collated. Extracts of case notes were anonymised and peer reviewed using an agreed assessment form.

Results: 228 patients were identified, 53% had relapsed and 65% had received at least one previous protocol of therapy resulting in comorbidities in 71%. An adverse event occurred within 30 days of chemotherapy in 50% of patients. 69% died during the admission, 12.5% died following discharge. Only 18% of patients were treated within a clinical trial. 58.6% of patients received good care. There were clinical failings in 27% and organisational problems in 10%. In 33.8% the decision to start therapy was not discussed in a multidisciplinary meeting. 17.6% of consent forms did not state the chances of benefit and 56% did not mention the risk of death. Only 49% had a formal assessment of performance status before starting chemotherapy. There were 58 key findings which led to 16 recommendations.

Conclusions: This is the first UK confidential enquiry into the quality of care in young oncology patients and has resulted in 16 recommendations to help improve care provided in hospitals for this group of patients.

FP018 SIOP19-1240 | PEPTALK3: Multi-Centre Service Evaluation of VZIG and Oral Aciclovir as Post-Exposure Prophylaxis Against Varicella in Children with Cancer in the United Kingdom

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Background/Objectives: Exposure to varicella (VZV) and its potential to cause morbidity and treatment delays remain significant for children with cancer in the UK where there is no universal varicella vaccination programme. Paediatric oncology practice varies across the UK in the choice of post-exposure prophylaxis (PEP) after exposure to VZV between varicella zoster immunoglobulin (VZIG) and oral aciclovir (ACV). However, since August 2018, there is a national shortage of VZIG with a recommendation for ACV to be given as PEP.

The objective of this study was to compare incidence and severity of chicken pox in children who receive either VZIG or ACV as PEP.

Design/Methods: PEPTalk3 is a prospective service evaluation of VZV exposure and PEP administration in children with cancer currently on or within 6 months of treatment with negative VZV serostatus at diagnosis across 17 UK paediatric oncology centres. Data collection commenced on 1 May 2018 and each patient was followed up after exposure to identify cases of breakthrough varicella.

Results: Sixty-eight patients have received PEP over 11 months (mean age 5.2 years, range 2.1 to 10.4 years). Underlying diagnoses were 43 acute leukaemia, 19 solid tumours and 6 other). 18 patients received VZIG and 50 received ACV. ACV patients received variable dosing, frequency and duration. Most exposures (59%) were at school, nursery or child-care while 18% were household exposures. There were 3 cases of breakthrough varicella following PEP—two who received VZIG and one ACV. Two patients required hospital admission and all three had chemotherapy delayed.

Conclusions: Only 4% of patients who received PEP developed breakthrough varicella. Preliminary data indicates ACV may have similar efficacy to VZIG but further data is required to estimate prevalence with accuracy. Wide variation between centres in regimens used for ACV PEP suggest guidelines are required.

Acknowledgements: With thanks to the PEPTalk3 participating centres

FPS 04: Bone Tumours (The Nollenburg Award Session)

FP019 SIOP19-0483 | Radiotherapy Dose Escalation in Unresectable Ewing's Sarcoma/PNET: Final Results of a Single Institute Phase III Randomized Controlled Trial

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Background/Objectives: Assess the impact of radiotherapy (RT) dose escalation on disease related outcomes in surgically unresectable Ewing's sarcoma/ PNET.

Design/Methods: Patients with non-metastatic unresectable Ewing's sarcoma/ PNET treated with definitive RT were accrued. Following induction Chemotherapy patients were randomised between standard dose RT (SDRT: 55.8Gy/31 fractions) vs. escalated dose RT (EDRT: 70.2Gy/39 fractions delivered in two phases: Phase I - 55.8Gy/31 fractions followed by Phase II - 14.4Gy/8 fractions boost to the post-induction chemotherapy (CTh) volume. The hypothesis assumed that EDRT would improve local control by 17% from a baseline of 65% in SDRT to 82% in EDRT.

Results: Between April 2005 to December 2015, 95 patients (SDRT: 47 and EDRT: 48) with a median age of 17 years (range 3-47) were accrued. Majority were males (59%). Pelvis (63%): SDRT-28 (29.4%), EDRT-32 (33.6%) was the commonest site of primary. The median values for maximum tumor dimension (9.7cm) and SUV max (8.2) were similar between both arms. After a median follow-up of 44 months (Range 6-165; SDRT vs EDRT: 38 months vs 47 months, $p=0.39$), the local control (LC), event free survival (EFS), and overall survival (OS) was 67.4%, 36.8% and 51.6% respectively. LC was significantly superior in EDRT as compared to SDRT (79.2% vs 55.3%, $p=0.02$). Difference in EFS (29.8% vs 43.8%, $p=0.20$) and OS (40.4% vs 62.5%, $p=0.08$) were not significant between SDRT and EDRT. RTOG > grade 2 acute skin toxicity was higher in EDRT as compared SDRT (10.4% vs. 2.1%, $p=0.08$). Median musculoskeletal tumor society (MSTS) score was 29 (range 26-30) in both arms. Second malignancy was documented in one patient.

Conclusions: EDRT results in improved LC with a trend towards improved OS and good functional outcomes without a significant increase in toxicities. Radiotherapy dose escalation should be considered for surgically unresectable non metastatic Ewing's sarcoma/ PNET.

FP020 SIOP19-1738 | Multicentric Study of Interval-Compressed Multiagent and Randomized Metronomic Chemotherapy for Patients with Localized Ewing Sarcoma: Results of the Latin American Pediatric Oncology Group Trial

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Background/Objectives: Locally advanced Ewing Sarcoma at diagnosis and the limitations in care delivery motivated pediatric oncologists from the Latin American Pediatric Oncology Group (GALOP) to organize a multicenter protocol to determine the efficacy and safety of a risk adapted regimen.

To investigate the feasibility, safety, overall survival (OS), and progression free survival of combined modality therapy that incorporates interval-compressed VDC/IE (Vincristine, Doxorubicin, and Cyclophosphamide/Ifosfamide, and Etoposide), and metronomic chemotherapy (MC).

Design/Methods: Prospective randomized trial. Induction chemotherapy (CT) consisted of 6 alternating cycles of VDC/IE, followed by local control, and then 8 cycles at Consolidation. Time interval between cycles at Induction and Consolidation were 14 and 21 days, respectively. After Consolidation, patients were randomized to MC (cyclophosphamide, oral, 25mg/m²/day, and vinblastine, iv, 3mg/m²/week), for 1 year.

Results: Between Aug'2011-Aug'2018, 282 patients (62.4% Male), median age 11.06-years were recruited across 34 centers from Argentina, Brazil, Chile, and Uruguay. According the site of origin, 37.6% were extremities, 46.1% axial, and 16% pelvic; size >8cm in 53.3%; and bone/extracranial in 76.6%/23.4%.

Overall response rate after Induction was 80.5%. Local treatment was Surgery (48.6%), RT (21.9%), or combination (29.4%). With a median follow up of 32.3 months (range

0.2-105), five-years OS and event-free-survival (EFS) were 69.3%, and 63.2%, respectively. Five-years OS and EFS of the 52 patients in the MC group were 75.5% and 69.2%, and of the 66 patients in the FUP group were 74.8% and 69.2%. The time interval between cycles at Induction was 14+/-2 days in 39.8% of patients.

Febrile neutropenia (Grade 3-4) during conventional CT and MC was present in 18.6% and 3.3%, respectively.

Conclusions: Implementation of a multi-institutional protocol in 4 countries in South America was feasible and resulted in outcomes that are comparable to those of groups in high-income countries. MC did not seem to improve outcome.

FP021 SIOP19-0347 | Prediction of Chemotherapy Response in Primary Osteosarcoma Using Machine Learning Technique on Radiomic Data

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Background/Objectives: Osteosarcoma is the most common malignant bone tumor before 25 years of age. Response to neoadjuvant chemotherapy determines continuation of treatment and is also a powerful prognostic factor. There are currently no reliable ways to evaluate it early. The aim is to develop a method to predict the chemotherapy response using radiomics from pre-treatment MRI.

Design/Methods: Clinical characteristics and MRI of patients treated for local or metastatic osteosarcoma were collected retrospectively in the Rhône-Alpes region, from 2007 to 2016. On initial MRI exams, each tumor was segmented by expert radiologist and 87 radiomic features were extracted automatically. Univariate analysis was performed to assess each feature's association with histological response following neoadjuvant chemotherapy. To distinguish good histological responder from poor, we built predictive models based on support vector machines. Their classification performance was assessed with the area under operating characteristic curve receiver (AUROC) from test data.

Results: The analysis focused on the MRIs of 69 patients, 55.1% (38/69) of whom were good histological responders. The model obtained by support vector machines from initial MRI radiomic data had an AUROC of 0.98, a sensitivity of 100% (IC 95% [100%-100%]) and specificity of 86% (IC 95% [59,7%-111%]).

Conclusions: Radiomic based on MRI data would predict the chemotherapy response before treatment initiation, in patients treated for osteosarcoma.

FP022 SIOP19-0848 | Conditional Deletion of RPS19 in Bone as a Potential Murine Model of Diamond Blackfan Anemia (DBA)-Associated Osteogenic Sarcoma (OS)

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Background/Objectives: DBA is a rare autosomal dominant, inherited bone marrow failure syndrome (IBMFS). The disorder results predominantly from a mutation in a gene encoding one of 80 ribosomal proteins (RP), leading to RP haploinsufficiency. The disorder is characterized by erythroid failure, congenital anomalies and a predisposition to certain cancers. The relative risk of all cancers is increased; observed/expected (O/E) ratio of 4.8. For OS, in particular, the O/E ratio is 42 (Vlachos *et al.*, *Blood* 2018). Recently Ajore and colleagues (*EMBO Molecular Medicine* 2017) described heterozygous inactivating RP gene mutations in 43% of 10,744 cancer specimens and cell lines. The vast majority of RP haploinsufficient specimens/lines were also mutated at TP53. Currently, there is no *in vivo* model phenocopying cancer predisposition in DBA.

Design/Methods: Using *Rps19* as a model, we generated *Rps19*^{+/-} conditional knockout mice allowing for rp haploinsufficiency restricted to bone. We then characterized this model with regard to bone development and tumorigenesis *in vivo*. As we hypothesize that this mouse model would be predisposed to OS, we put the *Rps19*^{+/-} mice on a *p53*^{+/-} or *p53*-null background. Molecular, biochemical and histologic studies were performed on these mice at different stages of development and colonies were established.

Results: We observed skeletal anomalies and defective bone maturation and mineralization consistent with DBA in the mice, which correlated with decreased RUNX2 expression and abnormal Wnt signaling. Importantly, all defects were rescued in a dose-dependence manner when p53 was depleted *in vivo*.

Conclusions: We have successfully generated an *in vivo* murine model recapitulating the skeletal defects observed in osteogenic sarcoma-prone patients with DBA. We highlight defective Wnt signaling resulting in improper RUNX2 transcriptional activation as an underlying mechanism. We are now in the process of characterizing this model for OS development as the colonies age.

FPS 05: Renal Tumours

FP023 SIOP19-0373 | Synchronous Bilateral Wilms Disease in the SIOP WT 2001 Study: Report from the Renal Tumor Group of the International Society of Pediatric Oncology (SIOP-RTSG)

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Background/Objectives: 5-8% of children with Wilms tumour (WT) have bilateral disease, presenting two challenges: to cure and to spare renal function. We report results of SIOPWT2001 for bilateral diseases.

Design/Methods: All patients with suspected bilateral WT were treated with pre-operative chemotherapy Vincristine/Dactinomycin V/A), advised to be given as long as tumours showed signs of regression, followed by Nephron sparing surgery (NSS). Post-operative chemotherapy was advised according to the highest local stage and histology. In case of associated nephrogenic rest or nephroblastomatosis (Nbm), monthly maintenance therapy with V/A was given, up to a total therapy duration of 1 year. Nbm only and metachronous bilateral disease were excluded from this analysis.

Results: 275 Stage V WT pts, either bilateral WT (BWT), or unilateral WT and contralateral NR/Nbm (WTNbm), were prospectively registered in the SIOP 2001 study. Median age was 25 months (55% females). Congenital abnormalities were found in 19% pts and 10% had a family history. 12% were

metastatic. Median duration of pre-operative chemotherapy was 80 days and 59 days for BWT and WTNbm, respectively. Out of 240 analysable surgeries, 56% had one sided NSS, 32% both sides NSS and 10% bilateral total nephrectomy. Local WT stage was I (60%), II (17%) and III (21%). Histological risk groups were Low Risk (7.3%), Intermediate Risk (74%) and High Risk (14%). 43% pts with BWT had concordant histology both sides. With a follow up median of 89 months, OS for BWT and WTNbm was, respectively, 84.6% (95% CI 78.1-91.7) and 93.7% (95% CI 89.0-98.7) at 10 years. Renal function was normal in 80% of pts. 11% had end stage renal function (ESFR).

Conclusions: With a good cooperation between oncologists, radiologists, and surgeons 90% of children with bilateral disease (BWT or WTNbm) can be cured with low% of ESRF.

FP024 SIOP19-0193 | 10-Year Results Of UK Childhood Cancer and Leukaemia Group's (CCLG) UK Relapsed Wilms Tumour (UKWR) Trial

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Background/Objectives: The UKWR trial aimed to improve the historical low survival rates after relapse through a national protocol, risk-stratified according to prior therapy. The trial also evaluated efficacy and toxicity of high-dose melphalan in the high-risk relapse group.

Design/Methods: Relapsed/refractory Wilms (70) or clear cell sarcoma (3) patients were allocated to treatment arms based on time to relapse and initial therapy. Arm A: Stage 1 Non-anaplastic histology who had only received Vincristine (VCR) or up to 2 doses of VCR+Actinomycin-D (ACT), relapsing >6m from diagnosis received 12m 'intensive' AVD: ACT+VCR+Doxorubicin (DOX). Arm B: Stage 2 non-anaplastic histology treated with VCR+ACT relapsing >6m from diagnosis received 8 alternating courses DOX/Cyclophosphamide (CPM) and CPM/Etoposide (VP16). Arm C: all other relapses received 6 alternating courses of Carboplatin (CARBO)/VP16 and CPM/VP16 followed by Melphalan+Autologous stem cell rescue

(M+ASCT). All patients were recommended to receive radiotherapy +/- surgery for sites of relapse.

Results: From 2002 to 2008, 73 children were enrolled: Arms A (12), B (9) and C (52). Median age was 5.3 years. Site of relapses were chest (n=43) and abdomen (n=39). Thirty-eight children (22 CR, 14 PR, 2 SD after initial treatment) received M+ASCT with no transplant related mortality. Twenty-five children died: 5 in arm A+B, and 20 in arm C, all from tumour related causes. The 5yr event-free (EFS) and overall survival (OS) for the whole group were 59% and 69%, and 74%/84% (arm A+B) and 54%/63% (arm C), respectively. Median follow up for alive patients is 65.4months (8.1-155.4).

Conclusions: Survival rates following risk-stratification including M+ASCT are 10- 15% higher than published studies for similar high risk groups that did not include high dose chemotherapy. The SIOP-Renal Tumour Study Group UMBRELLA protocol will include high dose melphalan in a risk stratified approach according to prior therapy, that will test this prospectively.

FP025 SIOP19-0758 | Towards More Efficient Detection of Genetic Predisposition in Pediatric Renal Tumors: A Systematic Phenotypic Characterization

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Background/Objectives: To determine the role of genetic predisposition, we evaluated phenotypic features and results of targeted genetic testing in a national cohort of children with Wilms tumor (WT) and non-Wilms renal tumors.

Design/Methods: Clinical data were collected of all Dutch children with a renal tumor (2015-2019). Patients were evaluated by a clinical geneticist and categorized: (A) highly suspected of a specific predisposition syndrome, (B) suspected without a clear candidate gene or (C) not suspected of genetic predisposition.

Results: A total of 112 patients (90 WT, 22 non-WT) were identified. Ninety-one (81%) patients were evaluated by a clinical geneticist; sufficient data were available of the remaining 21 to include them. Genetic predisposition was suspected (category A/B) in 77 patients (69%). Category A (N=32) included patients with features of Beckwith-Wiedemann syndrome (BWS, N=15), urogenital malformations (N=4), rhabdoid tumor (N=6), angiomyolipoma (N=2), cystic nephroma (N=2) or other features associated with specific syndromes (N=3). Category B (N=45) included bilateral/multifocal disease (N=20), WT before age 1 year

(N=6), familial WT (N=1), other family history (N=11), adult-type tumor (N=4) and/or other suggestive features (N=6). Targeted testing confirmed pathogenic germline mutations in six patients with WT, including germline *WT1* (N=4), *NF1* (N=1) and biallelic *BRCA2* (N=1) mutations. BWS was confirmed in five patients by *11p15* methylation analysis of blood-derived DNA. Pathogenic germline mutations were identified in 5/12 non-WT cases (*TSC2*, *DICER1*, *FH* and two *SMARCB1*). Overall, a molecular diagnosis was confirmed in 16/112 patients (14%).

Conclusions: Two-thirds of children with renal tumors have phenotypic features of genetic predisposition, but only in 14% germline aberrations are detected by targeted genetic testing. Genetic analysis of tumor and kidney tissue will help to identify mosaic aberrations, undetectable in blood. Moreover, we now offer whole exome sequencing and trio-analysis in a research setting, for patients where predisposition is not identified by targeted testing.

FP026 SIOP19-0230 | International Comparisons of Clinical Demographics and Outcomes in the SIOP Wilms Tumour 2001 Trial and Study (2002-2011)

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Background/Objectives: International comparisons of patient/tumour demographics and survival can shed light on areas for healthcare system improvement. The SIOPWT2001 trial and study registered patients at a near population-level in Scandinavia (NOPHO), France (SFCE), Germany (GPOH),

Netherlands (NL), UK/Ireland (CCLG). This retrospective posthoc analysis of the SIOPWT2001 database aims to make visible and suggest reasons for any variations.

Design/Methods: All protocol patients (unilateral Wilms tumour (WT), age > 6m, pre-operative chemotherapy) registered from the specified countries between 2002-11 were eligible for inclusion. Median follow-up was 46.2m. Univariable Cox and multivariable (MVA) log rank statistics were applied, with GPOH as reference for hazard ratios (HR) for event free (EFS) and overall survival (OS).

Results: A total of 2,334 eligible patients were registered by GPOH (n=791), SFCE (n=624), CCLG (n=612), NL (n=164) and NOPHO (n=143). There was little variation between country groupings in mean age at diagnosis (47 months overall) or distribution of histological risk groups (low/intermediate/high risk=5%/82%/13%, respectively). The distribution of disease stage varied by country. 16% (range 10-18%) were metastatic at diagnosis. For localised WT, there was variation in 5yr EFS by national group: 84%(CCLG), 89%(NOPHO), 90%(GPOH), 91%(NL), 91%(SFCE) (p=0.002) that retained significance only for CCLG in MVA (HR1.62, p=0.01). 5yr OS was 93%(CCLG), 94%(NL), 96%(NOPHO), 96%(GPOH), 98%(SFCE) (p=0.001). In MVA, only superior survival in SFCE was significant (HR 0.3, p=0.005). 5yr EFS/OS for stage IV did not vary significantly. Further analyses are in progress that will include tumour volume and patients registered in other European countries and Brazil, where patients were registered from selected centres only.

Conclusions: International benchmarking of survival rates from WT within a large clinical trial and study database can demonstrate statistically significant differences. Clinical interpretation should take account of variation in tumour stage but also treatment factors.

FPS 06: Palliative Care

FP027 SIOP19-0174 | High Intensity End-of-Life Care Among Children, Adolescents and Young Adults with Cancer Who Die in Hospitals: A Population-Based Study from the French National Hospital Database

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Background/Objectives: *Background.* Efforts to improve the quality of end-of-life (EOL) care depends on better knowledge

of the care that children, adolescents and young adults with cancer receive, including High Intensity End-Of-Life (HI-EOL) care. The objective was to assess the rates of HI-EOL care in this population and to determine patient- and hospital-related predictors of HI-EOL from the French national hospital database.

Design/Methods: This was a population-based, retrospective study of a cohort of patients aged 0 to 25 years at the time of death who died at a hospital as a result of cancer in France (2014-2016). The primary outcome was HI-EOL care, defined as the occurrence of ≥ 1 chemotherapy < 14 days from death, receiving care in an intensive care unit ≥ 1 time, > 1 emergency room admission, and > 1 hospitalization in an acute care unit in the last 30 days of life.

Results: The study included 1,899 individuals from 345 hospitals; 61.4% experienced HI-EOL care. HI-EOL was increased with social disadvantage (OR=1.30 [1.03;1.65], p=0.028), hematological malignancies (2.09 [1.57;2.77], p<0.001), complex chronic conditions (1.60 [1.23;2.09], p=0.001) and care delivered in a specialty center (1.70 [1.22;2.36], p=0.001). HI-EOL was reduced in cases of palliative care (0.31 [0.24;0.41], p<0.001).

Conclusions: A majority of children, adolescents and young adults experience HI-EOL care. Several features (i.e., social disadvantage, cancer diagnosis, complex chronic conditions and care in a specialty center) were associated with HI-EOL care and should now be discussed with patients, families and professionals in order to define optimal EOL.

FP028 SIOP19-0519 | Indwelling Pleural Catheters in the Management of Malignant Pleural Effusions in Young Patients with Solid Tumours: A New Option in the Armamentarium of Symptomatic Treatment

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Background/Objectives: Malignant pleural effusions (MPE) are not uncommon in children, adolescent and young adults (CAYA) with advanced solid tumours. There are no pediatric guidelines for MPE management. Our main objective is to describe the contribution of indwelling pleural catheters (IPC) for MPE management in CAYA with cancer, in a palliative care setting.

Design/Methods: Monocentric retrospective analysis of all patients aged 0-25 years old at death, treated for a solid tumor and deceased between 2008 and 2018 with a significant pleural effusion, defined as filling $\geq 1/3$ of thoracic space. Pleural port-a-cath and PleurX[®] were the two IPC used. IPC were considered efficient if more than 3 pleural aspirations retrieving ≥ 200 ml or ≥ 10 mL/kg had been performed between IPC insertion and death. IPC were not accessed in case of sampling failure or symptom regression.

Results: Significant MPE was present in 52/391 (13%) deceased patients (45/52 with sarcoma). MPE was symptomatic in 65% of cases. Median age at MPE diagnosis was 17 years [range: 0.6-25.9]. A lung mass and/or mediastinal lymphadenopathies were associated in 90% of cases. Initial MPE aspiration was performed in 25/52 patients. Nine patients had subsequent iterative thoracenteses. An IPC was inserted for 16 patients. Median time between catheter insertion and first puncture was 3.5 days [range: 0-18]. Using IPC, median volume of aspiration was 600 mL [range: 0-3.000]. IPC was efficient for 9/16 patients (56%). Although 8/9 patients with exclusive classical thoracentesis experienced transient improvement of respiratory symptoms post-aspiration, only 2/9 had efficient pleural aspirations overall.

Conclusions: IPC are an effective device to manage MPE in CAYA with solid tumours, in the palliative care setting. They are a safe and efficient alternative to iterative thoracentesis and allow early home discharges. This original tool will be helpful for thoracic symptom management as an alternative to iterative pleural punctures.

FP029 SIOP19-1654 | Shared Spiritual Beliefs Between Adolescents with Cancer and Their Families: An Exploration of Social Determinants of Spiritual Well-Being

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Background/Objectives: Little is known about shared spiritual beliefs among teens with cancer and their families or the social determinants of spiritual well-being. Objective was to understand religious well-being and shared beliefs of adolescents with cancer with that of their families.

Design/Methods: As part of multi-site (3) randomized controlled trial, the Spiritual Well-Being Scale of the Functional Assessment of Chronic Illness Therapy-Version 4 (FACIT Sp

EX 4) was completed by 84 teens with cancer and 84 family members at baseline. Through the FACIT Sp EX 4, spiritual beliefs about adolescent's cancer were assessed from family member and adolescents individually and total family congruence on religious/spiritual well-being. Prevalence Adjusted and Bias Adjusted Kappa (PABAK) measured congruence. Social determinants (gender, race, education, poverty) correlations were assessed using the generalized linear model.

Results: Adolescents (84) had a mean age of 16.9 years (range 14-20), and were 61% female and 81% Caucasian. Religious/spiritual classifications were identified as: Catholic (11), Protestant (60), Mormon (2), None/Atheist (7), and Other (3). "I have a reason for living," "I feel loved," and "I feel hopeful," received $>90\%$ congruence between adolescents and family member (s) with an Excellent PABAK score. Total agreement of "I feel peaceful," "I am able to reach down deep into myself for comfort," "I am able to forgive others for any harm they have ever caused me," and "I feel connected to a higher power (or God)," received $<68\%$ congruence with a Fair or Poor PABAK score. Hypothesized social determinants of spiritual well-being for families were not significant for gender, race, education, and poverty.

Conclusions: Adolescents and their families were in excellent agreement on having a reason for living, feeling loved, and hopeful. Adolescents and their families were in poor to fair agreement on being able to reach down deep into myself for comfort, connection to a higher power, and forgiveness.

FP030 SIOP19-1630 | The Influence of Religious Beliefs on Symptoms of Anxiety and Depression Among Adolescents with Cancer

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Background/Objectives: Understanding religious beliefs of adolescents with cancer is imperative to providing effective care. Objective was to describe the religious beliefs of adolescents with cancer and examine relationship of belief in spiritual healing with quality of life.

Design/Methods: Baseline, cross-sectional study of 84 adolescents with cancer who completed Brief Multidimensional Measurement of Religiousness/Spirituality and PROMIS-Brief measures of anxiety and depression. Two-sided Pearson Chi Square test or Fisher's exact tests or t tests were used.

Results: Adolescents' (N=84) mean age 16.9 years (range ≥ 14 – <21 years), 61% female, 81% Caucasian. 88% considered themselves religious/spiritual, 12% did not. 42% of adolescents reported they had a religious or spiritual experience that changed their life. When asked did they believe they will be spiritually healed from cancer by a miracle, 46% reported, Yes. Adolescents who believe in a miracle cure were significantly more likely to have no anxiety, than those who did not believe (28.2% vs. 7.3%, $p=0.0186$) and were significantly more likely to have no symptoms of depression, than those who did not believe (46.2% vs. 24.4%, $p=0.0414$). 7% believed their cancer was a punishment from God. The belief cancer was a punishment from God was not associated with anxiety or depression.

Conclusions: Belief in spiritual healing protected adolescents with cancer from symptoms of anxiety and depression. Study findings support the value of spiritual assessment and care as a fundamental component of quality psychosocial and spiritual care in AYA oncology. Integrated religious/spiritual care to meet the religious/spiritual needs of adolescents living with cancer provides support to the entire family and should be standard of care in pediatric hospitals, consistent with policy recommendations that spiritual care is part of holistic care for AYA patients with cancer.

FPS 07: Toxicity and Supportive Care 2

FP031 SIOP19-1053 | Genetic Ancestry-based Pharmacogenomics of Methotrexate Neurotoxicity in Acute Lymphoblastic Leukemia

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Background/Objectives: Hispanic patients with acute lymphoblastic leukemia (ALL) experience a high incidence of methotrexate-related neurotoxicity, potentially contributing to ethnic disparities in relapse and outcomes. The source of these disparities remains unknown, but is likely due to a combination of genetic and non-genetic factors. As Hispanics are a genetically diverse population with various degrees of European, African, and Native American genetic admixture, we sought to evaluate the association between genetic ancestry and methotrexate-related neurotoxicity in a prospective cohort of pediatric patients with ALL.

Design/Methods: Newly-diagnosed (2012–2017) pediatric ALL patients were recruited from three U.S. treatment

centers and followed for the incidence of neurotoxicity, defined as acute neurologic events following intrathecal and/or intravenous methotrexate therapy. Germline genome-wide data were generated and compared to publically available ancestral reference populations to estimate the proportion of European, African, and Native American genetic ancestry. Hazard ratios (HR) and 95% confidence intervals (CI) for the association between genetic ancestry and neurotoxicity were estimated with Cox proportional hazards models.

Results: Of 237 eligible patients aged 2.5–18.8 years at diagnosis (mean=8.6 years), 50% were self-reported Hispanic, 53% male, and 58% treated on high/very-high risk protocols. Overall, 32 (13.5%) experienced methotrexate-associated neurotoxicity within 12 months of diagnosis. The proportion of Native American ancestry was higher (p -value=0.02) in individuals who experienced neurotoxicity (mean=36.8%) than those without neurotoxicity (mean=24.2%). Every 10% increase in the proportion of Native American genetic ancestry was associated with a 13% increase in the risk of neurotoxicity (HR=1.13; 95% CI: 1.01–1.28) after adjusting for sex, age at diagnosis, and treatment risk group.

Conclusions: We identified an association between genetically-defined Native American ancestry and risk of methotrexate-related neurotoxicity, suggesting that biologic variability partly contributes to ethnic disparities in pediatric ALL toxicity. Leveraging genomic variability across diverse populations could lead to the identification of regions influencing neurotoxicity susceptibility.

FP032 SIOP19-1049 | Asparaginase-Associated Pancreatitis and Genetic Predisposition in Children Treated for Acute Lymphoblastic Leukemia

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Background/Objectives: Asparaginase-associated pancreatitis (AAP) is a severe complication in children treated for acute lymphoblastic leukemia (ALL). Genetic predisposition to chronic pancreatitis were described and could designate patients with high risk of AAP. Study objectives were to analyse the risk of AAP events among patients screened for 7 genes involved in chronic pancreatitis.

Design/Methods: Pediatric patients with AAP (defined by Atlanta criteria), treated in a single centre by FRALLE 2000 protocol for ALL between January 2000 and December 2010, were retrospectively studied. Severity was defined by CTCAE. *SPINK1*, *PRSS1*, *CTRC*, *CFTR*, *CPA2*, *ULK2* et

RGS6 genes were screened in patients and 138 controls without AAP.

Results: Among the 438 patients treated for ALL (73% B lineage, 27% T Cell), 15 patients developed AAP (3.4%). Median age was 6.6 year-old [1.1 – 13.7] with a sex ratio of 1.5. All AAP occurred during induction treatment after a median of 7 [1 – 9] E. Coli asparaginase infusions. Four cases (27%) were severe (grade 4) and 11 mild (grade 3). No death related to AAP occurred. Patients with AAP had less overall survival (93% vs 97% in controls, $p=0.41$). Of the 12 re-exposed to asparaginase, 7 patients (58%) developed a second AAP (100% if first AAP was severe). All second AAP were mild. Genetic predisposition was identified in 5 patients with AAP (33% vs 25% in controls, $p=0.54$): *SPINK1* ($n=3$), *CFTR* ($n=1$), *RG56* ($n=2$) and *ULK2* ($n=1$). None were *PRSS1*, *CRTC* or *CPA2* mutated. *SPINK1* variants were more frequent in patients with grade 4 AAP than patients with grade 3 AAP (50% vs 9%, $p=0.15$).

Conclusions: AAP is a complication with frequent life-threatening. Patients with severe AAP (grade 4) should not be re-exposed to asparaginase. Impact of genetic predisposition to pancreatitis still remains unclear. Systematic screening before asparaginase exposition in pediatric ALL doesn't seem to be justified.

FP033 SIOP19-0401 | Prevalence and Determinants of Tinnitus and Hearing Aid Use Among 2,948 Dutch Survivors of Childhood Cancer: A DCOG Late-Effects Study

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Background/Objectives: Tinnitus and hearing loss are serious late effects of childhood cancer treatment. In childhood cancer survivorship care, little information is available on occurrence and risk factors for tinnitus. The aim of this study was to examine the prevalence and determinants of tinnitus

and hearing aid use in a national cohort of childhood cancer survivors (CCS).

Design/Methods: Data was collected within the national DCOG-LATER cohort by a self-reported health questionnaire among 6,165 Dutch CCS treated between 1964-2002. Patient characteristics included gender, age at diagnosis, neuro/ear, nose, throat (ENT) surgery, (cumulative dose) platinum chemotherapy and cranial irradiation. Prevalence of tinnitus and hearing aid use were calculated for survivors compared to siblings, and per diagnosis subtype. To identify potential determinants, multivariate logistic regression analyses were applied.

Results: In total, 2,948 CCS and 1,055 siblings were included. Tinnitus was reported in 9.5% of survivors and 3.7% in siblings (OR 3.0, 95% CI 2.1-4.2), and hearing aid use in 4.4% of survivors and 0.8% in siblings (OR 6.9, 95% CI 3.2-14.7). CCS with tinnitus or hearing aid devices were mostly treated for acute lymphoblastic leukemia (26% and 20%), and central nervous system tumors (20% and 33%), respectively. Associated determinants for tinnitus were older age at diagnosis (OR 2.1, 95% CI 1.5-2.8), cisplatin (OR 2.0, 95% CI 1.4-3.0), cranial irradiation (OR 1.9, 95% CI 1.5-2.5), and neuro/ENT surgery (OR 1.8, 95% CI 1.1-2.8). Associated determinants for hearing aid use were cisplatin (OR 2.9, 95% CI 1.8-4.6), neuro/ENT surgery (OR 2.6, 95% CI 1.5-4.5), and cranial irradiation (OR 1.9, 95% CI 1.3-2.8).

Conclusions: Childhood cancer survivors are at increased risk for tinnitus and hearing aid use, which seems to be influenced by the mode of cancer treatment. We recommend improved surveillance for early detection in late effect clinics as well as development of prevention strategies.

FP034 SIOP19-1349 | Insight into Late Chronic Kidney Disease and Associated Risk Factors in Childhood Cancer Survivors: A French Childhood Cancer Survivor Study

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Background/Objectives: Very little is known about the long term risks and risk factors for kidney disease after childhood cancer. The aims of this study were to assess the incidence and

to evaluate the risks of chronic kidney disease (CKD) among 5-year childhood cancer survivors (CCS).

Design/Methods: The FCCSS (French Childhood Cancer Survivor Study) cohort includes 7670 5-year CCS diagnosed between 1946 and 2000 before age 21 in France. CKD was defined as decreased glomerular filtration rate (GFR) <60 ml/min/1.73m² and/or the presence of histological, morphological, biological abnormalities for more than 3 months. The cumulative incidence for CKD were estimated using the non-parametric Aalen–Johansen estimator. Time since childhood cancer diagnosis was used as time scale and death from causes other than CKD was considered a competing event.

Results: In this study 150 patients with CKD were identified and validated. These patients were followed for a median of 46.5 years (range 6.1–64.4) and were diagnosed of their CKD at a median age of 52.2 years (range 9.3–70). Among the CKD patients, there were 51 (34%) with end stage kidney disease (ESKD). The cumulative incidence 50 years after childhood cancer diagnosis (50y-CumInc) of developing all stages CKD and ESKD among all CCS was 5% (3.7%–6.6%) and 2.2% (1.3%–3.3%) respectively. The 50y-CumInc of CKD was higher among patients treated with radiation (Gray test, $P=0.002$) 7.2% (4.4%–10.9%) compared to 4.5% (3.1%–6.3%) with no radiotherapy.

Conclusions: Few studies have examined the long-term risk of CKD among CCS. In this study, patients treated with radiotherapy or nephrectomy were at highest risk of developing CKD. Studies are ongoing to determine the role of radiation dose, location and association with chemotherapy. These new findings will be useful for both survivors and those involved in their clinical management and follow-up.

FP035 SIOP19-0729 | Reproductive and Sexual Health in Adolescents and Young Adults Treated for Cancer: A Cohort Study Evaluating the Impact of an On-Site Dedicated Gynaecological Consultation

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Background/Objectives: The integration of sexual and reproductive health into routine practice remains insufficient among adolescents and young adults (AYAs) treated for cancer. We implemented an on-site gynecological consultation in Leon Berard Lyon Cancer Center since 2014, which was systematically suggested to female patients aged 15 to 25

diagnosed with cancer. This study aimed to evaluate the impact of this consultation on patient's management.

Design/Methods: We retrospectively analyzed medical records of AYAs who underwent a gynecological consultation at cancer diagnosis in Lyon Cancer center between April 2014 and December 2017. Ninety patients were included in the study.

Results: All the 90 patients were pubertal. Mean age at diagnosis was 18.0. This consultation was their first consultation with a gynaecologist for 67.8% patients (61/90). Fifty-three patients were still virgo and thus did not have any clinical gynaecological examination. Information on potential impact of treatment on fertility and on fertility preservation (FP) options was reported in patient's files in 98.9% patients (89/90), and FP was effectively performed in 53.3% patients (48/90) either by ovarian cortex cryopreservation, oocyte vitrification, ovarian transposition and/or GnRH agonists. Contraception was discussed in all the 37 sexually active patients. Thirty-seven (41.1%) patients needed hormonal contraception or treatment prescription. Additional gynaecological appointments were necessary for 56.7% patients (51/90), either during cancer treatment (26/90) and/or after the end of the treatment (41/90). Reasons for gynaecological follow-up after treatment were: ovarian reserve evaluation/fertility (27), contraceptive counselling (24), other reasons (21) (non-contraceptive hormonal treatment, breast follow-up...etc).

Conclusions: The implementation of a specific on-site gynecological consultation allowed to give systematic information on FP and contraception at cancer diagnosis. Integration of gynecologists in AYAs teams can facilitate access to disease-specific gynecological care during and after cancer treatment.

FP036 SIOP19-1655 | Knowledge About Past Medical History of Childhood Cancer: A Comparison of Self-Reported Data and Medical Files

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Background/Objectives: Adults treated for childhood cancer may face various late effects because of cancer treatment. Childhood cancer survivors (CCS) must be aware of these risks and of their medical history to be in capacity of preventing those late effects adequately. The aim of this study was to assess knowledge about past medical history in a large sample of adult CCS treated in distinct periods of time.

Design/Methods: Multi-center cross-sectional study conducted in France. A questionnaire was sent by mail to 5-year

CCS treated for a solid tumor or a lymphoma between 1970 and 2000. They were asked to report the name of their disease and to state if they knew the treatment they had. Their answers were compared to their medical files. Multiple regression analyses were conducted to identify predictors of accuracy of diagnosis, including sex, education, age at diagnosis, decade of treatment, and type of diagnosis and treatment recorded in medical files.

Results: Of the 2,198 respondents, 30% were treated in the 1970's, 42% in the 1980s and 28% in the 1990's. Overall, 83% of CCS accurately reported their diagnosis with precision, 11% were accurate, but not precise, 6% said they had a cancer or a tumor. Of those who had received alkylating agents or anthracyclins, 13% said were not sure or did not know the type of treatment they had. Accuracy of diagnosis was more likely in CCS who had a college degree (OR=2.4; 95% CI=1.5-3.7), who had received chemotherapy (OR=2.7; 95%CI=1.7-4.2) or radiotherapy (OR=2.0; 95%CI=1.3-3.1) and who had been treated in the 1990's (vs in the 1970's: OR=2.8; 95%CI=1.6-4.9).

Conclusions: A significant proportion of former patients do not know their past diagnosis or treatment. Accuracy was associated with decade of treatment, indicating that older patients, who are more at risk of developing late effects, are less aware of their medical history.

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FP037 SIOP19-1093 | Subgroup Specific Outcomes in Metastatic Infant Medulloblastoma Treated with Radiation Sparing Approaches

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Background/Objectives: Infant medulloblastoma is a major treatment challenge, and metastatic dissemination poses a particularly difficult clinical dilemma due to the severe side effects of radiotherapy. A paucity of prospective molecularly informed clinical trial data limits our ability to adequately risk stratify this patient population, specifically the role of radiotherapy. As such, molecularly subgrouped outcomes in clinically annotated cohorts would be highly desirable.

Design/Methods: Children with metastatic medulloblastoma (M2/M3) treated with radiation sparing approaches were identified in the Medulloblastoma Advanced Genomics International Consortium (MAGIC), and profiled using genome wide methylation arrays. Infants were only included if their initial treatment was as per an infant radiation sparing protocol, although radiation at the end of therapy was acceptable.

Results: Sixty-one children under age 4 treated for metastatic medulloblastoma with radiation sparing approaches were identified. Thirty-three (54.1%) were Group 3, 12 (19.1%) were Group 4 and 16 (26.2%) were SHH. 5-year event-free survival for Group 3 patients are 0.28 (95% CI 0.15-0.52), Group 4 is 0.53 (95% CI 0.26-1) and SHH is 0.6 (95% CI 0.36-0.99). However, when stratifying patients by those who received craniospinal irradiation, no radiation-free survivors within Group 3 or 4 were identified despite modern protocols incorporating transplant-based regimens, whereas no patient with a SHH tumour received radiotherapy. 5-year event free survival for Group 3 and 4 infants receiving craniospinal irradiation was 0.53 (95%CI 0.35-0.82).

Conclusions: In a molecularly characterized cohort of metastatic medulloblastoma treated with upfront radiation sparing approaches, molecular subgroup is a strong predictor of radiation-free survival. Our data suggests that Group 3 and 4 metastatic medulloblastoma frequently receive craniospinal radiotherapy as part of their treatment, however, metastatic SHH tumours have an acceptable outcome with chemotherapy only. Larger prospective studies are required to determine the dose, timing and role craniospinal irradiation in Group 3 and 4 medulloblastoma.

FP038 SIOP19-1608 | Identifying Distinctive LincRNA as Liquid Biopsy Marker of Medulloblastoma Subgroup Four

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Background/Objectives: Long non coding RNAs (lncRNAs) involvement in human cancers etiology is being increasingly proved. Cancer-secreted long non-coding RNAs (lncRNAs) in exosomes are emerging mediators of cancer-host cross talk communication in tumor microenvironments. The ability to monitor and detect tumor markers in real time enables access to tumor biology and may allow highly personalized treatment for each patient.

Design/Methods: We analyzed RNA sequencing of 36 Medulloblastoma samples and quantified the genome wide long non coding RNAs (lncRNA) expression levels. MB4 expression was further examined in microarray analysis on a larger cohort of medulloblastoma patient samples and a large cohort (n=1405) of patient samples with different types of brain tumors and normal brain. Finally, MB4 was quantified by RTPCR in the plasma of medulloblastoma patients.

Results: We identified a lincRNA that is distinctively highly expressed in group 4 (MB4). MB4 proved to be specific and highly expressed in group 4 Medulloblastoma. MB4 was detected in the plasma of medulloblastoma patients with active disease, or subtotal resection. MB4 was not detected

in patients that their tumors were grossly resected. MB4 expression is not detected in the serum of patients with medulloblastoma type SHH, penioblastoma, Ewing sarcoma and neuroblastoma.

Conclusions: We have found that MB4 lncRNA is a highly specific medulloblastoma tumor biomarker and is sensitive and noninvasive biomarker that can be quantified from a blood test. Thus MB4 quantification by RTPCR in the plasma of medulloblastoma patients is a noninvasive body fluid-based assay to examine for diagnosis and monitoring. Liquid biopsies increase the potential for a precise and personalized treatment based upon a blood test and allow pediatric patients and their physicians to have a minimally invasive diagnostic test. MB4 can be a good diagnostic marker, and in future both may also be a good target for therapy.

FP039 SIOP19-0414 | Treatment Results the Patients with Medulloblastoma of Molecular Subgroup 4

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Background/Objectives: To evaluate the treatment results among the patients of molecular subgroup 4, to determine the factors affecting the prognosis.

Design/Methods: From 1996 to 2017, the molecular subgroup was determined using the ILLUMINA850Kassay (Heidelberg, Germany) for 640 medulloblastoma: WNT subgroup comprised 77 (12%) patients; SHH subgroup, 115 (18%); subgroup 3, 171 (26.7%), subgroup 4, 277 (43.3%) patients. We analyzed the treatment results of medulloblastoma of molecular subgroup 4. In all the patients, initial removal of the tumor was performed. Most patients underwent a subtotal tumor resection. All the patients got chemoradiotherapy by the HIT protocol. There were 81 (29.2%) girls, 196 (70.8%)

boys, no patients under 3 years old, 91 (32.8%) patients aged from 3 to 6, 186 (67.2%) patients aged over 6. In 136 (49.1%) metastases or tumor cells were found during the initial examination (M+); in 130 (46.9%) there were no metastases or tumor cells (M0); in 11 (4%) the stage was not determined (Mx). 256 patients (92.4%) had the classic medulloblastoma subtype; 21 (7.6%) - the large-cell/anaplastic subtype. MYCN amplification was found in 26 (9.4%) patients. 192 (69.3%) got craniospinal radiation with total dose of 35.2Gy; 40 (14.4%) patients got reduced doses; 13 (4.7%) got no radiotherapy; 32 patients got unknown doses of radiation (11.5%).

Results: The progression-free survival (PFS) rate was 0.72 among the girls, 0.62 among the boys. The histological subtype had no significant effect on the results of treatment: PFS was 0.65 for classic medulloblastoma, 0.52 for the anaplastic/large-cell subtype. The presence of metastases significantly affected the survival: PFS was 0.70 for M0 and 0.61 for M+ ($p=0.008$). Patients with MYCN amplification had a significantly lower survival rate compared to the patients without it: 0.48 and 0.62, respectively ($p=0.01$). Patients who got standard doses of craniospinal radiation had a significantly higher PFS compared to those who got reduced doses or no radiation: 0.67 and 0.22, respectively ($p=0.00007$). The overall survival was also higher in patients who get standard doses of craniospinal radiation: 0.77 and 0.53, respectively ($p=0.001$). The reason for the lower efficiency caused by the reduction of radiation dose probably was the inadequate determination of the Mstage.

Conclusions: To differentiate the therapy and to reduce the craniospinal radiation dose in medulloblastoma of molecular subgroup 4, one should study the MYCN amplification and thoroughly analyze the MRI and CSF cytology for the tumor cells in a reference assay.

FP040 SIOP19-0911 | Role of Molecular Classification in Recurrent Ependymoma: Local Therapy of the PF-A Subgroup

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Background/Objectives: Recurrent ependymomas present a five-year survival of about 37%. Identification of molecular subgroups may help in finding the best therapy for each case.

Design/Methods: 60 patients with recurrent ependymoma and known molecular subgroup were examined as to age at recurrence; localization of and time to first recurrence; extent of surgery; as well as time and volume of radiation. Overall-survival (OS) was estimated based on Kaplan-Meier analysis to either date of death or last follow-up.

Results: Of 60 patients included, 48 were classified as PF-A, 9 as RELA, 2 as PF-B and one as YAP1. Median age at recurrence was 6.25 ± 4.2 years in the PF-A group and 12.9 ± 6.5 years for patients with RELA-fusions. Five-year OS was $42.3\% \pm 8.2\%$ in the PF-A-group, while no patients with RELA-positive tumors were alive after five years. PF-A tumors were metastasized in 38.8% with spinal metastases being the most predominant in 68.4%. Metastases in the RELA group were observed in 33.4%. In patients with PF-A tumors, gross-total resection (GTR) was achieved in 60% of patients; radiotherapy was applied in 51%. In this group GTR led to a significantly better survival (median OS: 70 ± 23 vs. 35 ± 14.5 months, $P=0.002$). A significant advantage of radiotherapy was found in neither local (58 ± 11.6 vs. 64 ± 31.8 months, $P=0.473$) nor metastatic (30 ± 23.9 vs. 42 ± 39 months, $P=0.936$) recurrences. However, a significantly better OS was found for patients with residual tumor receiving radiotherapy (wo/w 10 ± 7.8 vs. 49 ± 35 months, $P=0.033$).

Conclusions: PF-A tumors have a high tendency towards recurrence with spinal metastases. Maximal possible resection is the most important factor for long-term survival, while radiotherapy should mostly be considered in patients with remaining tumor after surgery. RELA-positive tumors show worse survival-rates at recurrence, but low case-numbers make deductions about the feasibility of treatments inconclusive.

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FP041 SIOP19-1126 | Risk-Adapted Therapy and Biological Heterogeneity in Pineoblastoma: Integrated Clinical-Molecular Analysis from the Prospective, Multi-Center SJMB03 and SJYC07 Trials

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Background/Objectives: Pineoblastoma is an aggressive embryonal tumor conventionally treated with high-dose CSI. We report outcome and molecular analysis of patients with pineoblastoma from two multi-center risk-adapted trials (SJMB03 for $\geq 3y$, SJYC07 for $< 3y$) and a non-protocol SJMB03-equivalent cohort (SJMB03-like).

Design/Methods: Fifty-three patients with pineoblastoma treated on SJMB03 (N=30), SJMB03-like (N=11), and SJYC07 (N=12) were included. High-risk (HR) disease was defined by metastasis (M⁺) (SJMB03/SJMB03-like/SJYC07) and/or residual tumor $\geq 1.5\text{cm}^2$ (R⁺) (SJMB03/SJMB03-like). The SJMB03 protocol comprised risk-adapted CSI (non-HR=23.4Gy, HR=36Gy) with boost and chemotherapy (cisplatin/cyclophosphamide/vincristine); the SJYC07 protocol consisted of induction (methotrexate/cisplatin/cyclophosphamide/vincristine), consolidation (non-HR=focal radiation, HR=cyclophosphamide/topotecan) and metronomic maintenance therapy. Available samples were profiled on MethylationEPIC array and analyzed with a reference brain tumor dataset. WES and RNA-seq were performed in a subset.

Results: Among SJMB03/SJMB03-like patients, 18 were non-HR and 23 HR (M+=17; R+ only=6). In SJYC07, 7 were non-HR and 5 HR (M+). 5y-PFS in patients on SJMB03/SJMB03-like therapy with non-HR and HR disease were 100% and $59.1 \pm 10.5\%$ respectively ($p=0.012$). Patients on SJYC07 with non-HR and HR disease had 5y-PFS of $14.3 \pm 13.2\%$ and 0% respectively ($p=0.23$). Unsupervised clustering of 40 methylation profiles resulted in 4 subgroups. Subgroup-1 (N=7) patients were younger (median=1.2y; range=0.5-5.7y), often metastatic (71%), and had epigenetic profiles that either associated with *RBI*-driven pineoblastoma ("PB_A") or formed a related cluster. Tumors in subgroup-2 (N=9; median=1.9y; range=0.4-14.4y) were heterogeneous and clustered with diverse reference classes. Subgroups-3 (N=6) and 4 (N=18) patients were older (median=8.4y; range=3.3-17y) and less frequently metastatic (subgroup-3=0%; subgroup-4=44%). Profiles from subgroup-3 formed a distinct cluster while those from subgroup-4 overlapped with

pineoblastoma methylation-class “PB_B”. Pathogenic alterations in the microRNA processing pathway were enriched in subgroups-3 and 4.

Conclusions: Children ≥ 3 y with non-HR pineoblastoma can be successfully treated with 23.4Gy CSI and chemotherapy. Moreover, molecular analysis uncovers a biologically diverse disease, with subgroup-specific differences in patient age and propensity for metastasis.

FP042 SIOP19-1108 | Primary Intracranial Sarcoma with *DICER1* Mutation - Treatment Results of a Novel Molecular Entity

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Background/Objectives: Sarcomas of the Central Nervous System (SCNS) constitute 0.7% of all sarcomas and 0.2% of brain tumors, with an incidence of 3 per 10 million people. Over the last 5 years we observed an increase of SCNS in Peru.

Design/Methods: This is a retrospective and analytic study. Between January 2005 and June 2018, 64 patients under 18 years old were diagnosed having primary SCNS. Tumors from 26 cases were molecularly profiled by DNA-methylation profiling and panel sequencing with constitutional DNA available in 18 cases.

Results: Median age was 6.1 years (range 2-17.5), M/F ratio 0.90; 56 patients (88%) had intratumoral hemorrhage at diagnosis. Headaches, vomiting and seizures were presenting symptoms; 03 patients had NF1 (7%) and 25 (39%) café-au-lait spots and/or freckling. Histology showed a pleomorphic and spindle cell without a distinct growth pattern. Methylation profiles of all 26 tumor samples clustered with

the newly described group “intracranial spindle cell sarcoma with rhabdomyosarcoma-like features and *DICER1* mutations”. 25/26 tumors harbored somatic *DICER1* mutations, 21/26 somatic TP53 mutations, 6/21 somatic *NF1* mutations and 5/26 somatic *NRAS* mutations. One additional germline *NF1* mutation was detected. None of the *DICER1*, *TP53* or *NRAS* mutations were found in the germline. Gross total resection was achieved in 37 patients (60%); 62 (97%) were supratentorial, eight patients had surgery only, 35 patients received chemotherapy/radiotherapy, nine radiotherapy only. Survival data was available for 60 patients. 26 patients (44.6%) recurred, 6 patients abandoned treatment and 23 died of disease. The two-year overall survival (OS) was 56% (95% CI: 43-74%) and EFS was 40.6% (95%-CI 26-62%).

Conclusions: The recently described group of primary SCNS with *DICER1* mutation seems to follow an aggressive clinical course with progression, even under multimodal therapy. Further investigation is warranted to decipher potential risk factors and to develop appropriate treatment strategies for this highly aggressive disease.

FPS 09: ALL: Biology and Prognostic Factors

FP043 SIOP19-1447 | Minimal Residual Disease (MRD) Predicts Outcomes in KMT2A-Rearranged But Not KMT2A-Wild Type Infant Acute Lymphoblastic Leukemia (ALL): AALL0631, A Children's Oncology Group Study

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Background/Objectives: MRD is a powerful predictor of outcome in leukemia. Overall outcomes for infants with ALL on AALL0631 were previously reported (SIOP 2016). Here, we report the impact of MRD on outcomes.

Design/Methods: Infants were risk stratified by KMT2A status and age: standard (SR): KMT2A wild type (KMT2A-wt); intermediate (IR): KMT2A-rearranged (KMT2A-r), ≥ 90 days; high (HR): KMT2A-r, < 90 days. SR patients received standard chemotherapy (Arm A). HR/IR patients were randomized after induction to intensive chemotherapy only (Arm B) vs chemotherapy plus lestaurtinib FLT3 inhibitor (Arm

C). Event-free and disease-free survival (EFS, DFS) were measured from study entry and randomization, respectively. 3-year EFS was 87%/41%/17% for SR/IR/HR; DFS was 39%/36% for Arms B/C. Flow cytometric MRD was measured at 3 time points (TP1: week 6; TP2: week 10; TP3: week 20).

Results: A threshold of 0.01% defined MRD positive (+) vs negative (-). MRD+ rates were associated with risk group. MRD+ rate (of N) at TP1/ TP2/ TP3 were: HR 65%(26)/ 43%(21)/ 14%(14); IR 54%(81)/ 30%(67)/ 11%(62); SR 15%(53)/ 15%(47)/ 5%(40). MRD+ rates for TP2 and TP3 did not differ significantly between Arm B and Arm C for either HR or IR patients. For all KMT2A-r patients (IR+HR), EFS for MRD+ vs MRD- was 25% vs 50% at TP1, 21% vs 46% at TP2 and 22% vs 51% at TP3 (all log rank p-values <0.02). For KMT2A-wt patients, there was no difference in EFS between MRD+ vs MRD- patients at any time point (log rank p-values 0.24-0.84).

Conclusions: MRD powerfully predicts EFS for KMT2A-r infants, but does not appear to predict EFS for KMT2A-wt infants. The lack of predictive value of MRD in KMT2A-wt infants is an intriguing finding given the strong predictive value of MRD in children >1 year of age with KMT2A-wt ALL, and suggests these leukemias may have a unique biology.

FP044 SIOP19-0620 | Application of Real-Time PCR Method for the Detection of Childhood BCR-ABL1-Like Acute Lymphoblastic Leukemia Cases

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Background/Objectives: To evaluate applicability of gene expression classifier built on real-time PCR data for the detection of BCR-ABL1-like pediatric ALL patients.

Design/Methods: The study was done on bone marrow samples of 147 primary pediatric BCP-ALL patients, included 10 BCR-ABL1-positive ALL patients, 59 cases with known structural or numerical aberrations and 78 'B-others' cases. We estimated expression of 15 genes by real-time PCR obtained

from the previously published 15-genes classifier (R. Harvey et al. ASH 2013). Δ Ct method was applied and ABL1 expression was used as control gene. After step-wise exclusion we selected 5 genes (IGJ, SPATS2L, MUC4, CRLF2, CA6) that allowed to built the best model based on hierarchical cluster analysis (HCA) and principal component analysis (PCA). BCR-ABL1-negative ALL patients who had expression data similar to BCR-ABL1-positive cases were attributed as BCR-ABL1-like ALL. IKZF1 gene status was evaluated by MLPA. Presence of ABL1, ABL2, CRLF2, IgH, JAK2, PDGFRb rearrangements were done by FISH.

Results: HCA and PCA showed that 11 'B-others' samples were clustered together with 9 BCR-ABL1-positive ones. IKZF1 deletions and high CRLF2 expression were more frequent in BCR-ABL1-like group in comparison to non-BCR-ABL-like (67% vs 11%, and 40% vs 6%, correspondingly; p<0.001 in both cases). Among 9 BCR-ABL1-like cases which were assessed by FISH, JAK2 rearrangements were found in 2, CRLF2 in 4. We did not detect any kinase fusions in 64 non-BCR-ABL-like 'B-other' patients (p<0.001). Cumulative incidence of relapse of BCR-ABL1-like patients was higher in comparison to non-BCR-ABL1-like 'B-other' patients enrolled into ALL-MB 2008 protocol (0.57±0.19 vs. 0.02±0.02, p<0.0001). The worst outcome was noted in case of combination of BCR-ABL1-like profile and IKZF1 deletions (EFS 0.00), while patients with isolated BCR-ABL1-like profile doing better (EFS 0.67±0.22).

Conclusions: Real-time PCR can be used as easy and reliable screening method for the detection of BCR-ABL1-like profile in 'B-other' ALL.

FP045 SIOP19-1157 | Minimally Detected Disease at End of Induction Affects Outcomes in Childhood B-Acute Lymphoblastic Leukaemia: Retrospective Analysis from a Tertiary Cancer Center in India

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Background/Objectives: Presence of minimal residual disease (MRD) at End-of-Induction (EoI) for acute lymphoblastic leukemia (ALL) is an important prognostic marker at levels ≥0.01%. However, value of Minimally Detectable Disease (MDD) <0.01% is being increasingly highlighted. We evaluated the impact of EoI MRD & MDD on outcomes of a uniformly-treated cohort of childhood B-ALL patients.

Design/Methods: B-ALL patients <15-years age treated on modified-ICiCle pilot protocol from February-2013 through

December-2016 were included. MRD was measured by standardised 10-colour FCM at EoI, and categorized as Group-A: MRD $\geq$ 0.01%, Group-B: MDD<0.01%, Group-C: MRD-undetectable. For initially Standard-risk (SR) and Intermediate-risk (IR) patients, Group-A received High-risk (HR) therapy from consolidation onwards, while Groups-B & C were treated as IR. EoI-MRD was correlated with 4-year event-free survival (EFS) and overall-survival (OS) by Kaplan-Meier on SPSSv21®.

Results: There were 1011 patients, male: female ratio-1.94:1, median-age 5-years (range:1-15). At median follow-up of 32 months (range:24-60) 4-year EFS and OS were 69.9 $\pm$ 3.6%, and 87.5 $\pm$ 2.6% respectively. Of 1011 patients, standard-risk (SR) were 303 (29.9%), intermediate-risk (IR)-365 (36.1%), and high-risk (HR)-343 (33.9%). Fifty-seven patients (5.6%) died in induction and 5 didn't undergo EoI-MRD. Of 949 patients evaluable post-induction, 4-year EFS and OS for MRD $\geq$ 0.01% was 50.8 $\pm$ 8.8% and 74.1 $\pm$ 10.4% respectively and for MRD<0.01%, 75.5 $\pm$ 3.8% and 90 $\pm$ 2.6% respectively (p <0.01). Patients in Group-A were 231 (24.3%), Group-B:77 (8.06%), and Group-C:641 (67.5%). Four-year EFS for Group A, B and C was 50.8 $\pm$ 8.8%, 62.2 $\pm$ 18.4% and 76.4 $\pm$ 3.8% respectively (p <0.01) and 4-year OS was 74.1 $\pm$ 10.4%, 81.4 $\pm$ 13.2% and 90.7 $\pm$ 2.6% respectively (p <0.01). For final risk-stratification HR, IR, and SR, 4-year EFS for was 61.0 $\pm$ 5.4%, 76.2 $\pm$ 6.2%, 80.9 $\pm$ 6.4% respectively (p <0.01), and OS, 82.7 $\pm$ 4.6%, 89.7 $\pm$ 4.8%, 92.5 $\pm$ 4.2% respectively (p <0.01). On pairwise comparison of Risk-group and MRD-Group, final-risk HR patients were significantly impacted if in Group-A & C (p =0.02), while all other combinations were not significantly associated.

Conclusions: Our study reiterated the robustness of MRD of $\geq$ 0.01% as an indicator for inferior outcome at EoI. MRD-undetectable, MDD and MRD-positive significantly impacted outcome of Pediatric B-ALL, and should be evaluated prospectively.

FP046 SIOP19-1066 | Impact of Cytogenetics on Outcome of B-Acute Lymphoblastic Leukaemia: Retrospective Analysis from Tata Memorial Hospital

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Background/Objectives: Increasing understanding of cancer biology and cytogenetic based-refinement of risk stratification are linked to improvement in childhood acute lymphoblastic leukemia (ALL) survival. The evolution of

Minimal Residual Disease MRD) at End-of-Induction (EoI) assessment response-based therapy adaptation has impacted prognostic value of traditional cytogenetics. We assessed their combined impact on outcomes of a large cohort of uniformly-treated patients with B-ALL.

Design/Methods: Patients <15years of age treated for B-ALL on a modified-ICiCLE pilot protocol from February 2013 to December 2016 were included. Cytogenetic findings as per fluorescence in situ hybridization (with/without MRD (positive defined as $\geq$ 0.01% as measured by standardized 10-colour flow cytometry at EoI) were correlated with 4-year event-free survival (EFS) and overall survival (OS) by Kaplan-Meier method on SPSSv24®.

Results: Of 1,011 patients, cytogenetic data was available for 1,005 (99.4%) patients. The frequencies of cytogenetic subsets were Trisomies- 427 (42.9%), ETV6-RUNX1- 141 (14.0%), TCF3-PBX1- 89 (8.9%), BCR-ABL1- 55 (5.5%) and MLLr- 19 (1.9%) while 274 (27.4%) showed no cytogenetic anomaly. Favorable cytogenetic positively impacted survival with 4-year EFS and OS being Trisomies (76.1 $\pm$ 2.5% and 88.9 $\pm$ 1.8%), ETV6-RUNX1 (75.9.3 $\pm$ 4.2% and 86.4 $\pm$ 3.3%), and TCF3-PBX1 (62.5 $\pm$ 5.5% and 83.0 $\pm$ 4.2%). Unfavorable cytogenetic subsets had poorer EFS and OS with BCR-ABL1 (20.0 $\pm$ 2.8% and 46.1 $\pm$ 11.2%) and MLLr (48.9 $\pm$ 13.9% and 73.7 $\pm$ 10.1%) respectively. Patients with no cytogenetic anomaly had 4-year EFS and OS of 55.4 $\pm$ 3.6% and 74.6 $\pm$ 3.4% respectively. When correlated with MRD, impact of cytogenetics persisted. While Trisomies and TCF3-PBX1 did better at MRD<0.01% as compared to MRD $\geq$ 0.01%, ETV6-RUNX1 showed no significant difference in both EFS (p =0.44) and OS (p =0.72) according to MRD levels. BCR-ABL1 had better EFS (p =0.035) but similar OS (p =0.13) while MLLr had better OS (p =0.025) but similar EFS (p =0.41) at MRD<0.01% as compared to MRD $\geq$ 0.01%.

Conclusions: The prognostic value of cytogenetics anomalies remains important in childhood B-ALL but is impacted by MRD-stratified approach of therapy escalation for MRD $\geq$ 0.01%. This MRD-stratified therapy escalation especially benefitted standard risk patients with ETV6-RUNX1.

FP047 SIOP19-0927 | Kinase Domain Mutations in PH-Positive Leukemias Mediate Biological Properties Beyond Resistance To Targeted Therapy by Kinase Inhibitors

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Background/Objectives: Introduction of tyrosine kinase inhibitors (TKIs) has revolutionized the treatment of BCR-ABL1-positive leukemias including CML and Ph+ ALL. However, the outgrowth of leukemic clones harboring resistant point mutations in BCR-ABL1 tyrosine kinase domain (TKD) poses a serious clinical problem. These mutant subclones are believed to expand due to disruption of the TKI/TKD interaction. However, due to the positioning of the resistant mutations at key positions of the BCR-ABL1 TKD, we hypothesized that these mutations have a biological effect on BCR-ABL1 downstream signalling.

Design/Methods: We have generated >50 Ba/F3 cell lines expressing BCR-ABL1 with various single and compound mutations. These cell lines were tested against a panel of TKIs and other inhibitors targeting different downstream signalling pathways activated by leukemogenic activity of BCR-ABL1.

Results: We observed several changes in the gene expression profile during clonal evolution. Various BCR-ABL1 mutants showed differential responses not only to TKIs, but also to drugs not directly targeting the kinase activity of BCR-ABL1, such as proteasome inhibitors and others. With specific regard to the highly resistant gatekeeper mutation, T315I, we could distinguish between changes attributable to reduction of BCR-ABL1 kinase activity by TKIs and changes specific for this mutant subclone. Interestingly, in contrast to wildtype BCR-ABL1 and several mutant subclones, the leukemic subclone displaying the T315I mutation was very sensitive to treatment with hydroxyurea. Molecular analyses revealed that acquisition of this mutation affected the expression of several genes, providing a biological basis for the intriguing effect of hydroxyurea.

Conclusions: Our data demonstrate that the impact of TKI-resistant mutations may go far beyond hindering the TKI/TKD interaction. Studying the differential downstream signalling in mutant BCR-ABL1 subclones should facilitate the understanding of their biological behavior and help establish their druggable vulnerabilities, as a basis for the development of novel effective treatment options in patients resistant to currently available TKI-based therapies.

FP048 SIOP19-1091 | Deep Targeted Sequencing in Chinese Pediatric Acute Lymphoblastic Leukemia Unveils Distinct Novel Relapse-Associated Genes

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Background/Objectives: Relapse occur in 15 to 20% of pediatric acute lymphoblastic leukemia (ALL) in China, relapsed leukemia has high rate of treatment failure and long-term

survival is poor. Several genes have been reported as driver genes of leukemia relapse, including SETD2, NR3C1, CREBBP. However, the genomic landscape of relapse Chinese B-ALL and the genetic basis behind it remains unexplored

Design/Methods: To comprehensively characterize the genetic alteration involved in relapsed pediatric B-ALL, we performed deep next generation sequencing of 185 genes on matched diagnosis-remission-relapse samples from 8 pediatric patients with B-ALL patients treated with CCLG-ALL-2008 or CCCG-ALL-2015 protocol

Results: In diagnostic samples, we detected 51 mutations in 29 genes, while 93 mutations in 48 genes were detected in relapse samples. 87.5% (7/8) patients gained new mutation genes during relapse, the average number of genes gained per patient was 4 (range 0-17). The gene mutations exclusively in relapse stage included genes involved in epigenetic modification, transcriptional factors, and signal pathways such as TP53 (n=4), NT5C2 (n=3), PCLO (n=3), and NUMB (n=2) mutations. Dynamic changes of clonal sizes were observed in most of the cases. Four cases have relapse-specific mutations panel in the founder clone at relapse. One case had the founder clone which was descendant of minor subclone at diagnosis, while the rest three cases had predominant clones at diagnosis that persisted to relapse, suggesting that in most cases the clones were not eradicated by therapy.

Conclusions: Here we use deep target sequencing to describe the clonal architecture and evolution of 8 pediatric B-ALL from diagnosis to relapse. We find a significant enrichment of mutations in some unreported genes at relapse. These results have implications for the early detection of mutations driving relapse. Further studies will be done to define the prognostic value of these genes.

FPS 10: Neuroblastoma: Clinical

FP049 SIOP19-0117 | Early Results from the HR-NBL1/SIOPEN Trial Randomizing Dose-Reduced Subcutaneous Interleukin2 (SCIL2) with Dinutuximab Beta (DB) Long-Term Infusion (LTI) in High-Risk Neuroblastoma Patients

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Background/Objectives: We tested dose-reduced scIL2 in combination with DB-LTI and oral isotretinoin and evaluated toxicity and efficacy in high-risk neuroblastoma patients (EudraCT:2006-001489-17).

Design/Methods: High-risk patients (stage 4 ≥ 1 y; stage 4 <1y with MYCN amplification (MNA); stage 2, 3, 0-21y with MNA) received high intensity induction (rapid COJEC or N5-MSKC and TVD for insufficient response), surgery, high dose therapy with busulfan/melphalan and local radiotherapy. Patients ≤ 9 months between diagnosis and HDT/SCT who achieved at least a partial response prior to HDT/SCT and without progression thereafter were randomized to receive up to 5 cycles of 100mg/m² DB-LTI (d8-17) $\pm$ 3x10⁶ IU/m² scIL2 (d1-5; d8, d10, d12, d14, d16) and 160mg/m² oral isotretinoin (d19-32).

Results: Between 04/2014 and 06/2018, 408 patients from 18 countries were randomized. Median follow-up is 1.8 years. The 2yrs-EFS and -OS for DB-LTI (205 pts) vs. DB-LTI&scIL2 (203 pts) was 64% $\pm$ 4% vs. 63% $\pm$ 5% (p=0.844) and 83% $\pm$ 3% vs. 74% $\pm$ 4% (p=0.337). For patients in CR the 2yrs-EFS was 69% $\pm$ 5% for DB and 66% $\pm$ 6% for DB&scIL2. Patients with evaluable disease prior immunotherapy, the end of treatment response rate was 57% (26% CR, 31% PR) vs 52% (27% CR, 25% PR) with 2yrs-EFS rates of 58% $\pm$ 7% and 64% $\pm$ 8%, respectively. Grade 3&4 toxicity was lower in the group with DB vs DB&scIL2 for fever (14%vs31%, p<0.001) and pain (7%vs18%, p=0.005), and no significant difference was seen for general condition (17%vs22%, ns), allergy (3%vs3%, ns), capillary leak (4%vs8%, ns), liver enzyme elevation (20%vs27%, ns) and neurological toxicities (2%vs2%, ns).

Conclusions: Our results indicate that DB-LTI and dose-reduced scIL2 clearly reduced the toxicity profile, but showed

absence of benefits of scIL2. DB-LTI achieved 2yrs-EFS in line with DB short term infusion (Ladenstein, Lancet Oncology 2018;) and a response rate >50% supporting its use as standard of care immunotherapy.

FP050 SIOP19-1385 | Long-Term Results for Infants with Neuroblastoma Treated Between 2000 and 2004 According to INES Protocols -INESFU- A SIOPEN Study

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Background/Objectives: One objective of INES-FU study was to assess the long-term survival of children younger than 1 year at diagnosis with neuroblastoma (NB).

Design/Methods: INESFU was a descriptive cohort follow-up. Infants with NB were enrolled in the SIOPEN-INES prospective multicenter European trial between 2000 and 2004.

Inoperable localized NB without MYCN amplification (MYCNA) were enrolled in 99.1. Stage 4S without MYCNA were enrolled in 99.2. Stage 4 without MYCNA were enrolled in 99.3. All MYCNA were enrolled in 99.4. The 99.9 arm was for all the infants who could not be enrolled in the other arms for any reason.

Staging were carried out according to International Neuroblastoma Staging System (INSS) then recoded using International Neuroblastoma Risk Group Staging System (INRGSS).

Results: We collected follow-up data for 739 patients. The median follow-up of our cohort is 10 years.

For the entire cohort, 10-years overall survival (OS) (+/- SE) is 91% $\pm$ 1% and 10-years event free survival (EFS) is 87% $\pm$ 1-3%. Four infants died of their disease more than 5 years after diagnosis.

For the entire cohort, infants younger than 6 months have significantly better survival: 93% $\pm$ 1% versus 88% $\pm$ 2%, $p=0.03$. Ten-years OS is respectively for groups 99.1, 99.2, 99.3 and 99.4: 99% $\pm$ 1%, 93% $\pm$ 3%, 96% $\pm$ 3% and 48% $\pm$ 8%. According to INRGSS, 10-years OS in L1 group is 99% $\pm$ 1%, 96% $\pm$ 2% in L2 group, 90% $\pm$ 3% in Ms group and 83% $\pm$ 5% in M group.

Conclusions: We confirmed excellent survival rates for patients under than 1 year without MYCNA which remain stable in the long-term. The excellent long-term survival rates of children under 6 months of age should encourage us to pursue therapeutic de-escalation strategies.

We thank: « 111 des Arts » and « Enfance & Cancer ».

FP051 SIOP19-1468 | Naxitamab-based Chemoimmunotherapy for Resistant High-Risk Neuroblastoma: Preliminary Results of "HITS" Pilot/Phase II Study

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Background/Objectives: Chemoresistant and relapsed disease are major obstacles to curing high-risk neuroblastoma (HR-NB). Anti-GD2 monoclonal antibody (MoAb) is effective in preventing relapse after remission but responses in relapsed or progressive disease (PD) are rare. We investigated the combination of humanized anti-GD2 MoAb naxitamab, (previously termed Hu3F8), irinotecan, temozolomide and sargramostim (GM-CSF): a pilot "HITS" protocol against resistant HR-NB now expanded to a phase II study (NCT03189706).

Design/Methods: Salient eligibility criteria included evaluable or measurable chemoresistant disease. Prior anti-GD2 MoAb and/or irinotecan/temozolomide (I/T) therapy was permitted. Each cycle comprised of irinotecan 50 mg/m²/day intravenously (IV) plus temozolomide 150 mg/m²/day IV or orally (days 1-5); naxitamab 2.25 mg/kg/day IV over 30 minutes, days 2,4,8 and 10 (total 9 mg/kg), and GM-CSF 250 mg/m²/day subcutaneously, days 6-10. Toxicity was measured by CTCAE v4.0 and responses by INRC.

Results: Forty-six (23 enrolled on protocol;23 on compassionate-use basis) heavily prior-treated patients (median age at enrollment: 6.6 years; median number of prior relapses: 2) received 175 (median 2; range 1-12) cycles. At enrollment, 7 patients had HR-NB refractory to induction chemotherapy while 39 had prior relapse. Toxicities included myelosuppression and diarrhea expected with I/T, and pain and hypertension expected with naxitamab. No other >grade 2 related toxicities occurred; treatment was outpatient. Early

responses, assessed after 2 cycles, were documented in 18 (39%) patients and were complete (n=9), partial (n=8), and mixed (n=1); 13 patients had stable disease. Responses were achieved in refractory (3/7;43%) and PD (15/39;38%) subgroups, in patients who had previously received I/T (12/34;35%) and/or anti-GD2 MoAb (14/36;39%), and in soft tissue (6/22; 27%) MIBG-avid skeletal sites (20/36;56%) and on bone marrow histology (9/12; 75%).

Conclusions: High-dose naxitamab-based chemoimmunotherapy is safe and effective against chemoresistant HR-NB. This ongoing phase II study may define a broader role for naxitamab which was recently granted breakthrough designation by the Federal Drug Administration of the US.

FP052 SIOP19-1003 | Temozolomide as a Single Agent or in Combination for Patients with High Risk Refractory or Relapsed Neuroblastoma: Excellent Tolerance and Sustained Disease Responses

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Background/Objectives: Phase II trial data proves temozolomide (TMZ) is effective and tolerable for neuroblastoma treatment, but there are no large cohort published data, little 'real-world' data, and variation in modality of use.

Design/Methods: Descriptive, retrospective study in 3 French centres for children with refractory/relapsed high-risk neuroblastoma (HR-NBL) diagnosed 1/1/04-31/12/17, follow-up to 31/10/18, receiving single-agent or combined TMZ, assessing efficacy and tolerability of TMZ.

Results: Refractory/relapsed disease was diagnosed at a median age of 4y9m (range 8m-18y11m) for the 147 children included.

Sixty-one had induction-refractory disease; 30 responded sufficiently to TMZ-based chemotherapy to proceed to high dose chemotherapy (HDC). At last follow-up, 21/30 were alive (18 CR/PR, 3PD), compared with 8/31 (5 CR/PR, 3 PD) in non-HDC cohort. Overall best response rate (CR/PR) was 48%. Median PFS was 1y1m (95%CI 6m-1y7m), OS was 2y9m (95%CI 1y10m-5y10m). Eighteen patients never progressed/relapsed over a median follow-up of 2y4m (range 7m-11y2m).

Eighty-six patients with relapsed disease received a median number of 3 (1-33) cycles, 36 received TMZ alone. Overall

best response rate was 44%, 31% had SD. Median PFS was 4m (95%CI 3m-5m), median OS 11m (95%CI 8m-1y1m).

Nineteen of the 147 patients received 12 or more consecutive cycles of TMZ-based chemotherapy, 13 are alive (9 CR/PR, 4 PD) with a median follow-up of 4y11m (range 1y7m-8y9m). Eight of these patients have stopped chemotherapy and are relapse-free with a median follow-up of 1y10m (range 4m-7y2m).

TMZ was well tolerated; toxicity delayed 8.8% of cycles, no-one required treatment withdrawal for toxicity. Performance scales were good ($\geq 80\%$) after 6 months treatment. No patients developed secondary malignancies, over a median follow-up of 12m (range 0m-10y10m).

Conclusions: TMZ-based regimens can gain, and maintain, disease control in HR-NBL, enabling consolidation for refractory disease. In relapse, prolonged use is well tolerated, with good performance score. Long-term survival was observed in some patients after treatment withdrawal.

FP053 SIOP19-0830 | Temozolomide versus Irinotecan-Temozolomide for Children with Relapsed and or Refractory High-Risk Neuroblastoma (RR-HRNB). Results of the Beacon-Neuroblastoma Randomized Phase II Trial, an ITCC-SIOPEN Trial

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Background/Objectives: One objective of the BEACON-Neuroblastoma (NCT02308527) randomized Phase II trial was to assess backbone chemotherapy activity for children with RR-HRNB.

Design/Methods: Patients aged 1-21 years with RR-HRNB were randomized in a 2x2 factorial design to: temozolomide (T) versus irinotecan-temozolomide (IT), with or without bevacizumab. Here we report the results of the irinotecan

randomization (T vs. IT), which had a probability-based Bayesian design. Primary endpoint was best overall response (complete or partial) during the first 6 courses; overall response rate (ORR) was calculated.

Results: From 2013 to 2018, 61 patients were randomized to treatment with T and 60 to IT; median age 5.8 years; 85 measurable (per RECIST) and 36 evaluable disease; 55 refractory and 66 relapsed disease; 22 had MYCN amplification. Baseline characteristics were balanced between the arms. Response data not available for 2 patients. 14 patients not assessable (NA) for response (did not receive treatment or stopped early) were considered non-responders (as per the protocol). Of 59 pts on T, 14 had responses [24%] (1CR, 13PR); 23SD; 13 PD; 9NA. Of 60 pts on IT, 10 had responses [17%] (3CR, 7PR). 36SD; 9 PD, 5NA. For ORR (risk ratio (RR) = 0.70, 95% credible interval 0.32 to 1.44). The probability that the RR for ORR was > 1.0 was 17%, meaning that IT did not show greater activity than T. In subgroup analyses, there was no interaction between T and IT and treatment with/without bevacizumab (heterogeneity test, $p = 0.7$). 44% T and 58% IT patients had grade ≥ 3 toxicities as per CTCAE v4.0; the largest difference was for diarrhea (0% T; 12% IT).

Conclusions: Irinotecan does not improve the response rate when added to temozolomide in RR-HRNB, but does increase the frequency of diarrhea. Longer follow-up is needed before assessing whether it impacts progression-free or overall survival.

FP054 SIOP19-0712 | Randomisation of Relapsed and Refractory High-Risk Neuroblastoma Patients Treated with Long-Term Infusion of Anti-GD2 Antibody Dinutuximab Beta with or Without Subcutaneous Interleukin-2, A SIOPEN Study

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Background/Objectives: Efficacy and toxicity of long term infusion (LTI) of dinutuximab beta (DB) with or without subcutaneous interleukin 2 (scIL-2) was determined in patients with high-risk relapsed/refractory neuroblastoma.

Design/Methods: Between 07/2014 and 07/2017, 160 patients from 11 countries were enrolled into an open label SIOPEN Phase II clinical trial (EudraCT 2009-018077-31) and randomly assigned to receive up to 5 cycles of 100 mg/m² DB-LTI (d8-17) and 160 mg/m² oral isotretinoin (d19-32) (81 patients) with and without 6x10⁶ IU/m² scIL-2 (d1-5; 8-12) (79 patients). Endpoints were toxicity, response rates and 2yrs-event free and overall survival.

Results: Patients were well balanced between arms according to stage, age, MYCN amplification, patients with relapse and remission status. Median follow-up was 2.6 years. The 2yrs-EFS and -OS for DB (81 patients) vs. DB combined with scIL-2 (79 patients) was 59%±6% vs. 65%±6% (p=0.721) and 79%±5% vs. 84%±4% (p=0.904). In 97 patients with evaluable disease, a response rate of 49% (9% CR, 40% PR) vs. 52% (26% CR, 26% PR) after treatment with DB vs. DB and scIL-2 was observed. Grade 3&4 fever (16% vs. 46%, p=0.000), allergic reaction (1% vs. 14%, p=0.004), hematological toxicity (46% vs. 66%, p=0.013) and neurotoxicity (0% vs. 8%, p=0.003) were significantly worse in the combination arm. Paraplegia possibly related to the treatment was observed in 2 patients in the combination arm, none in the arm without scIL-2, and one resolved to baseline. Pharmacokinetics and HACA responses between both arms were not different with overlapping antibody concentration-time curves and HACA responses of 15/81 (19%) (DB) vs. 16/79 (20%) (DB and scIL-2).

Conclusions: No significant difference in efficacy of DB alone compared to DB combined with scIL-2 and increased toxicity in the later arm suggest that this schedule of scIL-2 is of no additional benefit.

FPS 11: Lymphomas

FP055 SIOP19-1055 | Impact of Rituximab on Immune Status Following Therapy in Children with B-Cell Non-Hodgkin Lymphoma/Mature Acute Leukemia: A Report from Intergroup INTER-B-NHL RITUX 2010 Trial

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Background/Objectives: Rituximab in addition to standard LMB therapy improves survival of children/adolescents with high-risk B-NHL/B-AL. The immune related toxicity of rituximab, including the depth and duration of B cell and immunoglobulin deficiency, has not been described.

Design/Methods: The international randomized phase III trial compared LMB chemotherapy plus rituximab (375 mg/m² for a total of 6 doses) to chemotherapy alone in 328 patients (164/arm) < 18 years with high-risk mature B-NHL/B-AL. Immune laboratory evaluations included absolute lymphocyte counts and immunoglobulin levels at baseline (available for 211 and 257 patients respectively), end of treatment (188 and 168 patients) and one year (183 and 156 patients). Data on immunoglobulin infusions were collected.

Results: At baseline, 39% of patients had low B-cell counts, including 14% with profound B-cell lymphopenia (< 100/mm³), 59% had low CD4+ T-cells and 47% had hypogammaglobulinemia. At the end of treatment, patients in the rituximab group were more likely to have lymphopenia (79% vs 59%, p=0.0022), low B-cell counts (95% vs 64%, p<0.0001), profound B-cell lymphopenia (90% vs 55%, P<0.0001) and hypogammaglobulinemia (70% vs 47%, p=0.0019). By one year, only IgG, IgA, and IgM levels remained different between groups, with abnormal low values occurring in 56%, 18% and 23% of patients in the rituximab group vs. 25%, 5% and 9% of patients in the chemotherapy only group (p=0.0002, 0.023 and 0.027, respectively). Immunoglobulin replacement therapy was administered to 15.8% of patients who received rituximab and to 7% of those who received chemotherapy alone. There were no deaths attributed to infection during the post therapy follow-up period.

Conclusions: Children with high-risk B-NHL/B-AL receiving intensive chemotherapy with rituximab had significantly more lymphopenia, B-cell deficiency and hypogammaglobulinemia at the end of therapy. Hypogammaglobulinemia persisted at one year in more than half of patients whose therapy included rituximab.

FP056 SIOP19-0451 | Single-Centre Experience of B-Cell Lymphomas in Children at the Height of the HIV Epidemic in South Africa

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Background/Objectives: South Africa has seen an increase in B-cell lymphomas (BCL) associated with HIV/AIDS. The purpose of this study was to evaluate the outcome of children with BCL, assess the most common histology, and determine whether the HIV epidemic has increased the incidence.

Design/Methods: This was a retrospective review of patients with BCL at Red Cross Children's Hospital, Cape Town, between January 2003 and December 2015.

Results: Ninety-eight patients were diagnosed with BCL with a median age of 6.41 years. Sixty-nine patients were HIV-negative, 29 patients were HIV-positive. The annual incidence of BCL in the HIV-negative group was 4.3 vs 5.3 cases per year for 1991-2002 and 2003-2015, respectively. In the latter period, 2.2 additional cases of BCL were diagnosed in HIV-positive children. In the HIV-positive group, 19 (66%) had BL, 7 (24%) had Diffuse Large B-cell Lymphoma (DLBCL), 3 (10%) had other subtypes of BCL. Seven HIV-positive patients were not treated due to poor performance status, parent refusal or post-mortem diagnosis. In the HIV-positive group, one patient was LMB Risk Group A (3%), 19 patients were Group B (65%), 8 patients were Group C (28%). One patient had a primary CNS lymphoma. In the HIV-negative group, 8 patients were Group A (12%), 38 patients were Group B (55%), and 23 patients were Group C (33%). Overall 5-year event free survival was 81%; specifically, HIV-negative group: 84% (n=69) and HIV-positive group: 70% (n=22). Survival rates were not significantly different for Group B and C (*p*-value 0.20 and 0.37 respectively).

Conclusions: The outcomes for HIV-positive children with BCL were not significantly worse than those for HIV-negative children in the same time period. Although BL was the most common subtype overall for both groups, DLBCL was proportionally more common in the HIV-positive group. The HIV epidemic produced a modest increase in the incidence of BCL.

FP057 SIOP19-1497 | Value of FDG PET/CT for Staging and Response Assessment of Pediatric 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 standard for staging and response assessment in adult Non-Hodgkin Lymphoma (NHL), but there is still limited data in paediatric NHL.

Design/Methods: All patients aged 3 to 21 years with one of the 5 main paediatric NHL subtypes have been prospectively included in the French PET lymphoma study. PET/CT response was assessed using Deauville criteria. Staging was based on St Jude's classification. PET/CT results were used neither for staging nor for therapeutic decision.

Results: From 2011 to 2015, 229 patients were included. 149 (65%) patients had PET/CT at diagnosis: 57/89 (64%) Burkitt lymphoma, 21/24 (88%) diffuse large B cell lymphoma, 20/26 (77%) primary mediastinal B cell lymphoma, 29/61 (48%) lymphoblastic lymphoma and 22/29 (76%) ALK+ anaplastic large-cell lymphoma. With a median follow-up of 43.6 months, 3-year progression-free and overall survivals were 89.5% [84.5-93.1] and 95.5% [91.9-97.5]. PET/CT findings resulted in staging change in only 3/149 (2%) patients or 13/149 (8.7%) if we consider patients with bone lesions as stage IV, but none of those patients had treatment failure. At remission assessment, 89/172 patients (52%) had residual mass and PET/CT evaluation but none of the 62 patients with negative PET/CT had viable cells on histologic evaluation and/or further relapse. Among the 27 patients with positive PET/CT, 2 had viable cells on biopsy, 1 had no histologic evaluation but relapsed 3 months later, and the other 24 had no viable cells and/or no further relapse/progression.

Conclusions: In this first prospective PET/CT study in paediatric NHL, PET/CT findings have limited impact on initial staging and its results should not lead to a modification of treatment. For remission assessment, negative PET/CT is a very good indicator of complete remission. However, because false-positive PET/CT findings are frequent, biopsy is required to confirm persistent residual disease.

FP058 SIOP19-1257 | Management and Outcome of 108 Cases of Childhood Post Transplant Lymphoproliferative Disease (PTLD) in the Rituximab ERA – A Multicentre UK Study

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Background/Objectives: Post transplant Lymphoproliferative Disease (PTLD) is the most common malignancy in the paediatric transplant population. Since previous registry datasets, rituximab is now widely used in its treatment, as monotherapy or in combination with low dose chemotherapy, alongside a reduction in immunosuppression. Our experience using this approach over a 15 year period is presented.

Objective 1: To evaluate the resulting outcomes for overall survival (OS), event-free survival (EFS) and graft loss.

Objective 2: To co-relate features at presentation with outcomes.

Design/Methods: Retrospective, multi centre data was collected on children diagnosed with PTLD, post solid organ transplant, between Jan 2000-2015, across 5 major UK transplant and paediatric oncology centres.

Results: One hundred and eight patients were diagnosed with PTLD. The average age was 3 years 5 months (3 months – 17 years 2 months). Follow up duration 4 years 3 month (<1 month – 17 years 10 months). Upfront management was reduction in immunosuppression alone 24.1%, rituximab monotherapy 41.7%, (R) CP/COP 18.5%, other chemotherapy 9.3%, cytotoxic T lymphocytes 5.6%. Overall treatment involved exposure to cytotoxic chemotherapy (34%) and included anthracyclines (12%). Outcomes showed OS 1 year = 89.5%, 5 year = 85.1% and 10 year = 80.3%. EFS 1 year = 86.4%, 5 year = 78.5%, 10 year = 69.9%. Small post bowel transplant PTLD carried the worst prognosis. Immunosuppression prior to PTLD, histology, high risk disease site and management with or without chemotherapy did not statistically impact OS, EFS or graft loss.

Conclusions: OS and EFS using rituximab compare favourably with UK registry data, 1994-2004, where 5 year OS was 58% and EFS 56%. With rituximab and low dose chemotherapy even advanced disease showed good outcomes. However, numbers within the subgroups were small and larger studies, linked with biological data, are needed to identify high-risk groups requiring intensive treatment.

FP059 SIOP19-1097 | Genomic Characterization of a Pediatric Cohort with Non-Malignant Lymphoproliferative Disorders

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Background/Objectives: Pediatric non-malignant lymphoproliferative disorders (LPDs) are a clinically and genetically heterogeneous group of disorders. Misdiagnosis or delayed diagnosis often contribute to substantial morbidity or mortality. We aimed to define the genomic spectrum and clinical characteristics, including Epstein Barr virus (EBV) status and presence of hemophagocytic lymphohistiocytosis (HLH), associated with outcomes in a diverse cohort of children with non-malignant LPDs

Design/Methods: Patients at Texas Children's Hospital or collaborating referral centers who met criteria for non-malignant LPDs (lymphadenopathy lasting >3 months, splenomegaly, with or without recurrent or chronic Epstein-Barr virus infection) were offered participation in this research study, approved by the Baylor College of Medicine Institutional Review Board. Genetic testing was performed clinically or through research-based whole exome sequencing (WES).

Results: 51 subjects (from 47 different families) with non-malignant LPDs were identified. Research-based WES was performed in 88% (44/51) of patients; the remaining 7 patients had clinical WES performed. An approximately equal proportion of boys (n=26) and girls (n=25) were recruited into this study, and 51% (26/51) of patients were Hispanic. Fifteen subjects (30%) met HLH-2004 diagnostic criteria. Twenty-six patients (51%) had EBV-associated lymphoproliferative disorders (EBV-LPD). Only 5 of the 51 (~10%) developed malignancy, and 2 of these 5 patients experienced a history of persistent EBV viremia. Of the families who received research WES, potential disease causing genetic defects were identified in approximately 59%. Overall, 34% of patients had diagnoses that resulted in a clinical decision: 22% received chemotherapy and 12% received a bone marrow transplant. The Overall survival (OS) for the cohort was 54%. OS in patients with chronic EBV and HLH was 33%, and 48% respectively.

Conclusions: Pediatric LPDs represent a high-risk population with relatively poor overall survival despite designation as "non-malignant." WES identified a clinically-significant mutation in approximately half of the patients tested. This study supports complete evaluation and close follow-up for these patients.

FP060 SIOP19-0627 | Rituximab in Addition to LMB-Modified Chemotherapy Regimen in Pediatric Patients with Primary Mediastinal Large B-Cell Lymphoma: Results of the French LMB2001 Prospective Study

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Background/Objectives: Primary mediastinal large B-cell lymphoma (PMBL) is a rare entity predominantly affecting adolescents and young adults. The optimal immuno-chemotherapy regimen remains to be determined in this disease.

Design/Methods: French prospective LMB2001 study included all patients < 18 years with mature B-cell lymphoma. Treatment, stratified by stage and response to chemotherapy, included 4 to 8 courses of LMB chemotherapy without radiotherapy. In 2006, LMB 2001 study was further amended to introduce “LMB B/C-modified” chemotherapy for PMBL patients consisting of 2 Group B COPADM courses (with 3 g/m² of high-dose methotrexate and 1 single MTX intrathecal), followed by 4 Group C courses, i.e. 2 CYVE and 2 Maintenance 3. From 2007, rituximab was also given before each chemotherapy course (total 6 infusions).

Results: From September 2001 to March 2012, 42 patients with PMBL were registered. Median age at diagnosis was 15.8 years (R, 8.4 to 18.1). Thirty-three patients (79%) had bulky mediastinal mass > 10 cm. The most frequent involved organs were lung (n=15) and kidney (n=6), and 3 patients (7%) had bone marrow (n=1) or neuromeningeal involvement (n=2). Eighteen patients (43%) had LDH > 2N. Patients received a median of 6 chemotherapy courses with rituximab for 21 of them. With a median follow-up of 5.1 years (R, 1.2-10.8), 5-year event free (EFS) and overall survival (OS) were 88% (95%CI, 73.6%-94.8%) and 94.6% (95%CI, 79.8-98.7%) for the whole population. The 5-year EFS was 95.2% (95%CI, 70.7%-99.3%) and 80.9% (95%CI, 56.8-92.4%) (p=0.17) and 5-year OS was 100% and 89.9% (95%CI, 65.3%-97.3%) (p=0.18) for patients treated with and without rituximab, respectively. Indeed, only 1/21 patient treated with

rituximab and LMB B/C-modified chemotherapy had early treatment failure after RCOPADM1 but achieved prolonged complete remission with second-line chemotherapy and radiotherapy.

Conclusions: Intensive LMB-modified chemotherapy with rituximab achieved excellent outcome in children/adolescents with PMBL.

FPS 12: Survivorship

FP061 SIOP19-0463 | Impact of Radiation Dose and Volume on Declines in Intellectual Functioning (IQ) For Children Diagnosed with Medulloblastoma: A Report from the Children's Oncology Group (COG)

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Background/Objectives: We examined longitudinal intellectual functioning in children treated for medulloblastoma on COG phase III protocol ACNS0331.

Design/Methods: Children with standard risk medulloblastoma participated in neuropsychological testing at three timepoints over a 6-year period. Children aged 3-7 years were randomized to receive craniospinal irradiation (CSI) of either 23.4Gy (standard dose; SDCSI) or 18Gy (lower dose; LDCSI). Children aged 8+ received SDCSI. All children were also randomized to receive either a reduced volume radiation boost to the involved field (IFRT) or a standard boost to the whole posterior fossa (PFRT).

Results: Of 464 eligible patients, 354 (76%) completed some neuropsychological testing. The sample was predominantly male (65.3%), white (82.8%), and non-Hispanic (81.3%); mean age at diagnosis was 9.1 years (range 3-19). IQ was assessed at an average of 0.67 (T1), 2.95 (T2), and 4.90 (T3) years post-diagnosis. Mean estimated IQ was in the average range for the overall sample (T1=95.8+15.2; T2=94.8+14.0; T3=94.20+16.2) and declined only an average of 1.6 points over time. However, notable declines were observed for children in the younger age group (3-7 at diagnosis) who exhibited an 8-point decline in estimated IQ over time. Young children randomized to SDCSI exhibited greater IQ declines than those receiving LDCSI (-10.9 vs. -6.2, respectively; p=.025). Young children receiving PFRT also showed greater declines compared to the IFRT group (-9.75 vs -7.23, respectively).

Conclusions: Results of this prospective, randomized clinical trial suggest that young children (<8 at diagnosis) are particularly susceptible to the effects of radiation therapy, related to both dose of CSI and boost volume. However, similar results were not seen for older children, for whom IQ remained in the average range at up to 6 years post-diagnosis. Results suggest that strategies to limit CSI dose and/or boost volume in young children treated for medulloblastoma may lead to better neuropsychological outcomes.

FP062 SIOP19-1302 | Medulloblastoma Survivorship Outcomes are Related to Tumour Molecular Subgroup; A Meta-Analysis of the SIOP-UKCCSG-PNET3 and HIT-SIOP-PNET4 Trials

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Background/Objectives: Reduced health-related quality of life (HRQoL) and cognitive outcomes are common in children treated for medulloblastoma (MB). The 2016 WHO classification of brain tumours recognises four consensus MB molecular subgroups (MB_{WNT}, MB_{SHH}, MB_{Grp3}, MB_{Grp4}) and limited evidence in small cohorts suggest molecular subgroup may influence MB survivorship.

Design/Methods: Neurocognition measures (Wechsler Intelligence Scales, Kaufman Assessment Battery for Children, and Raven's Progressive Matrices) were collected in the HIT-SIOP-PNET4 MB trial and HRQoL (health status, HUI3; emotional and behavioural difficulties, SDQ; HRQoL, Ped-sQL) were additionally available for this and the previous SIOP-UKCCSG-PNET3 MB trial. Molecular subgroup was retrospectively determined in remnant tumour material and assessed for relationships to HRQoL and neurocognition alongside other treatment and clinicopathological features, in univariate and multivariate analyses.

Results: In a combined cohort comprised of SIOP-UKCCSG-PNET3 and HIT-SIOP-PNET4 patients (n=150), tumour molecular subgroup was significantly associated with parent- and child-reported HRQoL, even after taking into consideration other significant and reported HRQoL predictors (e.g. treatment, gender, age etc); MBGrp4 predicted significantly worse outcomes than MBSHH and MBGrp3 (p<0.05).

Furthermore, MBGrp4 predicted poorer patient- and parent-reported health status in HIT-SIOP-PNET4 (n=40/81, p<0.003). MBSHH showed a trend for exhibiting highest scores on all measures of cognitive performance, possibly related to tumour location. Within a restricted MBGrp4 cohort (n=35), HIT-SIOP-PNET4 treatment (p=0.041, B=-0.175) and classic tumour histopathology (p<0.001, B=0.516) were significantly associated with health status.

Conclusions: This combined analysis across two MB trials has identified relationships between tumour molecular subgroup and survivorship outcomes post-therapy (HRQoL, neurocognition), highlighting findings for assessment in larger series. Such cross-discipline, international trials-based studies have the potential to inform our current understanding of MB survivorship outcomes and could impact subgroup-directed disease management strategies in future.

FP063 SIOP19-1131 | Naïve T Cell Immunosenscence Associated with Thyroid Subsequent Malignant Neoplasm in Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study

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Background/Objectives: Reduced blood telomere content is associated with increased risk for subsequent malignant neoplasms of the thyroid (thyroid SMN) in survivors of childhood cancer. Here, we further investigated this association within leukocyte subsets.

Design/Methods: Survivors were enrolled to CCSS, a multi-center, retrospective cohort of 5-year+ survivors of childhood cancer. Survivors with thyroid SMN were matched to survivor controls without SMN by primary diagnosis, diagnosis year, chemotherapy, radiation field, and follow-up time. Telomere length (TL) was determined from viably frozen leukocytes by flow cytometry fluorescence in situ hybridization (Repeat Diagnostics), and transformed to age-adjusted percentiles based on age at collection. We compared frequency of very low (VL) and low (L) TL ($\leq 1^{\text{st}}$ and $> 1^{\text{st}} - \leq 10^{\text{th}}$ age-adjusted percentile), age-adjusted TL, and leukocyte subset proportions between cases and controls using McNemar's test, paired t-test, and Wilcoxon matched pairs signed rank test. Odds ratios were determined by conditional logistic regression.

Results: 46 out of 52 pairs had sufficient cell recovery for analysis. All survivors had age-adjusted TL below the population median. Cases had shorter age-adjusted TL than controls in lymphocytes ($p=0.04$), naïve T cells ($p=0.02$), B cells ($p=0.01$), and NK cells ($p=0.01$). Naïve T cell VL TL was observed in 9 cases vs. 2 controls, $p=0.04$ (OR for L/VL TL 2.8, 1.11-7.19, $p=0.03$). Naïve T cells also comprised a smaller proportion of all lymphocytes in cases vs. controls with high confidence immunophenotype data (median CD45RA+CD20- lymphocyte percentage: 24%, interquartile (IQ) range 19-32% vs. 39%, IQ range 30-50%, $n=40$, $p=0.002$).

Conclusions: Survivors of childhood cancer have shorter age-adjusted TL than population controls. This difference was most pronounced for survivors with thyroid SMN and particularly significant in naïve T cells, corresponding with lower cell frequency relative to total lymphocytes. Risk for SMN may be related to defects in T cell-mediated cancer surveillance from premature naïve T cell exhaustion.

FP064 SIOP19-1035 | Cumulative Burden of Chronic Health Conditions (CHC) In Survivors of Childhood Cancer: A Cloud-Based Risk Prediction and Visualization Tool from the ST. Jude Lifetime Cohort

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Background/Objectives: A limited number of risk-prediction models have been developed to predict a specific CHC. Multimorbidity risk-prediction models that account for the cumulative burden of disease while simultaneously accounting for competing risks are lacking.

Design/Methods: Clinically assessed CHCs (forming 32 categories) from 5522 childhood cancers survivors (mean age=35.3, range 18.9-67.9) were used to develop multimorbidity prediction models based on the cumulative burden approach. Prediction was made using two Poisson-process sub-models, a model for recurrent chronic disease events and a model for death as a terminal event. Risk-prediction models are based on user-defined terms including patient demographics (gender, race, age at diagnosis), chemotherapy exposures (cumulative dose: bleomycin, etoposide, cisplatin, carboplatin, vincristine, intravenous and intrathecal methotrexate, cyclophosphamide, anthracycline; yes/no exposed: steroids) and radiation exposures (dose: chest/neck, heart, brain, abdominal and pelvis). Predicted data are disseminated as a web-based tool with four interactive visualization

formats (cumulative burden line graphs, stacked bar charts, rank-order heatmaps, treemaps) using customized JavaScript.

Results: To demonstrate the utility of the tool, predicted cumulative burden was calculated for a hypothetical patient (10 year-old, white, male) receiving treatment either on Doxorubicin-Vinblastine-Vincristine-Chlormethine-Bleomycin-Etoposide-Prednisone with heart/chest radiation (STANFORD-V), Methotrexate-Doxorubicin-Cisplatin (MAP), or Dactinomycin- Doxorubicin-Vincristine with abdominal radiation (DD4A). By age 50, the model predicted that a patient would experience, on average, 6.2, 5.9 and 4.9 CHCs after completing each regimen, respectively. As for specific CHCs, arrhythmias, myocardial infarction and male reproductive disorders showed appreciable visual differences across the 3 treatment modalities, while obesity, strokes and seizures did not. Substantial variations were predicted within an individual patient, as well as between patients with different treatments, across different ages.

Conclusions: We have created a cloud-based, risk-prediction method and tool that provides clinicians and researchers an intuitive platform to instantaneously predict patterns for multiple CHCs concurrently for survivors of childhood cancer for use in research as well as patient-oriented education.

FP065 SIOP19-0452 | Effect of Risk-Stratified Therapy on Health Status and Sociodemographic Outcomes in Survivors of Acute Lymphoblastic Leukemia (ALL) in the Childhood Cancer Survivor Study

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Background/Objectives: Although survivors of childhood ALL treated in the 1990s have decreased risk for late-mortality, they reported long-term health status outcomes that were similar or inferior to survivors treated in earlier eras. However, the impact of risk-stratified therapy on health status and sociodemographic outcomes has not been evaluated.

Design/Methods: We estimated prevalence of poor general or mental health, functional impairment, activity limitations,

cancer-related pain or anxiety as well as sociodemographic outcomes among 5368 survivors of childhood ALL diagnosed from 1970-1999. Therapy combinations defined treatment groups representative of 1970s therapy (70s), standard- and high-risk 1980s and 1990s therapy (80sSR, 80sHR, 90sSR, 90sHR), and relapse/transplant (R/BMT). Outcomes were compared among treatment groups and to a sibling cohort using log-binomial models adjusted for age, sex and race to estimate relative risk (RR) with 95% confidence intervals (CI).

Results: Compared to 70s, 90sSR were less likely to report poor general health (RR [95% CI] 0.75 [0.57-0.99]), functional impairment (0.55 [0.40-0.74]), activity limitations (0.65 [0.47-0.89]) and cancer-related pain (0.62 [0.43-0.90]). Compared to 70s, 90sHR were less likely to report functional impairment (0.68 [0.47-0.99]) and activity limitations (0.65 [0.43-0.97]). Compared to 70s, a higher proportion of survivors from R/BMT reported adverse health status outcomes, albeit RR was not significantly different. Compared to siblings, 90sSR (0.80 [0.61-1.04]) and 90sHR (0.77 [0.51-1.15]) reported no difference in risk for being uninsured, attainment of <college degree (90sSR: 0.98 [0.88-1.09]; 90sHR: 0.85 [0.72-1.00]), or being employed less than full-time (90sSR: 1.29 [0.85-1.97]; 90sHR 1.38 [0.84-2.26]).

Conclusions: Survivors treated with therapy consistent with more recent ALL protocols had reduced risk for adverse health status compared to 70s and have sociodemographic outcomes similar to their siblings. Thus, poor health status in patients treated in more recent eras appears to be driven by those patients that relapse or require a BMT.

FP066 SIOP19-1063 | Medical Financial Hardship in Adult Survivors of Adolescent and Young Adult Cancers

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Background/Objectives: The long-term impact of cancer and its therapy can result in lifelong financial hardship in survivors, which can be categorized into material (e.g. problems paying medical bills), psychological (e.g. distress), and behavioural (e.g. forgoing care due to cost) domains. Medical financial hardship encompasses hardship in these domains related to medical care and costs, and has not been well characterized among adult survivors of adolescent and young adult (AYA) cancers.

Design/Methods: We identified a cohort of adult survivors of AYA cancers (diagnosed age 15-29; $n = 1,494$) and adults without a cancer history ($n = 234,487$) from the 2010-

2017 National Health Interview Survey. Financial hardship domains were compared between these groups using separate multivariable logistic regressions and hardship intensity (determined by co-occurrence of hardship domains) was compared with ordinal logistic regressions.

Results: The majority of survivors were more than 2 years from diagnosis (92.1%). Survivors were more likely to report at least one measure of hardship in material (39.3% vs 27.9%, $p < .001$) and behavioural (31.7% vs 21.6%, $p < .001$) domains, and hardship in all three domains (13.8% vs 8.8%, $p < .001$). Fewer survivors had no hardship in any domain (35.1%) than adults without a cancer history (42.3%, $p < .001$). Survivors were more likely to report at least one cost-related prescription medication non-adherence behavior (15.1% vs 10.5%, $p = 0.002$), such as skipping doses, or coping strategy behaviour (30.7% vs 23.0%, $p < .001$), such as asking for lower cost medications.

Conclusions: Adult survivors of AYA cancers are more likely to experience medical financial hardship across multiple domains compared to adults without a history of cancer. Healthcare providers must recognize these challenges because they may lead to poor health outcomes. More resources are needed to address this inequity and its potential impact on survivors' ongoing care.

FPS 13: AML and Stem Cell Transplantation

FP067 SIOP19-0410 | Lydia II Trial: Natural Killer Cells Infusions as Consolidation Strategy in AML Pediatric Patients

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Background/Objectives: Acute myeloblastic leukemia (AML) survival rate is stagnated in around 60%, being relapse the main problem. We propose including cellular therapy with haploidentical activated and expanded NK cells (NKAE) as adjuvant therapy in pediatric AML patients in complete remission and without indication of HSCT.

Design/Methods: Multicentric, open, prospective, non-randomized, phase II clinical trial to evaluate the efficacy and safety of allogenic NK cells infusion from haploidentical donor in pediatric patients affected by low and

intermediate risk AML in first complete cytological remission. After chemotherapy, patients received two infusions of NKA-E cells after a lympho-ablative treatment (cyclophosphamide 60mg/Kg, fludarabine 125mg/Kg). Donors were selected based on alloreactivity of KIR receptors. And their NK cells were activated and expanded for 3 weeks through co-culture of their peripheral blood mononuclear cells with the *Good Manufacturing Practices*-compliant K562-mb115-41bbl cell line

Results: 7 patients were enrolled, with a median of 7 years (1-16). In total, 14 cell products were infused with the following characteristics: NK cells (CD45+CD56+CD3-) 86.64 ± 11.36%; T lymphocytes (CD45+CD56-CD3+) 2.94 ± 3.55. A mean of 51.14 ± 53.99 × 10⁶ NK cells/kg and 0.69 ± 0.35 × 10⁶ T cells/kg were infused. Treatment and infusions were well tolerated. The main adverse event was neutropenic fever in one patient. After a median follow up of 530 days (371-813) all the 7 patients are alive. Two patients showed relapse at days +307 and +360 after NK cells infusion and received HSCT.

Conclusions: The results from this trial show that NKA-E cells infusion as consolidation strategy in pediatric patients with AML is feasible and secure. The therapeutic effect should be confirmed in a larger cohort of patients.

Clinical Trial Registry: Clinicaltrials.gov (NCT02763475) and EudraCT (2015-001901-15).

FP068 SIOP19-0564 | Independent Prognostic Impact of TET2 and ABCA3 Transcriptional and Post-Transcriptional Profiles in Pediatric Acute Myeloid Leukemia

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Background/Objectives: Despite recent progress, the relapse rate of pediatric non-promyelocytic acute myeloid leukemia (AML) stagnates around 50%. Transcriptional and post-transcriptional anomalies in cancer cells seem a promising source for new biomarkers. *TET2* and *ABCA3* are two genes with prognostic impact in adult AML. *TET2* is implicated in hematopoietic stemness and *ABCA3* in resistance to chemotherapy. We explored their transcriptional profiles in pediatric AML samples and aimed at building a specific prognostic score.

Design/Methods: Through exon-specific quantitative RT-PCR, we explored two sets of pediatric patients with AML taken from the ELAM02 clinical trial (exploratory, n=120

patients, and validation, n=150 patients) for *TET2* and *ABCA3* gene expressions, *TET2* exon 2 skipping and *ABCA3* exon 19 skipping. Cutoff values were determined using CutOff Finder in the exploratory set. Our transcriptional and post-transcriptional prognostic score (TPS) value was the weighed sum of the prognostic impact (1 for adverse and 0 for good prognosis) of each variable significantly associated with event-free survival (EFS).

Results: We identified in the entire cohort: high *TET2* gene expression (HR=0.34, 95CI[0.17 to 0.68], p<0.0001), high levels of *TET2* exon 2 skipping (HR=2.63 [1.30 to 5.32], p=0.007) and high *ABCA3* gene expression (HR=2.15 [1.13 to 4.47], p=0.04) as independent prognostic factors for EFS. Results were similar for overall and disease-free survivals. The TPS identified 4 groups of patients with significantly different prognosis and allowed a better prediction of outcomes than the current risk stratification (concordance index, c=0.71 versus 0.56).

Conclusions: *ABCA3* and *TET2* transcriptional profiles seem to better predict outcomes in pediatric acute myeloid leukemia than the current cytogenetic and molecular risk stratification. These promising results need to be validated in another set of patients. TPS performances could benefit from including more gene associated with stemness and response to treatment.

FP069 SIOP19-0994 | Association Between Global Methylation Status of Line-1 and Clinical Progression in Pediatric Myelodysplastic Syndrome

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Background/Objectives: Myelodysplastic syndrome (MDS) comprises a heterogeneous group of clonal hematopoietic stem cell diseases with an increased risk of evolution to acute myeloid leukemia (AML). Due to the heterogeneity and rarity of pediatric MDS little is known about its molecular pathogenesis. It has been showed that global hypomethylation plays a crucial role in genomic/chromosomal instability, leading to progression of various solid tumors. The aim of this study was to analyse the global methylation of LINE-1 in pediatric MDS patients and its association with subtypes, cytogenetics and disease evolution.

Design/Methods: Bone marrow cells were obtained from 71 pediatric patients with primary MDS. Forty six patients (65%) were classified at initial stage, refractory cytopenia of childhood (RCC) and twenty five (35%) at advanced stages,

refractory anemia with excess blasts (RAEB/ RAEB-t). We used as controls, the bone marrow cells obtained from 10 healthy pediatric donors. The cytogenetic analysis was performed by GTG and FISH. The global methylation profile of LINE-1 was studied by pyrosequencing.

Results: Pediatric patients present global hypomethylation in 97% (69/71) of the cases. Global hypomethylation was present from the initial stage (RCC) ($p < 0.01$), until the most advanced stages (RAEB/ RAEB-t) ($p < 0.005$) in relation to the donors. Patients with abnormal karyotypes ($p < 0.004$) had a higher percentage of global hypomethylation than donors, mainly with complex karyotypes ($p < 0.007$). The evolution of disease was observed in 35% of the patients (25/71). The decrease in methylation of LINE-1 is more evident in patients who presented clinical progression, with evolution to AML ($p < 0.003$).

Conclusions: These results suggest that global hypomethylation may contribute to the genomic/chromosomal instability during the development and progression from MDS to AML. Acknowledgment: Brazilian Ministry of Health (National Institute of Cancer/INCA, Brazil) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

FP070 SIOP19-0455 | CAR T-Cells Followed By CD34-Selected T-Cell Depleted (TCD) ALLO-HSCT is Associated with Low Toxicity and favorable overall survival

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Background/Objectives: Chimeric antigen receptor (CAR) T-cells have transformed the therapeutic options for patients with relapsed or refractory (R/R) B-cell acute lymphoblastic leukemia (B-ALL). The tolerability and outcome of allo-HSCT following CAR T-cell therapy is yet to be defined.

Design/Methods: We retrospectively reviewed patients with R/R B-ALL who received allo-HSCT following CAR T-cells. Transplant-related mortality (TRM) was estimated and overall survival (OS) was compared by disease status, time from CAR T-cells to conditioning, conditioning regimen, graft composition, and donor characteristics using log-rank analysis.

Results: Eighteen patients, with a median age of 14 (range 1-22), at time of allo-HSCT were included. All patients were in MRD-negative CR following CAR T-cells and prior to allo-HSCT. CR status included CR1 (n=7), CR2 (n=5), CR3

(n=5), and CR4 (n=1). Median time from CAR T-cells to the start of allo-HSCT conditioning was 46.5 days (range 20-126). Conditioning was TBI-based (n=15) or chemotherapy only (n=3). Donors were HLA-matched related (n=8), unrelated (n=6), or HLA-mismatched (n=5). Grafts included CD34-selected TCD PBSCs (Miltenyi) (n=9), unmodified BM (n=8) or cord blood (n=1). Two patients relapsed after CD34-selected TCD allo-HSCT but achieved CR following repeat CAR T-cells (n=1) and excision/local radiation (n=1). Three patients relapsed after unmodified allo-HSCT: one (n=1) achieved MRD-neg/CR following repeat CAR T-cells and two (n=2) died from disease. Three patients in the unmodified cohort died due to TRM (24-month TRM = 42% [3-80%]), including veno-occlusive disease (multi-organ failure/infection) (n=2) and GVHD (n=1), while no TRM was noted in the CD34-selected TCD cohort ($p=0.04$). The 24-month OS was 71% [50 to 93%], with 100% OS in CD34-selected TCD recipients and 40% in the unmodified recipients ($p=0.007$). No other factors significantly impacted OS.

Conclusions: CAR T-cells followed by a CD34-selected TCD allo-HSCT resulted in low toxicity (TRM) and favorable OS when compared to unmodified allo-HSCT.

FP071 SIOP19-0229 | Ruxolitinib in Children with Steroid Refractory Acute Graft Versus Host Disease: A Multicenter Study of the Pediatric Group of SFGM-TC

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Background/Objectives: We conducted a national multicenter retrospective study in France to evaluate efficacy and tolerance of ruxolitinib in children with steroid-refractory acute graft-versus-host disease (aGVHD) after allogeneic hematopoietic stem cell transplant (HSCT)

Design/Methods: Patients were recruited from the 15 pediatric transplantation centers in France. Transplanted patients were eligible if they met the following criteria: aged ≤ 18 years at transplantation, receiving a myeloablative allogeneic HSCT, irrespective of the stem cell source, having an acute GVHD of grade ≥ 2 and treated with ruxolitinib for steroid refractory acute GVHD. Treatment failure was defined by the

absence of improvement of aGVHD, deterioration of aGVHD in any organ by at least one stage, the development of acute GVHD manifestations in a previously unaffected organ, and the use of any additional agents to control the disease.

Results: Twenty-nine patients received ruxolitinib for steroid-refractory aGVHD. Six patients achieved a complete response at day 28 after the start of treatment but finally 19 patients (65.5%) achieved a CR with a median delay of 41 days (5 to 93). Two patients had a partial response. All patients who achieved CR or PR discontinued corticosteroid treatment. Eight patients showed treatment failure. Overall response rate was 72.4%. Twenty three of 29 patients were alive at a median follow-up of 685 days (177 to 1042 days) after the HSCT. Viral replication (including CMV, EBV and ADV) was observed in 51.7% of cases. We did not observe severe hematological adverse events and cytopenia requiring a modification of ruxolitinib doses always resolved. The median initial dose of ruxolitinib was 12.6 mg/m²/day with a huge range (6.3 mg/m²/d to 28.7 mg/m²/d). We could not demonstrate any relationship between initial dose and effectiveness.

Conclusions: Ruxolitinib may constitute a promising second line treatment for children with steroid-refractory aGVHD that should be validated in prospective large-scale pharmacokinetic and efficacy trial.

FP072 SIOP19-0378 | Defibrotide Treatment in Paediatric Patients with Severe/Very Severe VENO-Occlusive Disease/Sinusoidal Obstruction Syndrome (VOD/SOS) after Haematopoietic Cell Transplantation (HCT): Defifrance Interim Results

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Background/Objectives: VOD/SOS is a potentially fatal complication after HCT/high-dose chemotherapy. Defibrotide is approved for severe hepatic VOD/SOS post-HCT in patients aged >1 month in the European Union. DEFIFrance is collecting real-world data on outcomes in all patients treated with defibrotide across France. This interim analysis evaluated a

subgroup of paediatric patients (<18 years) with severe/very severe VOD/SOS post-HCT treated with defibrotide.

Design/Methods: DEFIFrance is an ongoing, multicentre, post-marketing study. Criteria used for VOD/SOS diagnosis were at the discretion of the treating physician per typical practice; severity was adjudicated by an expert steering committee member. Primary endpoints include Day 100 survival and Day 100 complete response (CR; total serum bilirubin <2 mg/dL and resolution of multi-organ failure [MOF] per investigators' assessment).

Results: As of 8 November 2018, 324 patients were included in DEFIFrance. Of these, 41 paediatric patients had VOD/SOS post-HCT, of which 23 had severe/very severe VOD/SOS and were included in this analysis. Median age was 8.5 (range, 0.4-17.5) years. MOF occurred in 5 (22%) patients. The Kaplan-Meier-estimated Day 100 post-HCT survival rate was 85% (severe [n=14]: 100%; very severe [n=9]: 53%); estimated survival rates were 68% and 55% at 6 and 12 months, respectively. The Day 100 post-HCT CR rate was 83%. Among evaluable patients with severe (n=13) and very severe (n=5) VOD/SOS, Day 100 CR rates were 100% and 40%, respectively. Day 100 VOD/SOS-related mortality was 15%; deaths after Day 100 resulted from causes other than VOD/SOS. Adverse events of interest occurred in 15/23 patients; common events included infection (n=7/23) and bleeding (n=4/23).

Conclusions: Among paediatric patients treated with defibrotide post-HCT for VOD/SOS, outcomes were better in those with severe versus very severe disease, highlighting the importance of early VOD/SOS diagnosis and treatment initiation. The incidence of adverse events of interest was consistent with previous studies.

FPS 14: Epidemiology and Pathways of Care

FP073 SIOP19-1600 | Place of Death Among Children with Cancer in Brazil: A Contemporary Population-Based Study

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Background/Objectives: Place of death can be a robust indicator of palliative care provision for children with cancer. This study aimed to identify factors associated with home death among children with cancer in Brazil and to describe time-trends.

Design/Methods: Population-based descriptive study, including all deaths due to cancer (ICD-10 C00-C97) among children (0-14 years) living in Brazil, in the period 2006-2013. Data source was National Information System

on Mortality and place of death was analyzed according to gender, age, race/skin color, region/state, cancer type and year of death. Logistic regression was employed to estimate crude and adjusted odds ratios (with corresponding 95% confidence intervals) for home death. Joinpoint regression was used to assess time-trends.

Results: Prevalence of home death was 3.9% (585/14,961 deaths), being more frequent for non-white compared to white children (OR=1.3, 95% CI 1.1-1.6). Age was significantly associated with place of death ($p < 0.001$). Children with solid tumors died more frequently at home compared to those with hematologic malignancies (OR=3.3, 95% CI 2.7-4.1), while those living in the North (OR=1.4, 95% CI 1.0-1.9), North-east (OR=1.9, 95% CI 1.6-2.3) and Midwest (OR=1.6, 95% CI 1.2-2.2) had higher chances of dying at home compared to the Southeast (most developed region). In the multivariate analysis, all variables remained as independent predictors of home death. Proportion of home deaths have significantly decreased over the years (APC=-6.1, 95% CI -10.9;-1.0).

Conclusions: A predominance of hospital deaths was observed, with a decrease in the proportion of home deaths over time. Non-White race, older age, solid tumors and residence at North/Northeast/Midwest conferred an increased chance of home death. We hope that the information generated in this research can be used to support public policies aimed at improving the supply of palliative care for children with cancer, benefiting both patients and their families with quality at the end-of-life.

FP074 SIOP19-0213 | Prospective Comparison of Travel Burden, Cost and Time to Obtain Pediatric Multidisciplinary Tumor Board Treatment Plan Through In-Person Visits vs. an AI Enabled Health Technology

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Background/Objectives: NAVYA is a clinically validated online cancer informatics solution that combines artificial intelligence (AI) and rapid review by Multi-Disciplinary Tumor Board (MDTB) experts at Academic Medical Centers (AMC) to deliver comprehensive multidisciplinary expert treatment plans to patients within 24 hours. This has significant implications in pediatric oncology where expertise

is concentrated only at a limited number of AMCs and not widely accessible. Prior research (SABCS and ASCO 2014-2018) showed 98% concordance of NAVYA with an AMC in India and 97% concordance with a US AMC.

Design/Methods: Parents of patients with age ≤ 18 yrs, who reached out to NAVYA between 2017-2019 but ultimately opted for in-person visit to an AMC were contacted by prospective phone follow up. Data was collected on three patient-centered outcomes (travel distance, cost, and time to receive MDTB treatment plan). This was compared using t-tests to a numerically balanced random sample of patients who used NAVYA to obtain treatment plans.

Results: Prospective phone follow-ups with 54 in-person patients and 123 NAVYA patients were analyzed. The groups did not differ significantly in demographics or disease characteristics. In-person patients and NAVYA patients differed significantly with respect to: 1) median travel distance (713 miles, IQR (296 -1089 miles) vs. 0 miles, ($p < 0.05$)) 2) travel related costs of \$2500 vs \$105 online processing fee 3) total time to receipt treatment plan (4.35 days IQR (1.1 days - 30.1 days) vs. 1.04 day IQR (0.4-2.5) ($p < 0.05$)).

Conclusions: Cancer informatics solutions that combine AI with human clinical expertise to generate MDTB treatment plans, vetted by pediatric oncology experts at AMCs, scale ready access to expertise, globally. For families of children with limited access to AMCs, such solutions eliminate travel burden, and significantly reduce cost and wait time. This positively impacts family finances and conveniences.

FP075 SIOP19-1119 | Access to Care for Childhood Cancers in India: Perspectives from Health Care Providers and the Implications for Universal Health Coverage

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Background/Objectives: Access to healthcare is an essential component of Universal Health Coverage (UHC). Individual and health system challenges in India lead to poorer health outcomes for childhood cancers compared to high-income countries. To understand these issues in-depth we sought to explore challenges to childhood cancer diagnosis and treatment in India, through perspectives of healthcare providers.

Design/Methods: This study was conducted in 7 tertiary cancer hospitals (3 public, 3 private and 1 charitable trust hospital) across Delhi and Hyderabad. We recruited 27 healthcare providers, which included oncologists (33%),

senior residents (15%), paediatric nurses (19%), social workers (19%), dieticians (7%) and psychologists (7%). Semi-structured interviews were audio recorded after obtaining informed consent. Thematic content analysis was conducted and organised using NVivo 11 software.

Results: Participants noted several barriers to accessing care such as insufficient infrastructure and supportive care, patient knowledge and awareness, social beliefs, and a weak primary healthcare system. However, these barriers were reflected upon differently based on participant perception, through three key themes: Firstly, perceptions of challenges varied depending on the type of hospital participants worked in, where charitable trust and private hospitals were better equipped to provide services; impacting the patient-provider relationship. Secondly, variation in participant roles meant a different degree of exposure to challenges families faced, where for example, social workers provided more in-depth accounts from their day-to-day interactions with families, compared to oncologists. Thirdly, participants varied in their individual perceptions of the severity of delay and recognition of stakeholder accountabilities, where governance was a major issue.

Conclusions: The health system challenges identified were similar across participants but variation was observed by hospital type, provider role and individual perceptions. This type of analysis is important when addressing access to care issues for emerging policies intending to achieve UHC.

FP076 SIOP19-0842 | Diagnostic Pathways for Children Diagnosed with Cancer in England

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Background/Objectives: Evidence about the frequency and clinical outcomes of children diagnosed with cancer by their diagnostic pathway is limited. Using Public Health England's internationally unique population-based data and Routes to Diagnosis methodology, we studied pathways for children at a more granular and clinically relevant level than currently available.

Design/Methods: We analysed cancer registrations, Hospital Episode Statistics and other administrative health data for

children (0-14 years) diagnosed with cancer, compared with results for age groups 15-24 and 25-44 (England, 2006-2015). Diagnostic groups were based on the International Classification of Childhood Cancer. Diagnostic pathways relevant to children were selected and grouped from those previously defined (Elliss-Brookes L et al, 2012. Routes to diagnosis for cancer - determining the patient journey using multiple routine data sets. *British Journal of Cancer*).

Results: The proportion of emergency presentations (EP) was higher among children (52%) than for 15-24 year olds (26%) and 25-44 year olds (13%). Proportions varied with age during childhood (maximum 60% for two-year olds, compared to 43% for 14-year olds) and varied by cancer type (i.e. 68% for leukaemia, 53% CNS, 46% renal tumours). For the majority of cancers types, EP one-year survival was higher for children than for older ages but the differences in survival across the diagnostic routes studied were markedly less varied; for all cancers combined the difference in survival after EP and GP referrals was 6% points for children, 10% points for ages 15-24 and 23% points for ages 25-44.

Conclusions: Our analysis provides a better understanding of diagnostic pathways for children with cancer and their prognostic implications. EPs account for a higher proportion of diagnoses among children than at older ages but are associated with a smaller survival disadvantage. Possible explanations for the higher prevalence among children include differences in referral guidance and differences in natural history and symptoms of childhood cancers.

FP077 SIOP19-0161 | Somatic Health Outcomes in Parents of Children with Cancer: A Nationwide Danish Cohort Study

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Background/Objectives: Parents of children with cancer often undergo severe psychological stress during their child's illness. It is possible that this stress may lead to an increased risk of somatic diseases, for example through lifestyle changes, but this remains almost unexplored.

Objective: To investigate whether parents of children with cancer have an increased risk of somatic disease after their child's diagnosis compared to parents of cancer-free children.

Design/Methods: We conducted a nationwide study using Danish registries to assess whether parents of children with

cancer had an increased risk of first hospitalization with somatic disease (using selected International Classification of Diseases 10th Revision (ICD 10) groups). From the Central Population Registry and the Danish Cancer Registry, we identified all parents of children diagnosed with cancer in Denmark between 1998 - 2013 (N= 7,797) and a matched control group (N= 74,388) of parents of cancer-free children. Cox proportional hazard models were used to estimate hazard ratios (HRs) with 95% confidence intervals (CIs) for selected disease groups in cohorts free of the specific disease in question. Analyses were adjusted for age and sex of parent and time since diagnosis.

Results: Parents of children with cancer had significantly higher risk of cancer (HR: 1.23; CI: 1.14-1.32), including lifestyle-related (1.17; 1.09-1.27) and tobacco-related cancers (1.2; 1.09-1.32) compared to parents of cancer-free children. They were also at an increased risk of diseases of the circulatory system (1.10; 1.03-1.17), digestive system (1.07; 1.02-1.15), and genitourinary system (1.09; 1.02-1.16).

Conclusions: The results suggest slight-to-moderate increases in risk for certain somatic diseases. As we were not able to account for shared genetics and environment, further research is needed to investigate causal mechanisms in order to improve outcomes in this population.

FP078 SIOP19-0796 | Global Variations and Time Trends in Incidence of Thyroid Cancer in Children and Adolescents - On Behalf of IICC-3 Contributors

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Background/Objectives: Thyroid cancer is more common in females than in males. Incidence increases with age and over time, especially where new diagnostic technologies are implemented. The thyroid gland is sensitive to ionizing radiation. Using large databases assembled by the International Agency for Research on Cancer, we present latest incidence in children and adolescents (age<20 years).

Design/Methods: Thyroid cancer data from 161 registries in 47 countries in 2008-2012 with a covered population <20 years of at least 1 million were analysed to assess geographical patterns. Temporal change was examined in 91 registries in 33 countries with at least 15 years data in 1998-2012 and quantified as rate ratio (RR) comparing the age-standardised rate (ASR) in 1998-2002 to the ASR in 2008-2012 with 95% confidence intervals. Incidence in age <20 years was compared

with that in age 20-74 years for 26 countries. All reported rates are per million.

Results: Based on 8401 cases, the overall ASR in 2008-2012 was 5.8, ranging from <2 in Africa, to >11 in Italy, Republic of Korea and Belarus. ASR was 2.3 in males and 9.3 in females (RR 3.9 [3.4-4.4]). The age-specific incidence rates increased exponentially from 0.2 in age 0-4 years to 15.6 in age 15-19 years. ASR increased between 1998-2002 and 2008-2012; RR=1.3 [0.9-1.8] in males and RR=1.4 [1.0-2.0] in females. The ASR in children and adolescents were correlated with those in adults (Spearman=0.61, p<0.01 in males and 0.59, P<0.01 in females); no correlation was seen for temporal changes.

Conclusions: The thyroid cancer burden is mostly born by females. Increasing incidence may be triggered by increasing socio-economic development in countries up-taking non-invasive diagnostic technologies. Despite of excellent prognosis, unnecessary interventions imply a life-long treatment and should be avoided. The effect of over-diagnosis may be confounded with potential risk factors.

FPS 15: Rare Tumours and Histiocytosis

FP079 SIOP19-0629 | Radiation Dose Adapted Strategy in Childhood Nasopharyngeal Carcinoma: A Proposal to Limit Burden of Treatment and Risk of Late Effects

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Background/Objectives: Childhood nasopharyngeal carcinoma (NPC) is a rare tumor with good prognosis but high risk of acute and long-term toxicities after high dose radiation therapy. Radiation dose adapted strategy according to neoadjuvant chemotherapy response could limit the risk of late effects.

Design/Methods: Bicentric retrospective analysis of children and adolescents (age <19years) treated for NPC with a radiation dose adapted strategy in Gustave Roussy and Institut Curie between 1990 and 2015 were selected. A radiological review of available imaging at diagnosis and after neoadjuvant chemotherapy was planned. Very good response (CR/VGPR) was defined as a primary size reduction in two axis ≥80%, and total radiation dose could be reduce <60Gy.

Results: Sixty-one patients (median age =14 years; range= 7.6-18.7) were included. Two neoadjuvant chemotherapy

regimens were used: A=cisplatinum-5Fluorouracile (n=17), B=cisplatinum and anthracyclines-based regimen (n=44). Radiological evaluations have been reviewed in 47/61 patients. After a median number of 2 courses (range=2-4), CR/VGPR was obtained respectively in 7/17 (41%) and 25/44 (57%) of patients treated with regimens A and B (p=0.4). A radiation reduction dose was performed in 4/7 CR/VGPR (regimen A) and 13/25 CR/VGPR (regimen B) patients with a median total dose of 50 Gy (range: 45.0-59.4). Twenty-two patients received adjuvant therapy (concomitant chemotherapy n=7, adjuvant chemotherapy n=17, interferon-beta n=3). After a median follow-up of 7 years (0.3-27), 17 events (11 progressions/relapses, 4 second cancers, 2 deaths) and 10 deaths occurred, resulting in 5-year EFS and OS of 76% (61.9-85.5%) and 84% (70.6-91.6%), respectively. Type of neoadjuvant chemotherapy regimen (A vs. B) was not correlated to EFS (HR=1.14, 95%CI=0.36-3.63, p=0.97) nor OS (HR=0.39, 95%CI=0.09-1.79, p=0.35). Radiation dose reduction was associated with better OS (HR=0.16, 95%CI=0.04-0.61, p=0.0497).

Conclusions: Radiation dose reduction in cases of CR/VGPR after first cisplatinum-based chemotherapy could be used safely in childhood NPC to limit the risk of late effects.

FP080 SIOP19-0152 | Esthesioneuroblastoma in Children: Is Cervical Prophylactic Nodal Irradiation Warranted? The French Pediatric Rare Tumor Group (FRACTURE) Contribution

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Background/Objectives: Esthesioneuroblastoma (ENB) is a rare neuroectodermal tumor which seldom occurs during childhood. Multimodal treatments are currently proposed but the necessity of cervical prophylactic nodal irradiation (CPNI) in pediatric patients is still unclear. Our objective was to describe cervical lymph node evolution to determine the potential need of systematic CPNI in pediatric ENB.

Design/Methods: Medical charts of all children (≤ 18 yo) affected by ENB, included in the French *Registre National des Tumeurs Solides de l'Enfant* and the database of the rare

pediatric tumor study group (*Fracture*), and treated in France from 01/1990 to 12/2015 were retrospectively analyzed.

Results: Eighteen patients were selected (10 male). Median age at diagnosis was 12.2 years (0.9–18). Tumor extension was Kadish-stage A (n=1), B (n=3), C (n=10), and D (n=4). Hyams histologic grades were I (n=1), II (n=3), III (n=6), and IV (n=6) (not defined 2 cases). Initial cervical spread was evaluated by MRI (n=15), CT scan (n=16), and PET/CT (n=7). Cervical node involvement was confirmed in 2/18 cases and one had cervical node dissection with neck irradiation (58 Gy). Among patients without cervical node involvement, only one patient had a CPNI (48 Gy). After a median follow-up of survivors of 7.6 years (3.8-17.9), no cervical nodal relapse occurred, whereas 10 patients developed neuromeningeal progression. Only 8 patients survived. Five-year overall and event-free survival rates were both 44.4% ($\pm 11.7\%$).

Conclusions: The necessity of systematic CPNI in pediatric ENB patients is not evidence-based. Despite a small number of patients, low incidence of cervical node relapse does not play in favor of CPNI. Poor prognosis of pediatric ENB is mainly related to neuromeningeal dissemination that should be considered during local treatment strategy.

FP081 SIOP19-0983 | Late Effects in Children, Adolescents and Young Adults with Nasopharyngeal Carcinoma Treated on the Multimodal GPOH-TRIALS NPC-1991, NPC-2003 and the NPC-Interim Registry

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Background/Objectives: Over the last decades nasopharyngeal carcinoma (NPC) in children and adolescents has been mostly treated with induction chemotherapy followed by radiochemotherapy. The GPOH-studies NPC-91 and NPC-2003 differ from other prospective studies in children with NPC by the application of a lower radiation dose to the primary tumor (59,4Gy) and by a 6 months lasting maintenance therapy with interferon- β . Event-free and overall survival rates have been >90% for patients with locoregional disease treated on the GPOH-studies. In this retrospective

analysis we investigated the long-term morbidities following treatment for NPC with the GPOH-concept.

Design/Methods: 156 patients with NPC diagnosed between 7/1992 and 6/2015 and registered in the multicenter trials GPOH-NPC-1991, -2003, and the interim NPC-registry were included. Of them 100 patients had at least 1 follow-up exam after the end of therapy and qualified for the analysis. Late effects were investigated using a questionnaire of 20 items.

Results: There were 65 males and 35 females with a median age at diagnosis of 14 years. Follow-up ranged from 1,4 years to 15,5 years with a median of 7,7 years. 93% of patients were in CR1, 6% in $\geq$ CR2, 1% had died at last follow-up. Major late effects were hypothyroidism (67%), xerostomy (32%), ototoxicity (30%), caries (17%) and trismus (10%), followed by chronic sinusitis (9%), skin fibrosis (6%), tinnitus (4%), lung fibrosis (4%) and osteoradionecrosis (4%). Xerostomy was grade I/II in all patients, 2 patients required hearing aids, 1 had received a cochlea implant. One secondary malignancy, a low-grade astrocytoma occurred 6 years after the end of therapy.

Conclusions: Late effects occur in the majority of patients treated for NPC. The incidence of severe late effects, however, appears to be lower than in previous published reports and might be attributed to lower radiation dosages and improvements in radiation techniques.

FP082 SIOP19-1253 | Pediatric Pulmonary Langerhans Cell Histiocytosis. Does Lung Lesion Severity Affect the Outcome

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Background/Objectives: In pediatric pulmonary Langerhans cell histiocytosis (P-LCH), typical chest radiological lesions are nodules and cysts. Pulmonary involvement has been excluded as a risk organ. We report our pediatric multi system pulmonary (MP-LCH) presentation and its relation to the outcome.

Design/Methods: Single centre retrospective analysis from 7/7/2007 to 31/12/2017 in 42 M-PLCH presenting with nodules or cysts, out of 251LCH patients. Pulmonary clinical and radiological presentations were correlated to overall and event free survival (OS) and (EFS) respectively. Patients were stratified as multisystem with or without risk organs (HR and LR respectively), and were treated according to LCH III protocol. The median follow up period was 42.5 months (1.2-137.5).

Results: Out of 42 patients, 17 failed 1st line treatment: Disease progression (DP) during induction n=7, reactivation (REA) after maintenance start n= 10. The 5 year OS is 72% and EFS 54%. The factors affecting OS are lung lesions severity: diffuse 57% vs localized 96% p0.05, radiological lesions resolution post induction: resolved 78% vs not progressed 91% vs progressed 0% p0.013, associated HR 50% vs LR 100% p0.003, no failure to treatment 100% vs DP 57% vs REA52% p0.001. Factors affecting EFS are respiratory manifestations 62% vs none 25% p 0.002, diffuse 28% vs localized 78% p0.001, bilateral 50% vs unilateral 67% p0.011, cleared post induction 54% vs not progressed 66% versus progressed 0% p0.001. HR with lung, 35% vs without 23% p0.65. LR with lung, 66% vs without 71% p0.62. The probability of survival of radiological nodules or cysts is 27%.

Conclusions: However pulmonary involvement has been excluded as a risk organ LCH, its severity as a matter of clinical or typical radiological manifestations has been proved to statistically jeopardize the outcome.

FP083 SIOP19-0733 | 2-Chlorodeoxyadenosine in Childhood LCH: Long-Term Efficacy and Tolerance

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Background/Objectives: The nucleoside analogue 2-chlorodeoxyadenosine (2CDA) has been reported active in Langerhans cell histiocytoses (LCH), especially for patients without risk organ (RO-) involvement. However, recurrence rate, permanent sequelae and long term tolerance data after such regimen are lacking.

Design/Methods: Childhood RO- LCH cases (age<18 years at diagnosis) treated by 2CDA monotherapy during these last 25 years included in the French LCH registry were retrospectively reviewed.

Results: A total of 44 patients were reviewed, with a median follow-up after 2CDA therapy at 2.7 years. At the beginning

of 2CDA therapy, 13 patients had a single system (SS) LCH with bone involvement, 21 had a RO- multiple systems (MS) LCH and 10 had a Lung + LCH. The median number of 2CDA course per patient was 6. At the end of 2CDA therapy, 33 patients (75.0%) were responders and response rate wasn't significantly correlated with the extension of the disease, disease localization or the *BRAFV600E* status. Considering only 2CDA responders patients, the 5 years reactivation rate after 2CDA discontinuation was 20.3%. Finally, the cumulative 5-years refractory/reactivation risk was estimated at 40.2% for this cohort. A total of 17 patients (38.6%) showed permanent sequelae, mostly diabetes insipidus (DI), and for 4 of them, the sequelae occurred after the 2CDA therapy (DI, n=3; pseudo neurodegenerative LCH, n=1). Almost all patients had a prolonged (~ 1 year) significant immune deficiency secondary to 2CDA therapy managed with appropriate prophylactic measures and without severe complication with the exception of one patient who experienced a fatal acute graft versus host disease after lung transplantation. One case exhibited a prolonged medullary hypoplasia after 9 courses of 2CDA. The 5-years overall survival rate was at 97.4%.

Conclusions: In RO- LCH, 2CDA monotherapy appears a safe and beneficial therapeutic option with appropriate management of the induced prolonged immune deficiency.

FP084 SIOP19-0813 | Changes in Clinical Presentation and Treatment of Pediatric Differentiated Thyroid Cancer (DTC)

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Background/Objectives: Paediatric DTC is rare disease with excellent prognosis but is diagnosed at advanced stage and has high recurrence rate. Recently, in adults there was significant increase in DTC<1 cm and increase use of rhTSH (recombinant human thyrotropin) in preparation for radioiodine treatment in advanced/metastatic disease. There are no such data in paediatric DTC.

The aim of this retrospective study was to evaluate changes in clinical presentation and results of radioiodine treatment in metastatic paediatric DTC treated in one centre over 40 years.

Design/Methods: 501 children with DTC (at diagnosis ≤ 18) were included. Children were divided in two groups, group A (diagnosed 1970-1999) and group B (2000-2015) to assess age at diagnosis, sex, stage and treatment. Statistical analysis was performed with *Statistica pl*, p<0.05 deemed significant.

Results: There was no age or sex differences between groups. However, there was a marked decrease in follicular with

respect papillary thyroid cancer. The mean tumour diameters decreased from 2.5 cm (1970-1990) to 1.2 cm (2010-2015). Before 1999 there was no case of pT1a tumour which was diagnosed in 36% of children during last 5 years. The rate of lymph nodes metastases (about 60%) and distant metastases (about 15%) was stable during studied period. However, there was decrease in diameter of lymph node metastases.

Metastatic disease was treated with 131-I, lately usually with rhTSH preparation. During last radioiodine treatment complete scintigraphic response was achieved in 63% and biochemical 23% (p<0.05). Complete scintigraphic and biochemical response treatment results were comparable in children prepared for the treatment with rhTSH or thyroid hormone withdrawal. No death was observed.

Conclusions: In accordance with adults there is a marked decrease in follicular cancer and locally advanced primary tumours in paediatric DTC, however this is not accompanied by decrease in metastases. rhTSH preparation for radioiodine treatment is effective in metastatic disease.

FPS 16: Psychosocial: Parent and Family Function

FP085 SIOP19-0279 | Effect on Parental Distress of a Home-based Psychological Intervention for Families of Children with Cancer (FAMOS): A Nationwide Randomized Controlled Trial

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Background/Objectives: Introduction: No convincing evidence-based model has been developed to relieve psychological symptoms in families of children with cancer. We evaluated the effect of a new psychotherapeutic intervention FAMily-Oriented Support (FAMOS), targeting the whole family after end of childhood cancer treatment on symptoms of post-traumatic stress, depression and anxiety among parents in a nation-wide randomized controlled trial (RCT).

Design/Methods: Families of children (aged 0-6 years) with cancer who were treated at one of the four pediatric oncology departments in Denmark were invited after end of intensive medical treatment. Families were randomly assigned using a computer-generated randomization (1:1) to care as usual or

to FAMOS, a cognitive-behavioural manualized home-based intervention with up to six sessions over a six months period for the whole family. We assessed symptoms of post-traumatic stress, depression and anxiety in parents using the Harvard Trauma questionnaire and the Symptom Checklist-90 at baseline, 6, and 12 months follow-up and estimated intervention effects in mixed method models.

Results: Findings: The FAMOS trial enrolled 109 families (204 parents). The intervention significantly reduced symptoms of depression at 6 months follow-up (estimated difference, -0.18; 95% CI -0.32 to -0.04 Cohen's d, 0.22). Intervention reductions in symptoms of post-traumatic stress (estimated difference, -0.10; 95% CI -0.20 to 0.01 Cohen's d, 0.18) and anxiety (estimated difference, -0.16; 95% CI -0.33 to 0.01 Cohen's d, 0.23) did not reach statistical significance.

Conclusions: This is the first psychotherapeutic family intervention targeting families of children with cancer after end of treatment, which in a randomized controlled design has shown that symptoms of depressions in the parents may be attenuated. (clinicaltrials.gov: NCT02200731).

FP086 SIOP19-0972 | Patterns of Parents' Pre-Disclosure Psychological Responses to Pediatric Oncology Genomic Sequencing

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Background/Objectives: In the context of next generation sequencing (NGS) to identify possible underlying cancer predisposition in children, parents qualitatively report hope, peace of mind, and perceived benefit, but also express worry and guilt around possible inheritance. Understanding the emotional impact of germline NGS on parents is essential to identifying targets for psychosocial screening and developing interventions as needed. This study identified patterns of parents' sequencing-related psychological reactions prior to germline NGS result disclosure and examined how demographic/clinical variables predicted patterns.

Design/Methods: Participants included 196 parents (69% mothers) of patients with cancer (41% liquid tumor, 31% brain tumor, 28% solid tumor) enrolled in a prospective study of clinical tumor and germline sequencing. Parents completed a modified Psychosocial Aspects of Hereditary Cancer Questionnaire (PAHC) prior to result disclosure. Classes of sequencing-related psychological reactions (i.e., worries, guilt, peace of mind, hope) were derived using Latent Class Analysis (MPlus). Logistic regression examined whether demographic/clinical variables predicted class membership.

Results: Approximately half of parents (53%; $n=105$) exhibited PAHC scores above established clinical cutoffs. Four classes emerged (entropy=.84; LMR=42.78, $p=.021$): Minimal Psychological Response (54%; minimal worries with moderate optimism [i.e., hope/peace of mind]), Worry with Optimism (22%; some worries with high optimism), Elevated Worry (13%; high worries with moderate optimism), and Future Worries (12%; worry about effect of testing on child's insurance/other children developing cancer). Parents were more likely in the Elevated Worry class if they were closer to time of consent ($OR=1.01, p=.014$), and less likely in the Future Worries class if the patient was black ($OR<.01, p<.001$) or deceased during the study ($OR<.01, p<.001$).

Conclusions: The majority of parents (54%) displayed minimal sequencing-related worries prior to NGS result disclosure; however, a subset (25%) with elevated pre-disclosure worry may warrant additional psychosocial screening and support. Development of parent-specific psychosocial screening instruments are warranted to further identify risk factors for distress in parents awaiting results of predictive germline testing.

FP087 SIOP19-0317 | Parental Functioning During Maintenance Treatment for Childhood Acute Lymphoblastic Leukemia: Effects of Cyclic Dexamethasone and Risk Group

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Background/Objectives: Dexamethasone has adverse effects on child's sleep and behavior. During maintenance treatment, pediatric patients with medium risk (MR) acute lymphoblastic leukemia (ALL) receive intravenous chemotherapy (including vincristine) and cyclic dexamethasone, whereas standard risk (SR) patients only receive oral chemotherapy, without dexamethasone. The effects of these treatments on parents are not well known. This study aims to compare parental sleep, distress and quality of life (QoL) between the MR and SR-groups and general population, and on and off dexamethasone within the MR-group.

Design/Methods: The Dutch longitudinal ALL11 add-on SLAAP [*SLEEP*]-study included patients (2-18 years) and their parents. One year after diagnosis, parents of patients in MR-maintenance treatment completed the MOS Sleep Scale, Distress Thermometer for Parents and SF-12 *twice*; once in a week with dexamethasone and once in a week without. Parents of SR-patients completed one measurement. Sleep problems, distress and QoL scores (off-dexamethasone) were compared to norm values and between the MR and SR-group. Additionally, score differences on and off-dexamethasone (MR-group) were assessed by multilevel regression analyses.

Results: Parents (80% mothers) of 122 patients (57% males; 75% MR, 25% SR) completed 191 measurements. Compared to population norms, all parents reported significant impairment in sleep and mental QoL. Parents of MR-patients also reported clinical distress (thermometer score ≥ 4), whereas parents of SR-patients did not (mean score 4.8 (2.4) vs 3.5 (2.4), $p=0.02$). In the MR-group, sleep problems, distress and QoL did not significantly differ on and off-dexamethasone.

Conclusions: During maintenance treatment, parents across both risk groups reported sleep and QoL impairment. In the MR-group, parental functioning did not differ on and off-dexamethasone treatment. However, the MR-group reported clinical distress while the SR-group did not, possibly reflecting a higher treatment burden including the overall strain of cyclic dexamethasone. This study highlights the need for ongoing psychosocial support across the entire treatment phase.

FP088 SIOP19-0141 | The Impact of Childhood Cancer on Parental Working Status and Income: Findings from a Nationwide Cohort Study in Denmark

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Background/Objectives: The intensive experience of having a child with cancer may have a substantial impact on parents' professional life. We aimed to assess the impact of childhood cancer on parental working status and income: i) over a follow-up period until 10 years after diagnosis, and ii) by period of diagnosis.

Design/Methods: We conducted a nationwide population-based cohort study based on Danish registry data. The study cohort consisted of all parents of children diagnosed with cancer before the age of 20 years in the period 1982-2014

($n=12,418$ case parents) matched (1:10) with parents of cancer-free children ($n=125,014$ comparison parents). We compared working status and income levels between case and comparison parents over a period of 10 years after diagnosis using logistic regression models to estimate odds ratios (ORs) and 95% confidence intervals (CIs). Interaction tests were used to evaluate differences by diagnostic period (1982-1999 vs. 2000-2014).

Results: Case mothers were more likely not working up to 9 years following diagnosis, whereas case fathers were more likely not working only in the second year following diagnosis (OR_{fathers}=1.19, 95%CI: 1.01-1.39). Among mothers of children diagnosed in the most recent period, the risk of not working was less pronounced during the first 4 years after diagnosis compared to mothers of cases diagnosed in the earlier period (pinteraction<0.05). Compared to comparison mothers, case mothers' income was more likely in the lowest quintile during the first 4 years after diagnosis, with the highest risk in the second year (OR=2.31, 95%CI: 2.10-2.55). No effect was observed for paternal income.

Conclusions: Our results suggest that the adverse effects of childhood cancer on parents' professional life are more pronounced in mothers compared to fathers and less pronounced in recent years. Continued efforts in providing comprehensive family support may further reduce the impact of having a child with cancer.

FP089 SIOP19-0402 | Health-Related Quality of Life in Parents of Long-Term Childhood Cancer Survivors: Swiss Childhood Cancer Survivor Study - Parents

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Background/Objectives: Childhood cancer places not only the children but also their parents at increased risk of impaired health-related quality of life (HRQOL). These impairments might persist long after the child's treatment has ended. We aimed to i) investigate HRQOL in parents of long-term childhood cancer survivors (CCS) compared to the general population, and ii) describe risk factors for impaired HRQOL in parents of CCS.

Design/Methods: We sent a questionnaire to parents of CCS (aged ≤ 16 years at diagnosis, survived ≥ 5 years, aged ≥ 20 years and alive at study) registered in the Swiss Childhood

Cancer Registry. We measured HRQOL using the Short Form-36 version 2 (SF-36v2), computing summary scores for physical and mental health. We used a weighted sample of parents of the general population ($n=454$, mean age=62 years, 58% women) as comparisons.

Results: In total, 751 parents (59% mothers, mean age=62 years) of 439 CCS responded to the SF-36v2. Among CCS-parents, 12% had a migration background and 10% were not living in a partnership. About a quarter (24%) of CCS-parents reported that their child suffers from late effects. CCS-parents reported better physical (47.9 vs. 46.3, $p=0.008$) and similar mental health (52.5 vs. 52.6, $p=0.855$) than comparison-parents. Among CCS-parents, fathers ($p=0.015$) and those with migration background ($p<0.001$) reported worse mental health. CCS-parents not living in a partnership reported worse physical health ($p=0.009$). CCS-parents whose child suffered from late effects reported worse physical ($p=0.018$) and mental health ($p=0.031$).

Conclusions: Despite the highly stressful event of cancer in their child, overall, CCS-parents fare well in the long term. Having been confronted with the life-threatening illness might have fostered increased appreciation of their own health. Fathers and parents with migration background or not living in a partnership are at higher risk for impaired HRQOL.

FP090 SIOP19-0654 | Impact of Family Functioning and Parent-Child Relationship Factors on Substance Use in Adolescent and Young Adult Cancer Survivors

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Background/Objectives: Adolescent and young adult childhood cancer survivors (AYA) are at risk for poor health outcomes that can be exacerbated by substance use. The primary objective of this research was to evaluate links between substance use and indicators of parent-child/family functioning to inform clinical intervention targets.

Design/Methods: Participants included 146 AYA (Mage=16.4, SD=2.38, range 12-21; 49% female), who were on average 8.5 (range 4.68-18.59) years post-diagnosis, predominately white (73%), and represented various cancer diagnoses (Leukemia=34%, Lymphoma=12%, Solid Tumor=37%, and Brain Tumor=17%). AYA and their caregivers (Mothers=86%) completed measures of family functioning (Family Environment Scale) and parent-child relationship quality (Parenting Relationship Questionnaire) at time 1. Two years later (time 2), AYA reported on cigarette, excessive drinking, lifetime marijuana, and lifetime drug use (not including marijuana). Demographic/medical information were obtained via medical chart review. Bivariate correlations

and chi-square analyses were used to examine links between demographic/medical factors and substance use. Partial correlations examined links between family functioning and the parent-child relationship quality with substance use while controlling for significant medical/demographic factors.

Results: Endorsement of excessive drinking (7.6%), lifetime marijuana use (17.9%), lifetime drug use (7.6%), and cigarette use (4.2%) were modest. Age was the only predictor of substance use, and subsequently controlled for in the partial correlations. Excessive drinking was not linked to any family or parent-child relationship variables. Time 2 AYA-reported drug and marijuana use were predicted by time 1 parent-reported relationship quality, but not family functioning indicators. Time 2 cigarette smoking was predicted by time 1 AYA- and caregiver-reported family functioning and caregiver-reported relationship quality.

Conclusions: This research documents the importance of understanding the role of family functioning and the quality of the parent-child relationship on future AYA substance use. These factors may be clinically relevant targets to improve substance use behaviors and ultimately assist in improving future health outcomes among AYA survivors.

FPS 17: Neuroblastoma 2

FP091 SIOP19-0587 | A Revised Children's Oncology Group (COG) Neuroblastoma Risk Classification System: A Report from the COG Biology Study ANBL00B1

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Background/Objectives: The COG risk classification system previously used the International Neuroblastoma Staging System (INSS). The pre-treatment INRG staging system (INRGSS) has been adopted internationally, requiring integration of INRGSS with known prognostic biological and clinical characteristics to evaluate outcomes and assess whether this incorporation will require revision to the established COG risk classifier.

Design/Methods: 4,037 newly diagnosed neuroblastoma patients were enrolled on COG ANBL00B1 between 2006-2014. Staging per the INSS and INRGSS was determined. Tumor biological and histologic features, including *MYCN*

status [amplified (A) versus not amplified (NA)], ploidy, histology, and segmental chromosome aberrations (SCA) including 1p and 11q LOH, were assessed centrally. 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 COG and INRG classification templates.

Results: Using the original COG risk classifier 1,309 low (LR), 992 intermediate (IR) and 1,736 high-risk (HR) patients were identified with 5-year EFS of 91.4±2.1%, 84.3±2.9%, 45.2±3.1%, and OS of 98.1±1.0%, 94.0±1.9%, 54.1±3.0%, respectively. Outcomes based on different combinations of clinical and biological prognostic factors were determined and compared for subsets of patients according to the COG (version 1) and INRG risk classification systems to develop a revised COG risk classifier that incorporates the INRGSS (version 2).

Conclusions: Use of INRGSS requires a revision to the COG risk classifier. By combining INRGSS and presence of SCA together with age, *MYCN* status, ploidy, and histology to determine outcome of patients treated with modern era therapies, we have been able to develop a revised risk classification to inform therapy and future COG clinical trial eligibility. Efforts underway to identify additional prognostic biomarkers (eg telomerase pathway alterations) may enable further refinement of risk groups to improve prognostic abilities and tailor therapies.

FP092 SIOP19-0782 | Genetic Alterations of ALK in High-Risk Neuroblastoma Patients. A SIOPEN Study

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Background/Objectives: In neuroblastoma (NB), the ALK receptor tyrosine kinase can be constitutively activated through genomic amplification or activating point mutations. We studied *ALK* genetic alterations in high-risk NB patients to determine their frequency and prognostic impact.

Design/Methods: Diagnostic NB samples from 1039 patients enrolled in the SIOPEN-HR-NBL1 trial were studied to determine the *ALK* amplification status (n=337), the *ALK* mutational profile (n=203) or both (n=499).

The sensitivity of *ALK* mutated/*ALK* amplified or *ALK* wild-type NB cell lines ((CLB-GA (R1275Q), CLB-GE (F1174V; ALK-A), SKNBE-2C (ALK wt)) to simultaneous or consecutive combinations of ALK tyrosine kinase inhibitors (TKIs) (crizotinib/lorlatinib) and/or chemotherapy (Etoposide and Doxorubicin) was then tested.

Results: Genomic *ALK* amplifications were detected in 4.4% of cases (37/836); all but 2 showed *MYCN* amplification. *ALK* mutations were detected at a clonal level (>20% mutated allele fraction, MAF) in 9.8% of cases (69/702) and at a sub-clonal level (MAF 0.5-20%) in 3.7% of patients (22/586). A significantly poorer OS and EFS was observed in cases with clonal *ALK* mutations, versus all others (3-years OS 47% +/- 6.4% versus 65% +/- 2%, logrank, p< 0.0001) and in those with *ALK* amplifications, versus all others (3-years OS 31% +/- 8.5% versus 66% +/- 1.9%; logrank, p<0.0001). A Cox proportional hazards procedure (n=450) retained stage 4 disease (as opposed to non-stage 4) and *ALK* amplification as factors with a higher hazard of relapse/progression (hazard 2.3 and 2.2, respectively), whereas *ALK* mutation, *MYCN* amplification and age>18 months were not retained. The consecutive treatment of Doxorubicin followed by Lorlatinib had a synergistic effect in *ALK* mutated/amplified NB cell lines

Conclusions: Genetic alterations of *ALK* (clonal mutations, amplifications) in high-risk NB patients are associated with poorer survival. Further preclinical data are required to determine optimal treatment modalities for integration of TKI in upfront treatment strategies of HR NB patients with *ALK* alterations.

FP093 SIOP19-1439 | Prognostic Significance of ATRX Aberrations in Neuroblastoma

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Background/Objectives: Loss-of-function somatic *ATRX* mutations or deletions in neuroblastoma (NB) were associ-

ated with older age at diagnosis (Cheung et al, JAMA, 2012). We have now expanded the cohort and extended their clinical follow up to determine its prognostic implications.

Design/Methods: With IRB approval, information on patients with somatic *ATRX* aberrations was retrospectively analyzed. *ATRX* sequencing was performed either by whole genome sequencing (~35x depth) or targeted exome sequencing (>500x depth using MSK-IMPACT or Foundation One platforms). Progression-free (PFS) and overall-survival (OS) were estimated using Kaplan-Meier analyses.

Results: Sixty-five patients (35 male; 30 female), diagnosed at 2-67 (median 8) years of age were identified. Forty tumors were analyzed before relapse and 25 after. Twelve (18%) and 53 (82%) patients had locoregional and stage M neuroblastoma at diagnosis, respectively. Most (62/63) evaluable tumors had unfavorable histology. *ATRX* was deleted in 38 (58%) tumors and mutated in 27 (42%). Of the mutations, 12 were missense or of unknown significance and 15 were nonsense or frameshift mutations. Coexisting *ALK* mutations were noted in 15 (23%) tumors; *MYCN*-amplification was not detected in any. High-dose chemotherapy was administered to 55 patients but only 16 (29%) achieved complete remission. At a median follow-up of 55 months, 5-year PFS and OS was 14% and 45%, respectively. Younger age at diagnosis was not prognostic ($p>0.1$ for PFS or OS for patients <5 years versus older). Patients with locoregional disease at diagnosis had an equally poor survival compared to those with stage M ($p>0.1$ for both PFS and OS). Patients with *ATRX* deletions and frameshift/nonsense mutations had significantly worse PFS compared to missense mutations or mutations of unknown significance ($p=0.03$, 5-year PFS 11% vs 27%).

Conclusions: *ATRX* aberrations were associated with chemorefractory neuroblastoma and poor survival outcomes regardless of stage and age at diagnosis.

FP094 SIOP19-1750 | Molecular and Phenotypic Evaluation of the Mesenchymal-Type Cell Population from Early-Phase Patient-Derived Cultures of Neuroblastoma for Personalized Drug Response Testing

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Background/Objectives: Ex-vivo evaluation of personalized models can facilitate individualized treatment selection for patients, and advance discovery of novel therapeutic options. We developed a system to consistently generate early-phase patient-derived cell cultures (PDCs) of neuroblastoma, evaluated its efficiency and utility, and compared the ability of PDCs and parallel xenografts (PDXs) to recapitulate original patient tumors, and predict potential treatment response.

Design/Methods: Fresh tumor explants from pre-treatment, post-treatment and relapse patients were cultured in 5 media conditions sequentially. In-vitro growth dynamics, morphology, immunoreactivity, gene expression and functional chemoresponse of PDCs were characterized, and compared with patient tumors and corresponding PDXs which were developed in parallel in NSG mice. Expression scores of 13 cancer-associated canonical pathways, and mesenchymal and adrenergic neuroblastoma gene signatures were evaluated using NanoString®, and compared with angiogenesis-related proteins in paired samples of culture media and patient serum. Cytotoxicity to human Cmax-equivalent concentrations of clinical drugs were tested in-vitro.

Results: Overall engraftment rate was 61.8%, with 30 PDC and 7 PDX lines generated from 34 specimens. Engraftment and establishment of log-phase growth was significantly higher with metastatic tumors ($P=0.05$). The optimal media condition could expand up to median 6.8×10^8 (8) cells over 9 passages, before the earliest clinical relapse events at day 209. PDCs displayed characteristic staining patterns of PHOX2B, TH and GD2 synthase. Concordance of *MYCN*, 1p and 11q status in PDCs versus patient tumors was 83.3%, 72.7% and 80.0% respectively. PDCs expressed predominantly mesenchymal neuroblastoma gene signature and showed upregulation of IL-6, which corroborated with protein expression in culture media and patient serum. *MYCN* vs non-*MYCN* amplified PDCs showed differential response to cyclophosphamide and topotecan in-vitro.

Conclusions: Early-phase patient-derived cultures representing the mesenchymal subpopulation of neuroblastoma reflect the molecular and phenotypic profile of patient tumors, and can be a potential platform for individualized real-time ex-vivo characterization and drug response testing.

FP095 SIOP19-0727 | Administration of Subcutaneous IL-2 is Associated with Strong Induction of Regulatory T Cells in High-Risk Neuroblastoma Patients Treated with Dinutuximab Beta, A SIOPEN Study

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Background/Objectives: We reported that co-treatment with subcutaneous IL-2 (scIL-2) did not have a beneficial effect in neuroblastoma patients treated with dinutuximab beta (DB). Here, we investigated treatment effects on regulatory T cells (T_{regs}).

Design/Methods: 160 patients from 11 countries enrolled into an open label SIOPEN Phase II clinical trial (EudraCT 2009-018077-31) were randomly assigned to receive up to 5 cycles of 100 mg/m² DB-LTI (d8-17) and 160 mg/m² oral isotretinoin (d19-32) (81 patients) with and without 6x10⁶IU/m² scIL-2 (d1-5; 8-12) (79 patients). T_{regs} (CD4⁺/CD25⁺/CD127⁻) were assessed by flow cytometry in every treatment cycle on d1 (prior to start of treatment) d8 (5 days of scIL-2 treatment, prior to start of DB LTI), d15 (3 days after end of scIL-2 treatment, 8 days of DB-LTI) and d18 (last day of DB-LTI).

Results: Prior to the treatment start, Treg levels were 47±20 cells/μl. Five days of scIL-2 treatment resulted in a 6-fold increase of Tregs (305±51 cells/μl) on d8. Following the combined treatment a slight reduction of Tregs counts on d15 and d18 compared to d8 was observed (219±33 and 154±48 cells/μl, respectively). Moreover, we found an increase of the peak levels in subsequent cycles compared to the first cycle except for cycle 4 (385±48, 493±126, 342±51 and 517±68 cells/μl for cycle 2, 3, 4 and 5, respectively), indicating Tregs accumulation during the whole treatment period with DB and scIL-2.

In contrast, patients receiving DB without scIL-2, showed similar Tregs levels on d8 compared to the baseline (85±52, 84±45, 112±70 and 93±47 cells/μl for cycle 2, 3, 4 and 5, respectively), and Tregs remained low during DB-LTI on d15 and d18, confirming that Tregs induction was mediated by scIL-2.

Conclusions: IL-2-dependent induction of Tregs may partially explain the lack of beneficial effects of IL-2 co-treatment in immunotherapy with DB.

FP096 SIOP19-1645 | A Curative Approach to Central Nervous System Metastases of Neuroblastoma

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Background/Objectives: Neuroblastoma metastatic to the central nervous system (CNS NB) is associated with significant mortality (median survival <6 months, <10% survival at 36 months). Intraventricular compartmental radioimmunotherapy (cRIT) with the radio-iodinated murine IgG1 monoclonal antibody ¹³¹I-Omburtamab targeting tumor cell-surface glycoprotein B7-H3 offers a therapeutic strategy. We analyzed the overall survival of patients with CNS NB treated with ¹³¹I Omburtamab -cRIT at Memorial Sloan Kettering Cancer Center (MSK) starting in 2004 through April 2, 2019.

Design/Methods: After radiographic and/or pathologic confirmation of CNS NB, cRIT eligible patients underwent temozolomide/irinotecan-based chemotherapy, craniospinal radiation therapy, ¹³¹I- Omburtamab cRIT plus systemic immunotherapy. cRIT administration involved a 2mCi tracer of intra-Ommaya ¹²⁴I- or ¹³¹I-8H9 with nuclear imaging and CSF sampling for dosimetry followed by 1 or 2 therapeutic injections of 10-70 mCi ¹³¹I- Omburtamab. Disease evaluation included serial MR brain/spine, MIBG, CT, and bone marrow evaluation. Patients were treated on IRB-approved protocol. Data are presented as overall survival after detection of CNS metastasis.

Results: 108 patients with CNS NB were treated; median follow-up 6.3 years. cRIT injections were well tolerated in the outpatient setting with myelosuppression being the most common adverse event. At analysis, the median OS is 3.7 years [95% CI: 1.9 to 7.5]. The 2-year OS rate is 57% [95% CI: 47 to 67%]. The 5-year OS rate is 41% [95% CI: 31 to 52%]. The 10-year OS rate is 37% [95% CI: 26 to 48%]. Subgroup analyses identified age at NB diagnosis (≤18 months), and relapse restricted to CNS as being favorable markers of long-term survival.

Conclusions: Despite advanced CNS involvement, 2 year OS is 57%, > 40% of patients treated with ¹³¹I- Omburtamab remain disease free. This compares favorably to median survival of 5.5 months reported in the literature. Long term cure of CNS NB is feasible.

FPS 18: Brain Tumours 2

FP097 SIOP19-0076 | Long-Term Follow-Up of AIEOP 2nd Series of Children and Adolescent with Primary Intracranial Ependymoma

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Background/Objectives: This Italian prospective study, between 2002-2014, stratified patients by surgical resection (complete=NED vs incomplete=ED) and centrally-reviewed histology. Grade2/NED patients received focal radiotherapy (RT) up to 59.4 Gy with 1.8 Gy/day, grade3/NED received 4 courses of VEC (vincristine, etoposide, cyclophosphamide) after RT. ED patients received 1-4 VEC courses, second-look surgery, and 59.4 Gy followed by an 8 Gy boost into 2 fractions on still measurable residue. NED children aged 1-3 years with grade 2 tumors could receive 6 VEC courses alone after surgery.

Design/Methods: Due to the well-known possibility of late relapse in childhood ependymoma we re-analyzed data at 109 months median follow-up also including 450k methylation profile on posterior fossa (PF) available samples.

Results: At the time of this report PFS/OS at 5/10 years were 66/58% and 80/74%, respectively. Of the 63 relapsers at median 20 mos, 53 had died at median 46 mos: 9 relapsed after 5 years (66-113 mos) and 3 died. Of these 9, relapse was local in 7, metastatic in 1, combined in 1, 5 patients were below age 3 and female, 7 had PF tumor. Their survival after relapse was not different from that of precocious relapsers.

At univariable analysis, age over 3 years, supratentorial origin, complete surgery, grade 2, absence of shunt were favorable factors for PFS and OS.

58 PF samples were analyzed for methylome:13 were classified as group B (45 as group A). Only 1 patient locally relapsed in group B at 96 months after radiation; other risk factors were equally distributed among group A/B patients.

Conclusions: Same prognostic factors remained at almost 10 years follow-up;5.6% of patients had late relapses;14.2% relapsed patients were late relapsers. Their OS after relapse was not better than early relapsers'. Group B patients confirmed better prognosis at long-follow-up but all patients had received «at least» adjuvant radiation. Modern trial outcomes need a long-time to be evaluated as successful.

FP098 SIOP19-1479 | Chemotherapy Strategies for Young Children Newly-Diagnosed with Medulloblastoma up to the Era of Molecular Profiling – A Comparative Outcomes Analysis

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Background/Objectives: Survival had been poor in several multi-center/national studies since the 1980s, attempting to delay, avoid or minimize brain irradiation in young children with medulloblastoma. The introduction of regimens in Germany, incorporating both intravenous high-dose (HD-MTX) and intraventricular (IVENT-MTX) methotrexate, as well as regimens in North America incorporating marrow-ablative chemotherapy with autologous hematopoietic cell rescue (HDCx+AuHCR), have reported encouraging outcomes. The objective of this report is to perform a comparative outcomes analysis of these differing strategies.

Design/Methods: Data from 17 prospective multi-center trials published between 1990 and 2018 for children under six years old with medulloblastoma were reviewed; event-free (EFS) and overall survivals (OS) were compared.

Results: The two trials using full dose craniospinal irradiation with or without chemotherapy reported 5-year survivals of 32-38%. Three trials using standard chemotherapy with delayed irradiation reported 2-4-year EFS and OS of 23-34% and 31-46%. Two trials employing standard chemotherapy with irradiation avoidance for all patients reported 3-5-year EFS and OS of 22-33% and 34-43%. Four trials incorporating HD-MTX with or without IVENT-MTX reported 5-10-year EFS and OS of 56-59% and 67-80%, and 31% and 59% respectively; one trial with HD-MTX without IVENT-MTX for desmoplastic/nodular medulloblastoma (DN-MB) reported 2 year EFS and OS of 52% and 92%. Finally, five trials employing induction chemotherapy, with or without HD-MTX, followed by single or tandem HDCx+AuHCR have reported 3-5-year EFS and OS of 45-60% and 60-70%.

Conclusions: The best survivals are observed in trials including HD-MTX and IVENT-MTX or including HD-MTX during induction followed by HDCx+AuHCR. Because histology/biology (classic and large-cell/anaplastic *versus* DN-MB; SHH *versus* non-SHH subtypes) have crucial prognostic roles, event-free and irradiation-free survival advantages require analysis in these settings. The benefit of these trials appears true for all young children with medulloblastoma. Risk-adapted treatment stratification may be improved by molecular profiling of SHH- and non-SHH medulloblastoma.

FP099 SIOP19-0653 | A Metronomic Antiangiogenic Combination Therapy Prolongs Survival for Patients with Recurrent Medulloblastoma: Experience in 20 Consecutive Patients

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Background/Objectives: Prognosis of patients with recurrent medulloblastoma is dismal with 3-year survival rates ranging between 18% and 22% despite intensive therapy including high-dose chemotherapy with stem cell rescue. An evolving alternative approach to conventional chemotherapy is to target neovascularisation by interfering with tumor angiogenesis at various levels. We report on 20 consecutive patients with recurrent medulloblastoma treated with an antiangiogenic combination therapy.

Design/Methods: From 11/2006 to 02/2018, 20 patients with recurrent medulloblastoma (14 first, 6 multiple

recurrences) started an antiangiogenic metronomic multi-targeted combination therapy for their recurrence. Therapy included IV bevacizumab, oral thalidomide, celecoxib, fenofibrate, and etoposide alternating every three weeks with cyclophosphamide, and augmented with intraventricular therapy (etoposide and liposomal cytarabine). Median age at start of antiangiogenic therapy was 10 (1-24) years.

Results: As of 03/2019, 9/20 patients with medulloblastoma are alive, seven in CR 125, 123, 123, 96, 57, 52, and 47 months after first initiating antiangiogenic therapy. All seven patients in CR are off therapy for a median of 45 months (7-107 months). Two patients are alive with progressive disease for 95 and 41 months after start of recurrence therapy. 5-year-OS is $49.5 \pm 11.3\%$ and 5-year-EFS is $25.0 \pm 9.7\%$. One patient died of an accident in CR 23 months after initiation of antiangiogenic therapy. Therapy was generally well tolerated and toxicities were manageable.

Conclusions: The proposed antiangiogenic regimen appears to be a promising strategy to prolong survival and potentially cure patients with recurrent medulloblastoma. The approach is currently being evaluated in an international phase II protocol (MEMMAT; ClinicalTrials.gov Identifier: NCT01356290).

FP100 SIOP19-0725 | Treatment of Relapsing Patients with Intra Cranial Germ Cell Tumors: The French Experience

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Background/Objectives: Optimal strategy for treatment of relapsing intracranial malignant germ cell tumors remains ill-defined. Authors describe the French experience over a 25-year period.

Design/Methods: Relapsing patients were retrieved by their participation in the SFOP-TGM 90-92 SFOP or GCT 96 protocols and from National Childhood Solid Tumour Registry (RNTSE).

Results: The cohort included Group A: documented germinomas (n=14), Group B: patients treated as germinomas without histopathological proof (n=5) and Group C: secreting germ cell tumours (n=25).

Patients all received standard dose chemotherapy, and some high dose chemotherapy (VP16 Thiotepa with stem cell rescue) and/or various type of radiation.

The 5 year EFS and OS post relapse are: 79% [47 to 93%] and 86% [54 to 96%] respectively in group A, 20% [1 to 58%] and

80% [20 to 97%] respectively in group B, 56% [35 to 73%] and 60% [38 to 76%] respectively in group C.

Among 14 Group A patients, 7/12 receiving high dose versus 3/3 receiving standard dose chemotherapy, and 9/11 re-irradiated versus 1/3 not re-irradiated are CR2.

Among 21 Group C patients, who had received radiation in first line, 10/15 receiving high dose versus 1/6 receiving standard dose chemotherapy, and 7/11 re-irradiated versus 4/10 not re-irradiated are CR2.

Conclusions: The outcome of relapsing germinoma is favourable and intensity of second line remains matter of debate. High dose chemotherapy with radiotherapy, when its feasible, should remain the reference for treatment of a relapsed non germinoma, though more active treatments are warranted.

FP101 SIOP19-1364 | Pharmacokinetics of Oral Vinorelbine in French Children with Recurrent or Progressive Primary Low-Grade Glioma: Results of the Multicentric Ovima Phase II Study

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Background/Objectives: Over the last three decades, the role of chemotherapy in the management of pediatric Low-Grade Glioma (LGG) has dramatically increased. Vinorelbine, a semisynthetic vinca-alkaloid, showed encouraging results in children with progressive LGG. There is a crucial need for pharmacokinetic (PK) data of oral vinorelbine in this population. The aim of this work was to assess the PK profile of orally administered vinorelbine in French children with recurrent or progressive primary LGG.

Design/Methods: A multicentric, open-label, single-arm intervention phase II study was conducted. Patients, aged between 6 and 18 years, with histologically confirmed recurrent or progressive primary LGG or typical optic pathway glioma, were included. Children received oral vinorelbine (60 mg/m² on Days (D) 1, 8 and 15 of Cycle (C) 1 and 80 mg/m² on D1, 8 and 15 of C2 to C12). Blood samples were collected at D1 of C1 and C2 and plasma concentrations were analyzed by a validated LC-MS/MS method. PK parameters were estimated by non-compartmental analysis using Phoenix WinNonlin® software (version 8.0, Certara, Inc.)

Results: PK analysis included 29 patients. Median age (range) was 12 (7-17) years, with male/female ratio of 1.07. Estimates of clearance (CL/F), volume of distribution (Vz/F), half-life (t_{1/2}) and their interindividual variability (CV%) at the 60 mg/m² dose level, were 536 L/h (60.8%), 8.22 L (62.3%) and 10.6 h (22.2%), respectively. A similar PK profile, without accumulation of vinorelbine in the body, was observed between the first and the second cycle. Clearance was found to increase with age (p = 0.005). Sex had no statistically significant effect on vinorelbine clearance (p = 0.43).

Conclusions: A high inter-individual variability of vinorelbine PK parameters was observed in French children with LGG. Further investigation will be performed to explore PK variability based on demographic, physio-pathological markers and genetic factors using population approach.

FP102 SIOP19-0116 | Preterm Birth in Offspring of Long-Term Survivors of Childhood Central Nervous System Tumors: A National Cohort Study

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Background/Objectives: Central nervous system (CNS) tumors represent the most common solid malignancy in childhood. With the improvement of treatment, more than 70% of children with CNS tumor is surviving beyond 5 years. However, it is largely unknown whether treatments of CNS tumor will affect the subsequent pregnancy outcomes, such as preterm birth, among long-term CNS tumor survivors.

Design/Methods: Patients who were diagnosed with CNS tumors under 15 years of age between 1958 and 2015 were identified from the Swedish Cancer Register. Unconditional logistic regression was used to estimate the association between long-term CNS tumor survivors and risk of preterm birth by using children whose parents without CNS tumor as the reference. Conditional logistic regression was used to examine the risk of preterm birth among children of CNS tumor survivors who had more than one child after their diagnosis, and using the first child as the reference.

Results: A total of 518 mothers and 368 fathers were diagnosed with childhood CNS tumors. As compared to the children whose parents without CNS tumor, the risk of preterm birth was significantly higher among children of female CNS tumor survivors (adjusted OR=1.57, 95% CI =1.14-2.17). A higher risk of preterm birth was also found among children of male CNS tumor survivors with an adjusted OR of 1.72 (95 CI% = 1.19-2.48). The risk of preterm birth was lower among the children born subsequently as compared to the first childbirth of both female and male survivors (adjusted OR for female = 0.30, 95% CI =0.07-1.30; adjusted OR for male = 0.70, 95% CI =0.22-2.25), but the association was not significant.

Conclusions: Our study provides evidence for a higher risk of preterm birth among offspring whose parents diagnosed with CNS tumors in childhood.

FPS 19: Epidemiology: Risk Factors

FP103 SIOP19-0361 | Maternal Illnesses During Pregnancy and the Risk of Childhood Cancer: Findings from the UK Childhood Cancer Study (UKCCS)

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Background/Objectives: Although maternal illnesses have long been suspected risk factors for childhood cancer, it remains uncertain whether infections and other conditions in pregnancy increase the risk of childhood malignancies. Using highly-reliable information directly extracted from maternal medical records, this study aims to provide new insights in the aetiology of childhood cancers.

Design/Methods: The UKCCS is a national case-control study including 3,812 children with cancer (cases) and 7,586 controls. Maternal medical information was obtained from general practitioner (GP) and obstetric records. Maternal clinically-diagnosed illnesses were coded using standardized procedures to the International Classification of Diseases (ICD-10). Haemoglobin levels were also abstracted from obstetric records. The data from obstetric and GP records were pooled and available for 2,886 (75.7%) cases and 5,502 (72.5%) controls. Associations between maternal illnesses during pregnancy and several types of childhood cancer were assessed using unconditional logistic regression models adjusted for sex, age, year of birth, having a primary care record abstracted, and having an obstetric record abstracted.

Results: Whether using haemoglobin level (<10g/dL) or medical diagnosis, maternal anaemia was associated with childhood acute myeloid leukaemia (OR=2.36 95%CI [1.59-3.52]). Children born to anaemic mothers were also more

prone than others to develop several types of embryonal tumours. Increased risk for non-Hodgkin lymphoma was observed in those with records of maternal infections during pregnancy (OR=1.51 [1.07-2.13]), in particular urinary tract infections (2.36 [1.46-3.81]). Analyses also suggested positive associations between pre-eclampsia, polyhydramnios, severe hyperemesis, diabetes mellitus, and some types of childhood cancer, but due to low frequencies and borderline associations, these associations require cautious interpretation.

Conclusions: These findings support an association between some maternal illnesses in pregnancy and the risk of cancer in the offspring. Further studies using unbiased data sources will help unravel these relations.

FP104 SIOP19-0514 | Children with non-Chromosomal Structural Birth Defects Demonstrate Differences in Cancer Profile and Age at Diagnosis

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Background/Objectives: Non-chromosomal structural birth defects (BDs) are an established risk factor for childhood cancer. Nonetheless, the descriptive epidemiology of cancer in children with non-chromosomal BDs is not well characterized.

Design/Methods: We linked data from birth certificates, birth defects registries, and cancer registries for >10 million live births in Texas, Michigan, North Carolina, and Arkansas (the Genetic Overlap Between Anomalies and Cancer in Kids [GOBACK] Study) to investigate cancer risk in children with BDs. Present objectives were to determine whether there were differences in the distributions of cancers diagnosed and age at diagnosis by BD status. We performed a case-only analysis comparing children with cancer and no BD (N=12,986) to children with cancer and one or more BDs (N=1,616).

Results: A larger proportion of children with BDs were diagnosed with embryonal tumors (26.6% vs. 18.7% in those with no BD, p<0.001). Specifically, neuroblastoma (12.5% vs. 8.2%, p<0.001) and hepatoblastoma (5.0% vs. 1.3%, p<0.001) each accounted for a larger proportion of diagnoses in children with a BD. Conversely, a smaller proportion of children with BDs were diagnosed with leukemia (20.3% vs.

30.7%, $p < 0.001$), acute lymphoblastic leukemia (12.4% vs. 24.5%, $p < 0.001$) and Hodgkin lymphoma (1.1% compared to 2.5%, $p < 0.01$). Median age at first cancer diagnosis was significantly younger in children with BDs for most cancers including: leukemia, lymphoma, astrocytoma, medulloblastoma, ependymoma, neuroblastoma, retinoblastoma, hepatoblastoma, nephroblastoma, sarcomas, and germ cell tumors (all $p < 0.05$). Differences in the proportion of at least one major childhood cancer subtype were evident in every age group (<1 year, 1-4 years, 5-9 years, and 10-18 years).

Conclusions: These population-based data suggest that children with non-chromosomal structural birth defects exhibit a distinct cancer risk profile with proportionally more embryonal and germ cell tumors but proportionally fewer hematologic malignancies. Children with birth defects are also diagnosed younger than unaffected peers for the majority of childhood cancers.

FP105 SIOP19-0400 | Preterm Birth and Risk of Childhood Cancer

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Background/Objectives: Preterm birth itself, or treatments associated with it, such as nitric oxide, may give rise to an increased risk of cancer during childhood and early adulthood, particularly that of hepatoblastoma. The impact of prematurity on the risk of other childhood malignancies needs to be clarified.

Design/Methods: In our population-based registry study we combined data from the Finnish Medical Birth Registry (MBR) and Finnish Cancer Registry (FCR). A total of 2,192 patients diagnosed with cancer under the age of 20 years and 10,960 age- and sex-matched controls were identified from the FCR and MBR. Information on gestational age, birth weight, diagnoses and treatments during the first 7 days of life was obtained from the MBR. Gestational age was categorized into three groups: early (<32 weeks) and late preterm (32-36 weeks) and term birth (≥ 37 weeks). A total of 141 (20.7%) cancers were identified in the exposed vs. 1,888 (16.1%) cancers in the unexposed group. Conditional logistic regression modelling was used to evaluate the cancer risk of preterm children compared to children born at term.

Results: Risk for any cancer by the age of 20 years was significantly higher for children born preterm compared to children born at term (crude OR 1.33, 95% CI 1.15-1.75, adjusted OR 1.50, 95% CI 1.25-1.80). The risk was especially high for early

preterm children born before 32 gestation weeks (crude OR 1.78, 95% CI 1.15-2.75) remaining elevated after adjusting for maternal age, smoking, parity and birth weight (adjusted OR 2.13, 95% CI 1.32-3.43).

Conclusions: Preterm, especially early preterm birth, seems to be associated with childhood cancer risk. Our results warrant further research about the given treatments and morbidity during the first days of life to clarify mechanisms behind increased cancer risk.

FP106 SIOP19-0716 | Parental Tobacco Smoking and Risk of Childhood Leukemia in Costa Rica: A Population-Based Case-Control Study

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Background/Objectives: The role of environmental and behavioral exposures on childhood leukemia etiology is poorly understood. We examined the association of maternal and paternal tobacco smoking at different time windows of exposure with the risk of acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) in Costa Rican children.

Design/Methods: We conducted a population-based case-control study based on the Costa Rican Childhood Leukemia Study. Cases ($n_{ALL}=252$; $n_{AML}=40$) were diagnosed between 1995 and 2000 (age <15 years at diagnosis) and identified from the Costa Rican Cancer Registry and the National Children's Hospital. A total of 578 frequency-matched population controls were sampled from the National Birth Registry. Exposure of tobacco smoking was assessed via face-to-face interviews using questionnaires. We used unconditional logistic regression models to examine the association of paternal and maternal tobacco smoking before conception, during pregnancy, and after birth with risk of childhood ALL and AML, adjusted for child sex, birth year, parental age, and parental education.

Results: Paternal smoking before conception, during pregnancy, and after birth was associated with an increased risk of childhood AML (Odds Ratio (OR): 2.50, 95% CI: 1.22-5.12; OR: 3.19, 95% CI: 1.53-6.64; and OR: 2.80, 95% CI: 1.37-5.74, respectively). Maternal smoking before conception and during pregnancy was also associated with a modest, but imprecise increase in AML risk (OR: 1.43, 95% CI: 0.53-3.88; and OR: 2.66, 95% CI: 0.84-8.50, respectively). We observed

null associations for maternal and paternal smoking and ALL in the offspring.

Conclusions: Our results suggest an association between parental smoking and risk of AML, but not ALL, in Costa Rican children. These findings add to the established evidence of numerous health risks associated with smoking and highlight the potential harm of smoking during sensitive windows of the development of fetus and child.

FP107 SIOP19-0435 | Variations and Trends in Incidence of Lymphoid Leukaemia in Children: Results from 131 Population-based Cancer Registries Around the Globe – On Behalf of ICCC-3 Contributors

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Background/Objectives: Acute lymphoblastic leukaemia (ALL) is the most frequent cancer type diagnosed in children. The aetiology of ALL remains largely unknown. Incidence patterns and comparison of occurrence between populations and over time stimulates aetiological research and is informative for health policy. Using the most up-to-date data collected for the International Incidence of Childhood Cancer (IICC) project we analysed global incidence of childhood ALL to promote aetiological research and implementation of childhood cancer control policies.

Design/Methods: We used incidence data collected in all 131 registries in 65 countries and territories around the globe which were able to provide high quality data for each calendar year in the period 2001–2010 for children diagnosed with ALL before the age 15 years. The analyses by age, gender, and geographical region were complemented by assessment of temporal change in incidence by using comparable data covering (roughly) the decade of the 1980s.

Results: The overall age-standardized incidence rate (ASR) for the entire decade of 2001–10 was 34.8/million person-years based on 68,705 cases. The highest age-specific rate was observed in children aged 0–4 years (52/million). Incidence rates varied substantially between and within the described regions. While the highest incidence was seen in White Hispanic children in the USA (51.1/million), the lowest overall rate was observed in Sub-Saharan Africa (7.9/million), where ASRs ranged from 6.5/million in Kyadondo (Uganda) to 28.5/million in Reunion (France). Compared with the 1980s, the global ASR has increased from 30.4 (95% CI 30.0–30.8)

to 34.8/million person-years (95% CI 34.5–35.1). The increase was seen in virtually all compared regions; it was particularly pronounced in Sub-Saharan Africa, where the ASR doubled.

Conclusions: The observed geographical and temporal incidence patterns suggest a link of the ALL incidence with socioeconomic development of a population, which may play a role for both aetiology and clinical detection of this malignancy.

FP108 SIOP19-0509 | Risk Factors for the Development of Second Neurotoxic Events Among Children Being Treated for Acute Lymphoblastic Leukemia

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Background/Objectives: Methotrexate is a critical chemotherapeutic agent in acute lymphoblastic leukemia (ALL) therapy, but its efficacy may be limited by neurotoxicity. Methotrexate-associated neurotoxicity can lead to treatment modifications and jeopardize long-term survival, particularly in patients who experience recurrent neurotoxicity following methotrexate re-challenge. The objective of this study was to evaluate factors associated with incidence of multiple neurotoxic events among pediatric patients with ALL.

Design/Methods: Pediatric patients undergoing therapy for ALL at Texas Children's Cancer Center (2012–2017) were prospectively followed for the incidence of methotrexate neurotoxicity, which was defined as any neurologic event (e.g., aphasia, seizure, altered mental status) following intrathecal (IT) and/or intravenous (IV) methotrexate. Available biologic samples were genotyped and associations with neurotoxicity were evaluated for 51 variants previously linked to clinical neurotoxicity in scientific publications. Odds ratios (OR), 95% confidence intervals, and p-values for the association between neurotoxicity and potential risk factors were estimated with multivariable logistic regression.

Results: The study sample (n=200) was 56.0% male, 59.0% Hispanic, with a mean age at diagnosis of 8.5 years. Forty patients (20.0%) experienced methotrexate neurotoxicity. Of the 35 patients re-challenged with IT methotrexate, 15 (42.8%) experienced an additional neurotoxic event, including 13 Hispanics (86.7%). Time to IT methotrexate re-challenge was significantly less (p=0.013) for patients who experienced subsequent events (mean=64.6 days; range: 28–161) compared to those who did not (mean=145 days; range: 42–430). Genotype data were available for 160 individuals, including 31 neurotoxic cases and 11 with multiple events. A missense variant in chromosome 15q21.3 was associated with

neurotoxicity risk overall (OR=2.33, p-value=0.025) and risk of multiple neurotoxic events (OR=4.18, p-value=0.005).

Conclusions: Understanding the predictors and mechanism of methotrexate neurotoxicity is vital for improving outcomes. We identified time to IT MTX re-challenge and a genetic variant on chromosome 15 as potential factors influencing the likelihood of subsequent neurotoxicity following methotrexate re-challenge.

FPS 20: Soft Tissue Sarcomas

FP109 SIOP19-0748 | European Pediatric Soft Tissue Sarcoma Study Group MTS-2008 Study: First Results of a Study for Metastatic Rhabdomyosarcoma

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Background/Objectives: Historically, patients with metastatic rhabdomyosarcoma have an event free and overall survival (EFS and OS) of 27% and 34% respectively (Oberlin, J Clin Oncol 26:2384). The main goal of this study was to improve outcome by giving nine courses of intensive multiagent chemotherapy, with radiotherapy+/- surgery, followed by 1 year of maintenance chemotherapy.

Design/Methods: Between 2008 and 2016, patients <21 years with metastatic rhabdomyosarcoma received 4x21-day cycles of IVADo (ifosfamide, vincristine, actinomycin-D, doxorubicin) +5 cycles of IVA followed by maintenance chemotherapy (12x28-day cycles of low-dose oral daily cyclophosphamide + weekly intravenous vinorelbine on days 1, 8 and 15). Radiotherapy and/or surgery to locoregional

disease and metastatic sites were advised after the sixth IVA cycle whenever feasible.

Results: Overall, 273 patients were enrolled with a median follow up of all living patients (n=115) of 43.8 months (range 6.3-110.5); patient and disease characteristics did not differ from the Oberlin pooled cohorts. The 3-yr EFS was 36.9% (95%CI 30.9-42.8), and OS was 48.2% (95%CI 41.8-54.2%). Patients with 0, 1, or 2 "Oberlin risk factors" had a 3-yr EFS of respectively 55.7% (36.9-71.0), 50.0% (38.4-60.6), and 44.6% (32.0-56.4), whereas patients with 3, or 4 factors had dismal 3-yr EFS of 12.1% (4.8-22.9) and 11.1% (1.2-29.8) (p<0.0001). Treatment was manageable, and 63.6% of those that started maintenance therapy completed maintenance therapy. Sixty percent of patients received radiotherapy to their loco-regional site only.

Conclusions: Patients with metastatic rhabdomyosarcoma with up to 2 'Oberlin risk factors' had improved survival compared to a cohort from pooled European and US studies (Oberlin et al, J Clin Oncol 26:2384-2389). Survival for this group was comparable to the most recent reported COG study, ARST0431 (Weigel et al. J Clin Oncol 34:117-122), applying 54 weeks of dose-compressed intensive multiagent chemotherapy. For patients with ≥3 risk factors prognosis remained dismal and new approaches are needed.

FP110 SIOP19-1261 | Assessing the Risk Profile of Rhabdomyosarcoma (RMS) Patients in a New Classification System for the Next European Paediatric Soft Tissue Sarcoma Study Group (EPSSG) Protocol

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Background/Objectives: In Europe treatment for patients with RMS is tailored according to 6 different risk factors: histology, result of initial surgery, tumour primary site and size, nodal involvement and patient's age. The combination of these factors identified 4 risk groups (low, standard, high and very high risk) in the RMS2005 protocol stratification. In this study we analysed 1) the validity of the adopted stratification; 2) the impact of fusion genes on outcome; 3) the possibility to modify the stratification system in future EpSSG protocols.

Design/Methods: Overall 803 patients enrolled in the RMS2005 protocol, whom all the data was available, have been considered for this analysis. The 5-year EFS according risk group, tumor and patients characteristics was calculated and univariate and multivariate analysis performed.

Results: The RMS2005 stratification resulted effective in predicting outcome according to the 4 risk groups (5-year EFS: low 96.2%, standard 76.4%, high 64.4%, very high 49.3%, $p < 0.0001$). When fusion status replaced histological subtype the stratification seems to better identify those patients at higher risk of relapse (fusion positive RMS with nodal involvement: EFS 40.4%). The analysis by subgroup demonstrated that young patients with small tumors at unfavorable sites (subgroup D, standard risk) have similar prognosis to patients with tumours > 5cm and/or age > 10 (subgroup E, high risk). The analysis by primary tumour site demonstrated that bladder-prostate and liver-biliary RMS had a satisfactory outcome (EFS 75.8% [65.6-83.4] and 76.5% [54.2-88.9], respectively).

Conclusions: These results prompted EpSSG to elaborate a new classification for the next protocol: a) fusion status will replace histological subtype; b) subgroup D and E will be unified; c) bladder-prostate and liver-biliary will be considered favorable primary tumor sites.

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FP111 SIOP19-0696 | Marrow Involvement In Pediatric Rhabdomyosarcoma - Can FDG PET-CT Replace Bone Marrow Procedure?

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Background/Objectives: Bone and marrow involvement in Rhabdomyosarcoma (RMS) has poor outcomes. Bone marrow biopsy (BMB) is considered as a reference standard for evaluation of marrow involvement in pediatric RMS. FDG

PET CT is being routinely used to stage RMS for detecting other metastatic sites. Purpose of this study was to evaluate the accuracy of FDG PET CT to detect marrow disease.

Design/Methods: This IRB approved prospective study included treatment naïve consecutive patients of RMS from Jan 2014 to Dec 2016. Conventional staging was done with FDG PET/CECT incorporated with CT chest and BMB (bilateral iliac bone) within a week of each other.

Review of FDG PET/CT images for marrow involvement was done blinded to BMB report which was reference standard.

Diagnostic accuracy of FDG PET for marrow involvement was calculated. Correlative imaging and follow up studies used to validate discordant results.

Results: 77 patients were analysed, median age 4.5 yrs and M: F 2.5:1.

BMB was positive in 4/77 patients.

FDG PET-CT was positive in 10/77 – 4 matched with BMB (true positive) and 6/10 with only FDG (false positive).

All 67/77 FDG negative had negative BMB (true negative).

There were no false negative results.

Statistical analysis showed a PPV of 40% with NPV at 100%.

Discordant findings in 6 patients correlated with lytic sclerotic lesions on CT in 4, positive MRI in 1 and complete resolution on follow up scan in one patient. All these patients had poor outcomes

Conclusions: FDG PET CT has a high NPV (100%) to exclude marrow involvement in pediatric RMS.

It has the potential to replace invasive BMB avoiding the risks and associated procedural complications and hence can be used as a single stop shop staging investigation.

It can save procedural time and also prove to be cost effective.

FP112 SIOP19-0388 | Prognostic Significance of FDG-Positron Emission Tomography (FDG-PET) Response Post Chemotherapy and Definitive Radiotherapy in Pediatric Rhabdomyosarcoma

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Background/Objectives: Persisting residual mass at the end of therapy are known in rhabdomyosarcoma (RMS), who have been treated with definitive radiotherapy to the primary site, but their prognostic significance is uncertain. Tumor response as assessed by anatomic imaging is not prognostic, but there

are limited studies based on FDG-PET response. We report the prognostic significance of persistent FDG avidity in residual masses at end of treatment in pediatric RMS who have undergone definitive RT as primary local therapy.

Design/Methods: Children <15 years with Group 3 or 4 RMS treated on a uniform chemotherapy protocol, who received definitive radiotherapy for local control from June 2013–December 2017, and had a FDG-PET CT at 3-months post radiotherapy were retrospectively analyzed for outcomes.

Results: Forty-seven children formed the study cohort, Group 3–42 and Group 4–5 with M: F–1.6:1. Median age was 5.2 years (range 1–15 years). PAX3/7-FKHR fusion positivity was present in 11/34 (32.3%) patients tested. FDG-PET CT scan done 3-months post-radiotherapy showed FDG avid residual masses in 10 patients (21.3%), morphologic only (FDG negative) residual mass in 15 patients (31.9%) and no residual in 22 patients (46.8%). At a median follow up of 22 months (range 5–67 months), 2-year EFS and OS of patients with FDG avid residual mass are 25% (95% CI: 3.7–55.8) and 51.4% (95% CI: 11.8–81.3) and for those with morphologic only or no residual are 71.8% (95% CI: 53.8–83.7) and 86.9% (95% CI: 68.4–94.9) respectively. Presence of metabolic residual disease on PET-CT scan 3-months post definitive RT [HR–4.64 (95% CI: 1.07–20.09)] and metastases [HR–4.06 (95% CI: 1.57–10.54)] affected outcomes. On multivariate analysis, metabolic residual disease post definitive RT alone showed a trend to affect outcome [HR–4.51 (95% CI: 0.89–22.88)], $p=0.06$.

Conclusions: Persistent metabolic activity in residual disease at the end of therapy in RMS may portend poorer prognosis, and help better identify patients who would benefit from additional local therapy (surgery) or alternative chemotherapy strategy.

FP113 SIOP19-0536 | Genome-Wide Association Study of Pediatric Kaposi Sarcoma Reveals Novel Genetic Association with the Disease: A Report from the Baylor Pediatric HIV-Related Malignancy Consortium

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Background/Objectives: Kaposi sarcoma (KS) is among the most common pediatric cancers in sub-Saharan Africa. Even after introduction of anti-retroviral treatment regimens, KS has been shown to be the most frequently diagnosed cancer in children where HIV remains highly prevalent. Two-year overall survival in children is approximately 50%. Although it is

the most common HIV-associated malignancy, only 1.5% of children with HIV develop KS, oftentimes despite adequate control of HIV. There are no known genetic risk factors for HIV-associated KS; therefore, we conducted a genome-wide association study (GWAS) of pediatric KS.

Design/Methods: Germline DNA from 46 HIV+ pediatric KS cases and 92 HIV+ cancer-free controls recruited from the Baylor-Uganda Pediatric HIV Center of Excellence was genotyped on the Illumina Infinium Multi-Ethnic Array. We tested the association between variants and pediatric KS risk in PLINK. Odds ratios (OR) and 95% confidence intervals (CIs) were estimated using log-additive logistic regression.

Results: After quality control, 896,703 autosomal markers were analyzed. A missense variant in *MAVS* was found to be highly associated with KS: OR=4.5 (95% CI: 2.3–8.8, $p=9.8\times10^{-6}$). *MAVS* codes for mitochondrial antiviral signaling protein (MAVS), a protein central to host anti-viral interferon response. Dysfunction of MAVS is known to increase human herpesvirus-8 (HHV-8) gene expression and viral load. HHV-8 infection is oncogenic and is required for KS development. Despite the small sample size, these findings pass the threshold typically accepted by the National Human Genome Research Institute as statistically suggestive ($p\leq1\times10^{-5}$).

Conclusions: A GWAS of pediatric KS revealed a biologically plausible variant associated with disease in a gene involved in the antiviral response to the oncogenic HHV-8 virus. If replicated, these findings carry implications for the pathogenic mechanisms underlying regional prevalence of this lethal disease as well as potential novel targets for therapy.

FP114 SIOP19-0869 | Larotrectinib Efficacy and Safety in Pediatric Patients with TRK Fusion Cancer

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Background/Objectives: *NTRK1*, 2, and 3 gene fusions are oncogenic drivers in pediatric and adult malignancies. Larotrectinib, an FDA-approved selective TRK inhibitor, was well tolerated and efficacious in pediatric patients with TRK fusion cancer in a phase 1 study (Laetsch et al Lancet Oncol 2018). We report updated efficacy and safety data for larotrectinib in pediatric patients with TRK fusion cancer.

Design/Methods: Pediatric patients (<18y) with non-CNS TRK fusion cancers in larotrectinib clinical trials NCT02637687 and NCT02576431 were included. Most patients were treated at the FDA-approved dose. Larotrectinib was administered until complete surgical resection, disease progression, withdrawal, or unacceptable toxicity. Response was assessed by investigator (INV) and independent review committee (IRC) using RECIST v1.1.

Results: By July 30, 2018, 38 children with TRK fusion cancer were enrolled. Median age was 2.3y (range 0.1–14); 14 were <1y. Eighteen had infantile fibrosarcoma, 15 other soft tissue sarcoma, 2 thyroid cancer, and 1 each gastrointestinal stromal tumor, melanoma, and mesoblastic nephroma. Fusions involved *NTRK1*, 2, and 3 in 18, 2, and 18 patients, respectively. Thirty-two patients had received prior cancer therapy and 6 were treatment naïve. In 34 evaluable patients by INV, overall response rate (ORR) was 94%: 35%CR, 53%PR, 6%PR pending confirmation, and 6%SD. In 29 evaluable patients by IRC, ORR was 83%: 21%CR, 62%PR, 14%SD, and 3%PD. Median duration of response (DoR) by INV was not reached (range 1.6+ to 26.7+months); DoR was >1y in 84% of patients. At data cut-off, 28 patients (74%) remained on treatment; 4 patients discontinued after complete surgical resection, 4 discontinued due to disease progression, and 1 discontinued for other reasons. Adverse events were mostly grade 1–2.

Conclusions: Larotrectinib demonstrated a high and durable response rate and was well tolerated in children with TRK fusion cancer, highlighting the importance of NTRK testing in children with cancer.

FPS 21: Liver and Germ Cell Tumours

FP115 SIOP19-1338 | Armored GPC3 CAR T Cells for Children with Relapsed/Refractory Liver Tumors

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Background/Objectives: Hepatoblastoma (HB) and hepatocellular carcinoma (HCC) are the two most common pediatric liver cancers. Available chemotherapies for unresectable or metastatic HB are less effective and associated with significant toxicities. Immunotherapy may help these children. Glypican 3 (GPC3) is an attractive immunotherapeutic target: it is expressed in the majority of HBs and HCCs and not expressed in non-malignant tissues. One effective immunotherapeutic approach is using chimeric antigen receptors (CARs) to redirect T cells to specifically destroy tumor cells, but this immunotherapy has limited efficacy in patients with solid tumors due to limited expansion and persistence of T cells.

Design/Methods: We systematically examined the antitumor properties of T cells co-expressing an optimized GPC3-CAR with IL-15, IL-21 or both (15.GBBz, 21.GBBz and 21.15.GBBz, respectively) in preclinical models of liver cancer.

Results: GPC3-CAR T cells co-expressing IL-15 and/or IL-21 effectively kill GPC3-positive tumor cells and produce effector cytokines in an antigen dependent manner. Constitutive IL-15 and IL-21 expression induces enrichment of less differentiated T cells after initial expansion (Naïve/stem cell memory CD8 T cell subset: 21.15. GBBz 29.2% vs GBBz 13.3%, $p < 0.05$) and protects from apoptosis during repeated killing of tumor cells (21.15. GBBz 40.6% vs GBBz 20.2%, $p < 0.05$). Importantly, the combined expression of both IL-15 and IL-21 induces the highest peak expansion and sustained persistence GPC3-CAR T cells in vivo (Area under the curve: GBBz: 32.4, 15.GBBz: 66.2, 21.GBBz: 21.1 and 21.15.GBBz: 94.7; $p < 0.0001$; $=0.17$; <0.0001 for 21.15.GBBz, respectively) leading to superior survival HCC xenograft bearing mice ($p < 0.001$, Log-rank).

Conclusions: Our results indicate that the co-expression of IL-21 and IL-15 enhances the antitumor properties of GPC3-CAR T cells. Based on these results, we are now recruiting children in Cohort 1 of a Phase 1 trial to evaluate the safety, expansion, persistence and antitumor activity of GPC3-CAR T cells in children with liver cancers (GAP; NCT02932956).

FP116 SIOP19-0589 | Feasibility of Dose-Dense Cisplatin-based Chemotherapy in Japanese Children with High-Risk Hepatoblastoma: A Result from JPLT3-H Study

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Background/Objectives: A prospective study, SIOPEL-4, demonstrated that dose-dense cisplatin-based chemotherapy and surgery dramatically improved outcome of children with high-risk hepatoblastoma. However, feasibility and safety of this regimen has not been clarified in Japanese patients.

Design/Methods: JPLT3-H was a prospective and single-arm study to evaluate safety profile of SIOPEL-4 regimen in Japanese children with newly diagnosed hepatoblastoma with either metastatic disease or low alpha-fetoprotein.

Results: A total of 15 patients were enrolled. Median age was two years (range:0-14). Three patients were female. PRETEXT stage was II in 2, III in 7, IV in 6 patients. All patients had lung metastasis, and there were no patients with low alpha-fetoprotein. Eight patients completed the protocol treatment, while seven patients discontinued it prematurely due to causes other than severe toxicities: progressive disease (4); no fulfillment of the criteria for lung metastasis (1); patient's desire to discontinue (1); and transfer to a non-participant hospital (1). Among patients who completed the protocol treatment, eight (100%) patients had grade 3-4 hematological toxicity (anemia, neutropenia, thrombocytopenia or leukopenia). All patients had grade 4 neutropenia and seven (88%) had grade 4 thrombocytopenia. Six (75%) had at least one episode of febrile neutropenia. One patient had grade 4 hypomagnesemia. Other grade 3 or 4 toxicities were anorexia, nausea, mucositis, elevation of liver enzymes, fever, infection, and fatigue. No unexpected severe toxicities were documented in all the enrolled patients.

Conclusions: Toxicity profile of JPLT3-H was comparable with that of SIOPEL-4. Dose-dense cisplatin-based chemotherapy may be feasible among Japanese patients with high-risk hepatoblastoma.

FP117 SIOP19-0010 | Long-Term Survival in Patients with Primary Intracranial Germ Cell Tumors Treated with Surgery, Carboplatin based Chemotherapy Followed by Radiotherapy

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Background/Objectives: In the present study, we performed a retrospective review of patients receiving carboplatin based chemotherapy followed by radiotherapy for newly diagnosed primary intracranial germ cell tumors. In order to identify an optimal germ cell tumor treatment strategy, we evaluated treatment outcomes and toxicity and compliance.

Design/Methods: This study included 110 consecutive patients with newly diagnosed primary intracranial germ cell tumors. The drug doses and administration schedule of carboplatin-etoposide (CARB-VP) were as follows: carboplatin (300 mg/m² daily for 1 days), and etoposide (100 mg/m² on days 1 to 3). Ifosfamide-carboplatin-etoposide (ICE) treatment comprised ifosfamide (1500 mg/m² daily for 3 days), carboplatin (300 mg/m² daily for 1 days), and etoposide (100 mg/m² daily for 3 days). Patients with germinomatous germ cell tumors (pure germinoma or germinoma with STGC) basically receive three cycles of CARB-VP and a total dose of 30Gy whole ventricular radiotherapy. We delivered combination therapy consisting of combined ICE chemotherapy and craniospinal irradiation followed by the complete resection of the residual tumor for nongerminomatous malignant germ cell tumors.

Results: The median follow-up time was 11.0 years (range, 0.5–37.8 years). The 5-year total survival rates of germinomatous and nongerminomatous germ cell tumors were 97.2% and 66.7%, respectively. The 10-year and 20-year total survival rates of germinomatous germ cell tumors were 95.7% and 90.0%, respectively. Adverse events related to carboplatin based chemotherapy are not detected. Furthermore, no treatment-related deaths were observed.

Conclusions: Our treatment with surgery, carboplatin based chemotherapy followed by radiotherapy is effective in treating primary intracranial germ cell tumors, especially in germinomatous group.

FP118 SIOP19-0797 | Development of Nomogram for Prediction of Survival of Patients with Childhood Extracranial Germ Cell Tumors

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Background/Objectives: *Introduction.* The value of serum tumor marker of alfa-fetoprotein (AFP) assessed by marker half-life (HL) analysis in the follow-up was show to predict survival in patients with poor prognosis childhood extracranial germ cell tumors.

The aim of the study was to assess the prognostic value AFP half-life in long-term outcomes.

Design/Methods: Data regarding 46 patients aged less than 18 years old with extracranial germ cell tumors prospectively accrued were obtained. Serum AFP was assessed at baseline (M0) and after 2 cycles of chemotherapy (M1). AFP HL rate was calculated for each patient using a logarithmic transformation: $HL = T \cdot \log(2) / \log(M0/M1)$, with $T = 42$ days.

Results: The median follow-up was 8 years (range, 1 months to 21 years). Median HL for all patients was 15.6 days (range, 3 – 138 days). A cut-off point at 6 days of HL was found. The ROC curve area was 0.647 ± 0.0896 . The maximum Youden index was 0.3869. An unfavorable decline in AFP was predictive of overall survival (OS). The 8-years OS rates were $85.2 \pm 7.9\%$ and $50.1 \pm 12\%$ in patients with $HL \leq 6$ days weeks and with $HL > 6$ days, respectively ($p=0.01873$). Nomogram for prediction of OS of patients with childhood extracranial germ cell tumors based on unfavorable AFP decline was built.

Conclusions: Performance of the nomogram was excellent. It may be helpful for physicians when making a decision. Prospective studies of using the nomogram in patients with childhood extracranial germ cell tumors based on serum tumor marker decline are warranted.

FP119 SIOP19-1534 | Validation of the Magic Germ Cell Tumor Risk Stratification

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Background/Objectives: A new risk stratification for metastatic non-seminomatous pediatric germ cell tumors (NS-GCT) was published in 2015 by the Malignant Germ Cell International Consortium (MaGIC) based on analysis from 25 years of clinical trial data provided by Children's Oncology Group and Children's Cancer and Leukemia Group (United Kingdom, UK). The MaGIC risk stratification identified age ≥ 11 y, advanced stage disease and extragonadal or ovarian primary site as adverse prognostic indicators; this risk

stratification served as the basis for three new international clinical trials. To validate the risk stratification, the model was tested in two independent datasets provided by the UK and Brazilian Pediatric Germ Cell Tumor Clinical Trial groups.

Design/Methods: The MaGIC risk stratification was tested in the two datasets. The 366 Brazilian patients with NS-GCT were treated on one of three protocols: TCG91, TCG99, TCG2008, and the 45 UK patients were treated on GC3, a trial not included in the original validation. A non-mixture cure model was used to characterize the relationship between variables and event-free survival. The likelihood ratio test of a p-value >0.05 was used to eliminate terms using stepwise selection. The predicted probability of remaining event-free survival was estimated from the 2015 model. The C-index at 5 years (Uno et al. Statist Med 2011) was used to assess the robustness of this prediction.

Results: A model fitted with the three covariates (age, site, stage) showed that all were significant, in the same direction, and with similar coefficients as in the original risk model. On stepwise selection, age was eliminated at $p=0.08$. Stage and non-gonadal sites were significant predictors of outcome in the validation dataset. The C-index at 5 years after enrollment was 0.40 (95% CI 0.34-0.46).

Conclusions: The original MaGIC risk stratification was verified in two independent datasets from the UK and Brazil, supporting its use in prospective clinical trial design.

FP120 SIOP19-0260 | The Avian Embryo as a New Patient-Derived Xenograft Model to Explore Germ Cell Tumors Etiology, Heterogeneity and Therapeutic Screening

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Background/Objectives: Germ cell tumors (GCTs) arise from pluripotent germ cells (PGC), primarily in the gonads, but also in extragonadal sites along the body midline and the brain. The etiology of extra-gonadal GCTs and GCT metastasis is still debated, mainly because of the lack of model recapitulating GCT history and migration behaviors. In the same line, *in vivo* patient-driven analyses of tumor migration and chemosensitivity are not even intended in current animal models. Our main objective was to develop an avian Patient-Derived Xenograft (PDX) system that reproduce GCTs heterogeneity and clinical features.

Design/Methods: Based on previous experiments on neuroblastoma, we conceived an avian model of GCTs in which

tumorigenesis is driven in HH25 chick embryos either in gonadal site by grafting GCTs in the migration path of PGCs, or in extra-gonadal brain site. We set up the technique with NCC-IT and Tera2 GCT cell lines. We then extended it to 3 GCTs patient samples, harvested from fresh surgical resections and preserved in DMSO freezing medium: one mediastinal yolk sac tumor with pulmonary metastasis in a 6-year-old boy, one multimetastatic testicular mixed GCT in a 17-year-old patient and one mixed testicular GCT with lymph nodes extension in a 15-year-old patient.

Results: Cell lines grafted in the migration path of PGCs formed visible tumors in avian primitive gonads 5 days after engraftment while grafts in the developing brain replicated secondary foci in 2 days. Similar graft experiments on GCTs patient samples confirmed a rapid and highly reproducible tumor intake in the embryo for both paradigms. IV injection of 5.1 mg/kg cisplatin into embryos grafted with samples validated its efficacy to reduce the tumor volume of avian replicas of cisplatin-responding patients in 48h.

Conclusions: Our GCT avian model opens exciting possibilities ranging from the study of GCTs etiology to the evaluation of novel drug/combination efficacy on patient-derived material.

FPS 22: Experimental Therapeutics and Cancer Immunology

FP121 SIOP19-1103 | Olaparib Associated with Irinotecan in Children and Adolescents “with Relapsed or Refractory Tumors” – ARM D of the European AcSé-ESMART Trial

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Background/Objectives: AcSé-ESMART is a proof-of-concept, phase I/II, multicenter, prospective basket trial designed to explore targeting agents in a molecularly enriched cancer population; treatment arms with targeted agents as single agent or in combination regimens are explored independently.

Arm D explores the PARP inhibitor olaparib in combination with irinotecan. The design is based on the hypothesis

that in pediatric cancer pathogenic *BRCA* alterations are extremely rare and proliferative capacity is high requiring a sensitisation approach. Preclinical data in pediatric cancer suggest PARP inhibitor activity in other genomic alterations impairing homologous recombination and demonstrate synergy with irinotecan. We here report the results of the Phase I part.

Design/Methods: Children and adolescents with relapsed/refractory cancer and comprehensive molecular profiling (whole exome/RNA sequencing) at relapse were eligible. Dose-escalation followed a CRM design of pre-specified dose combinations of oral olaparib and iv irinotecan. Plasma for pharmacokinetics was collected.

Results: From October 2016 to April 2018, 27 patients (19 sarcomas, 3 brain tumors, 5 other) with a median age of 15 years (range 4;22) were enrolled over 4 dose levels. Dose limiting toxicities occurred in 7 of 24 evaluable patients (gastrointestinal (n=4), febrile neutropenia (n=1), thrombocytopenia (n=2)). The RP2D was defined as olaparib 90 mg/m² BID day 1-10 and irinotecan 20 mg/m² day 4-8. Twenty-three patients evaluable for response received a median of 2 cycles (range 1-30+). Confirmed partial responses were seen in one patient each with osteosarcoma, pinealoblastoma and neuroblastoma; time to progression was 22.4, 50 and 96+ weeks, respectively. Eight patients experienced disease stabilization (median 14.8 weeks, range 9;42.3). Biomarker analysis including pharmacokinetics is ongoing to identify factors associated with clinical benefit.

Conclusions: The RP2D of the combination is olaparib 90 mg/m² BID day 1-10 and irinotecan 20 mg/m² day 4-8. Preliminary activity led to the ongoing Phase II part of the arm.

FP122 SIOP19-1372 | Phase 1/2 Trial to Assess the Activity of Entrectinib in Children and Adolescents with Recurrent or Refractory Solid Tumors Including Central Nervous System (CNS) Tumors

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Background/Objectives: We report the efficacy of entrectinib, a CNS-penetrant oral inhibitor of Trk, ROS1 and ALK tyrosine kinases, in children with solid or CNS tumors.

Design/Methods: Eligible patients ≤ 20 y had recurrent/refractory solid tumors. After determining the recommended dose in all-comers, disease-specific expansion cohorts of CNS and solid tumors harboring target aberrations in *NTRK1/2/3*, *ROS1* or *ALK*, and of neuroblastomas (NBL) regardless of mutation spectrum, were enrolled. Investigator-assessed response was classified as complete (CR) or partial response (PR), stable (SD) or progressive disease using RANO (CNS tumors), RECIST (solid tumors), or Curie score (NBL).

Results: 29 patients aged 4.9m–20y (median 7y) were enrolled (May2016–October2018). Entrectinib was well tolerated. The dose-limiting toxicities seen were: elevated creatinine, dysgeusia, fatigue, and pulmonary edema. The recommended dose was 550mg/m² daily. All responses occurred at doses ≥ 400 mg/m². In CNS tumors (n=6), all high-grade with gene fusions, confirmed responses were: 1 CR (*ETV6-NTRK3*); 3 PR (*TPR-NTRK1*, *EEF1G-ROS1*, *EML1-NTRK2*); 1 SD (*GOPC-ROS1*); 1 has yet to be evaluated (*KANK1-NTRK2*). In extracranial solid tumors (n=8), 6 had a fusion of whom 1 achieved a confirmed CR (*DCTN1-ALK*); with 3 PR (*TFG1-ROS1*, *EML4-NTRK3*, *ETV6-NTRK3*), and 2 SD (*KIF5B-ALK*, *ETV6-NTRK3*). In NBL (n=15): 3 had confirmed SD (no fusions), and 1 has yet to be evaluated (*ALK-F1174L*). Median duration of therapy: 2.79m (range 0.2–17.7m) for all patients; 10.51m (range 3.8–17.7m) for responders; 1.84m (range 0.2–11.1m) for non-responders. Median time to response: 1.89m (range 1.0–1.9m).

Conclusions: Entrectinib produced striking, rapid, and durable responses in children with refractory CNS/solid tumors harboring *NTRK1/2/3*, *ROS1* or *ALK* fusions. No responses were seen in tumors lacking aberrations in target kinases. These results support the continued evaluation of entrectinib as a targeted therapeutic in solid tumors with positive target gene fusions, especially high-grade CNS neoplasms.

FP123 SIOP19-1241 | Patient-Derived Xenografts (PDX) Development in Mappysacts - A Pediatric Precision Cancer Medicine Trial in Relapsed and Refractory Tumors

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Background/Objectives: Overall 5-year survival of children and young adults with cancers is around 80% albeit it greatly varies between tumor types. Predictive preclinical models and novel therapeutic strategies are therefore a clinical imperative.

The multicenter, precision cancer medicine trial MAPPY-ACTS aims at identifying the individual molecular tumor profile in relapsed or refractory pediatric patients and suggesting them to the most suitable matched targeted treatment. One major ancillary aim is the establishment and characterization of relevant preclinical models mainly patient-derived xenografts (PDX).

Design/Methods: Tumor material from biopsy or resection was transplanted into immunocompromised mice into the renal capsule, subcutaneously or orthotopically. Models were characterized by histology, whole exome and RNA sequencing, low-coverage whole-genome sequencing (LcWGS), methylome analysis, compared to the patient's profile, and in their growth behavior.

Results: From the first 566 patients with recurrent or refractory cancer included in 18 clinical MAPPYACTS trial centers, 96% of patients and their parents consented to the preclinical model development. A total of 259 samples were transplanted in 9 research units; so far 89 tumors engrafted successfully and are established models (34.4% tumor take rate) with a median delay in tumor take of 3 months. These include 48 sarcomas (rhabdomyosarcoma, osteosarcoma, Ewing sarcoma, undifferentiated sarcoma, malignant nerve sheath tumor, rhabdoid

tumor, synovial sarcoma), 17 non-CNS tumor (neuroblastoma, nephroblastoma, carcinomas, hepatoblastoma), 9 CNS tumor (gliomas, ependymoma), 13 leukemias (B-ALL, T-ALL, AML), 2 lymphomas (anaplastic large cell lymphoma, Burkitt lymphoma), as well as some rare tumors (colon adenocarcinoma, pinealoblastoma, pleuropulmonary blastoma). Histology and sequencing revealed a high concordance with the primary patient's tumor profile and heterogeneity. Most frequent alterations were *TP53* mutation, *CDKN2A/B* deletion, *RB1* mutation, tumor specific fusions, equivalent to findings in primary samples.

Conclusions: This new PDX biobank of unique recurrent childhood cancers provides a crucial support for basic and translational research in pediatric malignancies.

FP124 SIOP19-0493 | Comprehensive Characterization of Tumor Immune Microenvironment in Children and Adolescents with Relapsed or Refractory Cancers: The Immunoacts Project

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Background/Objectives: IMMUNOACTS is an ancillary study of MOSCATO-01 (NCT01566019) and MAPPY-ACTS (NCT02613962), two sequential prospective precision medicine trials recruiting children/adolescents with recurrent/refractory malignancies, with the purpose of comprehensively study the tumor microenvironment (TME).

Design/Methods: Patients <18 years at diagnosis underwent on-purpose tumor biopsy/surgery of recurrent/refractory malignancies for molecular characterization by whole exome (100x, tumor/paired germline) and bulk RNA sequencing (RNAseq). Immunohistochemistry (IHC) was performed with a panel of 12 antibodies (CD3, CD8, FOXP3, PDL1, CD20, CD68, CD163, CD47, HLA-I, HLA-II, NKp46, CD57), plus LAG3, IDO1, CSF1R in selected samples.

Results: From December 2012 to October 2018, contributive molecular profiling was available for 439 patients (88% solid and 12% hematologic malignancies). RNAseq analysis confirmed that pediatric cancers are poorly immunogenic or

“cold” with mainly no/low immune infiltrate (estimated $\leq 5\%$). TME had a common pattern across all histologies, with a predominance of macrophages (M2 > M0 > M1), very few T-cells, and even rarer dendritic cell, B-cell, and NK-cell infiltrates. M0 macrophage phenotypes were inversely correlated to M2 and activated NK cells. Cancer-associated fibroblasts were observed in most of the samples. Significant lymphocytic T-cell infiltrate (CD4+ memory resting and CD8+) was observed in 10% of samples. PDL1 expression in solid tumors was generally low. High expression of B7-H3, TIM3, STING, CXCR4, CSF1R and CD47 in specific tumor types was also displayed. Multiplex IHC confirmed the predominance of M2, while NK cell infiltration was mainly restricted to peritumoral sites. Correlation of TME with genetic tumor aberrations, constitutional features and tumor response to immunotherapies is currently ongoing, as well as the design of de novo signatures specific of pediatric cancers.

Conclusions: Our results confirm the poor immunogenicity of pediatric cancers, and the main role of innate immunity dominated by macrophages. Potential immunological targets will be further explored to guide the design of new therapeutic strategies. C. Pasqualini/A. Marchais: first co-authors.

FPS 23: Precision Medicine and Cancer Predisposition

FP125 SIOP19-1611 | Molecular Characterization of Pediatric Tumors: An Analysis of 1026 Cases from the International AACR-GENIE Database

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Background/Objectives: Analysis of somatic genomic alterations of children and adolescent tumors included in the international GENIE database from 2017 to 2019 (N=1,306).

Design/Methods: AACR-GENIE (American Association for Cancer Research Project Genomics Evidence Neoplasia Information Exchange) is an international data sharing initiative gathering clinical-grade cancer genomic adult and pediatric data from 8 participant reference centers. Dataset includes 1,306 pediatric cancers (patients aged between 0-18 years). Data cleaning included re-classification of histological subtypes. We limited our analysis to tumors genotyped with one of the 4 largest gene panels to have a homogeneous population. The panel intersection represented 206 genes among which 190 were included in the Cancer Gene Census database.

Data were imported in a local database and used for descriptive statistics.

Results: A total of 1,026 tumors from 971 patients were analyzed. Embryonal tumors (33%), sarcomas (24%) and gliomas (19%) were the most represented histological subtypes. No genetic alteration was found to be specific of the pediatric population. Seven hundred and fifty-nine tumors (74%) presented at least 1 somatic mutation, among which 747 (98%) presented less than 10 somatic mutations. TP53 was the most frequently mutated gene (in 8% of the tumors). Six-hundred and eight tumors (59%) presented at least one copy number variations (CNV) and MYCN was the most frequently affected gene, in 13% of the tumors. Further analysis deciphered the landscape of alterations within canonical cancer driving pathways, and explored more deeply these alterations for specific histological subtypes (*i.e.* sarcomas, compared with the adult cohort).

Conclusions: AACR-GENIE database includes the largest pediatric cancer genomics cohort, with represented pathologies covering the histological subtypes encountered in this age group. Our results provide insights on genetic alterations, oncogenic drivers and molecular targets to be developed in this pediatric population.

FP126 SIOP19-0926 | Can Pediatric and Adolescent Patients with Recurrent Tumors Benefit from a Precision Medicine Program? The European Mappyacts Experience

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Background/Objectives: The international prospective precision medicine trial MAPPYACTS (NCT02613962) aims at defining a molecular profile in recurrent/refractory malignancies in order to suggest the most adapted salvage treatment.

Design/Methods: Patients < 18 years-old at the time of initial diagnosis underwent on-purpose tumor biopsy/surgery of their recurrent/refractory malignancy for molecular characterization by WES and whole RNA sequencing. Results were reviewed in a dedicated weekly molecular tumor board (MTB), followed by discussion with the treating physician in a clinical MTB (CMTB). Whenever possible, patients were enrolled subsequently in clinical trials based on CMTB recommendations.

Results: From February 2016 to October 2018, 500 patients have been included in 17 centers in France, Italy and Ireland. Median age at inclusion was 13 years. Molecular profiling was performed on samples in 433 patients and was contributive for 390 patients. For 271/390 patients (70%), there was at least one genetic alteration that could represent a potential therapeutic target and 8% had alterations considered as “ready for use”. Among them, 19 (7%) died before the CMTB. With follow-up censored in January 2019, 72 patients (27%) were treated with at least one matched targeted agent, 57 of them in a clinical trial, mostly the proof-of concept AcSé-ESMART trial (NCT02813135). Of the 166 patients (61%) that did not receive the matched treatment recommended by CMTB (80 still on follow-up), main reasons were: response/stable disease under previous therapy (50), another treatment (48), rapid disease progression/death (30) and legal representative refusal (12).

Conclusions: MAPPYACTS profiling allowed tailored targeted treatment, mainly through early clinical trials, in patients with recurrent pediatric cancer. Since most detected molecular findings are within the investigational or hypothetical evidence level, therapeutic proof-of-concept trials that are exploring targeted therapies in molecularly enriched patient populations are crucial to improve knowledge and potentially outcome.

*P. Berlanga/G. Pierron/L. Lacroix are co-first authors and G. Schleiermacher/B. Geoerger are co-last authors.

FP127 SIOP19-0836 | Performance of an E-Health Decision-Support Tool for Identifying Cancer Predisposition Syndromes in Canadian Pediatric Oncology Centres

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Background/Objectives: Multiple challenges limit physicians' capacity to rapidly identify cancer predisposition syndromes (CPS) in pediatric oncology. To improve physician detection of a CPS, we developed an eHealth tool called "MIPOGG", which contains 140 tumour-specific decisional algorithms that generate a recommendation for genetic evaluation based on the likelihood of a CPS. We aimed to evaluate the performance of MIPOGG for timely detection of CPS among children with cancer in Canada.

Design/Methods: Through a multicentre Canadian collaboration, we identified patients diagnosed with cancer (0-18 years) between 2000-2018 and who had a confirmed CPS. Two independent clinicians applied the appropriate MIPOGG tumour algorithm to each case using retrospective data abstracted from medical charts at the time of cancer diagnosis to determine the proportion of patients who would have been identified by MIPOGG as requiring a genetic referral. We evaluated whether the application of MIPOGG resulted in recognition of CPS at an earlier timepoint than physicians.

Results: We identified 422 patients with a cancer diagnosis and a confirmed CPS in 10 Canadian sites (solid tumours n=208, brain tumours n=196, hematological malignancies n=18) with sufficient information for application of the tool. MIPOGG identified 419 (99.3%) patients with a CPS as requiring a genetic referral at the time of cancer diagnosis. Family history did not contribute to MIPOGG's decision for genetic referral in 258 (61.6%) cases. Seventeen patients developed more than one malignancy prior to CPS recognition by physicians, all of which would have been identified for genetic referral by MIPOGG at the time of the first cancer.

Conclusions: MIPOGG is applicable in various clinical settings and contributes to the standardisation of genetic referrals in pediatric oncology. MIPOGG enhances physician-based CPS recognition and may decrease time to CPS recognition. MIPOGG is currently undergoing more robust validation steps and will soon be available to the medical community.

FP128 SIOP19-1016 | Parental Expectations Around Return of Updated Germline Genomic Results in Pediatric Oncology

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Background/Objectives: Despite increasing integration of germline genetic testing into the care of pediatric cancer patients, variant analysis is an evolving field and results can be reclassified over time. These reclassifications may have important clinical consequences for patients who have previously undergone predispositional testing. When sequencing is conducted in the context of clinical research, the obligation to return updated, individual results is a source of scientific debate. In clinical oncology trials, pediatric oncology parents strongly desire return of research results that may impact their child's health, but preferences for updated genomic information, and over what timeframe, remain poorly understood.

Design/Methods: Parents whose children underwent cancer germline genomic testing in the context of a prospective clinical trial were asked about their expectations for receiving updated genomic results, including preferences for receipt of new information should their child expire.

Results: Of 197 parental respondents, 96% (n=189) believed researchers have a responsibility to contact families with updated genomic results. The majority (n = 119; 63%) expect updated results no matter how long it has been since initial testing, unless they ask the researchers to stop, while 31% (n=59) limited the obligation to return new results to the duration of contact with the institution, even if this extends into adulthood. Asked about their desire for updated results following the death of their child, 68% (n=133) said yes, but 19% (n=38) were uncertain, and 11% (n=21) preferred no further contact or did not answer (n = 5; 3%).

Conclusions: Expectations for return of updated genomic results are high and not limited by time from original testing. While most parents desire updated information after the loss of a child, nearly one-third are uncertain or have concerns. These results indicate a need for clear communication at the time of testing that aligns parental expectations around receipt of new genomic information over time.

FPS 24: Retinoblastoma

FP129 SIOP19-1265 | Results of a Second Multicenter Prospective French National Study on the Postoperative Treatment of Unilateral Retinoblastoma after Primary Enucleation

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Background/Objectives: The objective of this prospective study was to assess overall and event-free survival in patients with Reese-Ellsworth group V unilateral retinoblastoma treated by primary enucleation with or without adjuvant therapy depending on histopathologic risk factors. Lower cumulative chemotherapy dose than in the previous published study was evaluated in some cases (Aerts, J Clin Oncol 2013).

Design/Methods: Between February 2010 and November 2018, 125 patients were included and divided into four groups on the basis of risk factors for extraocular relapse and metastasis assessed on centralized histologic examination of enucleated eyes and standardized criteria. Group 1 with minimal or no choroidal involvement and/or prelaminar or intralaminar or no optic nerve involvement received no adjuvant therapy. Group 2 with only massive choroidal involvement received two courses of Vincristine Carboplatin. Group 3 with intra- or retrolaminar optic nerve and/or anterior segment involvement (with or without massive choroidal involvement) received 2 cycles alternating VP16 Carboplatin and Vincristine Cyclophosphamide. Group 4 defined by invasion of the surgical margin of the optic nerve and/or microscopic extrascleral involvement received six courses of conventional adjuvant chemotherapy with intrathecal Thiotepa, high dose chemotherapy (VP16, Carboplatin, Thiotepa) with autologous stem-cell rescue.

Results: Ninety patients were included in group 1, 7 in group 2, 28 in group 3. Median follow-up was 36.3 months. Staging did not show any distant metastasis at diagnosis. No disease progression, relapse, distant metastasis or secondary malignancy occurred during follow-up. Adjuvant chemotherapy

was well tolerated, with limited toxicity. The EFS and OS are 100%.

Conclusions: The incidence of histopathological risk factors is lower than in the previous study. No event occurred in the 7 group 2 patients treated with a lower chemotherapy cumulative dose. These preliminary data confirm the excellent prognosis of risk-adapted post-enucleation therapy but need to be confirmed with a higher patient number and longer follow-up.

Acknowledgments: RETINOSTOP

FP130 SIOP19-1321 | Intrathecal Topotecan as Part of Retinoblastoma Treatment

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Background/Objectives: Previous results show that minimally disseminated disease (MDD) in the cerebrospinal fluid (CSF) is a major route for retinoblastoma dissemination. We proposed the use of intrathecal topotecan (ITtpt) based upon its activity and safety profile.

Design/Methods: ITtpt was used in 2 patient groups: Group A) as treatment of Central Nervous System (CNS) dissemination and B) as part of the adjuvant treatment in case of intraocular pathology risk factors or extra ocular non-CNS disease. ITtpt was given at 0.4 mg diluted in isotonic saline.

Results: We report 18 patients (8 unilateral, 7 bilateral, 3 trilateral) treated in our centers between 2010 and 2018. The median (range) age at first dose of ITtpt was 2.5 years (0.6-5). Patients received a median of 6 applications of ITtpt (total 112). Group A: (CNS involvement) included 10 patients. Nine of them received treatment of CSF dissemination (2 ITtpt alone and 4 combined with other treatments) and 3 for the treatment of MDD. Three of 5 patients with positive cytology had a complete response and all patients with MDD became negative after 2 doses of ITtpt and intravenous (i.v) chemotherapy. The remaining patient with trilateral retinoblastoma received i.v chemotherapy and ITtpt as palliative treatment. All patients with MDD are alive and disease-free (median 28 months) and all the other patients died of CSF dissemination. Group B: included 8 patients who received i.v chemotherapy and ITtpt as adjuvant treatment. One patient died of CSF relapse and all others are alive and disease-free (median of 4 months). No grade III/IV adverse events related to ITtpt were observed in any patient.

Conclusions: ITtpt cleared the CSF malignant cells in 75% of the patients with no serious adverse events. However, patients with positive CSF cytology ultimately relapsed. ITtpt may be further explored as components of the treatment of high risk retinoblastoma.

FP131 SIOP19-1251 | Extraocular Retinoblastoma: A 9-Year Experience at Children Cancer Hospital in Egypt (CCHE)

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Background/Objectives: This study was performed to evaluate the extraocular protocol of COG [ARET0321] and to describe demographical and clinical characteristics of patients diagnosed with extraocular retinoblastoma disease.

Design/Methods: Eighty-nine patients were diagnosed with extraocular retinoblastoma in Children Cancer Hospital in Egypt (CCHE) during the period of January/2010 till June/2018 with follow-up period till the end of December/2018. Patients were classified according to International Staging System Classification and treated according to COG protocol [ARET0321] for extraocular retinoblastoma. All patients received four cycles of induction chemotherapy [Cisplatin, Vincristine, Etoposide, Cyclophosphamide/Mesna] followed by radiotherapy for stages II / III or followed by consolidation myeloablative treatment [Etoposide, Melphalan, Carboplatin], stem cell rescue and radiotherapy for stages IVa and IVb. We collected all potential factors: patient's demographics, first clinical presentation, staging, treatment regimens and response. All of them were analyzed.

Results: Eighty-nine patients presented with mean age 2.7 years with range (1.5 month – 10.9 years). Most of the patients presented with stage II (37, 41.5%) and IVb (33, 37%) followed by stage III (25, 28%) and stage IVa (10, 11.2%). Five-year overall survival was [55.1% (95% CI, 45.2 – 67.2%)] with 37 deaths and event-free survival [55.1% (95% CI, 43.6 – 65.3%)] with 39 events. The event was defined as relapse, progression, second malignancy, and death. Five-year event-free survival for each stage: II, III, IVa, and IVb were 69.6%, 71.4%, 36%, and 24% respectively. Eleven patients with stages IVa and IVb were undergone bone marrow transplantation, one patient died with 5-year overall survival [88.9% (95% CI,

70.6 – 100%)] and event-free survival [80.8% (95% CI, 60 – 100%)].

Conclusions: The four cycles of these chemotherapy followed by radiotherapy are a good treatment regimen for stages II and III. Bone marrow transplantation revealed a promising treatment option for stages IVa /IVb.

FP132 SIOP19-0563 | Impact of Therapy on Quality of Life in Patients Treated for Retinoblastoma

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Background/Objectives: Treatment of retinoblastoma (Rb) has changed over time, from a combination of local treatments with systemic chemotherapy (CT), external beam radiotherapy (EBR) and enucleation (E) to new conservative treatments such as intraarterial (IAC)/intra-vitreous (IVC) administration of chemotherapy. Limited data are available regarding their impact on health-related quality of life (HRQoL) in cured patients. We assessed HRQoL in Rb survivors and compared the results between the four different treatment modalities.

Design/Methods: This is a population-based cross-sectional study. HRQoL was assessed using the KIDSCREEN-52 questionnaires for parents and patients sent out to all RB survivors (aged 3-20 years) who were entirely treated at our centre and had a minimal follow-up of 3 years since end of treatment. A total score was established and the scores of each dimension were compared between the four groups.

Results: Seventy-eight Rb survivors and their parents participated. The overall total score was 43.10/50 (SD=6.03). Rb survivors who received primary CT scored significantly higher than the other groups for total HRQoL and school environment dimension score; they scored significantly higher compared to E in psychological well-being, and higher than EBR in self-perception and autonomy dimensions. Variables associated with a lower score were older age at study time and at diagnosis, self-reported questionnaire and unilaterality.

Conclusions: Our results show that the perceived HRQoL by Rb survivors was globally very good and that the HRQoL differed according to the treatment received. Patients treated with EBR have, as expected, the worst HRQoL. To our surprise, systemic chemotherapy, although related to more general side effects, scored best in almost all domains, even when compared to the newer local chemotherapies (IAC/IVC). Further data are needed to confirm these observations.

IPSO

IPSO: FPS- Basic Research and Technology Developments

IPSO01 SIOP19-1451 | Minimally Invasive Surgery (MIS) in Pediatric Oncology: Experience in a National Pediatric Oncology Center

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Background/Objectives: Minimally invasive surgery (MIS) has become increasingly common in various pediatric surgical conditions. However, the experience of MIS in pediatric cancer patients is still limited. We report our experience of MIS in a national pediatric oncology center.

Design/Methods: A retrospective review of all patients who underwent a laparoscopic or thoracoscopic procedure at Princess Máxima Center for Pediatric Oncology between 1st January 2015 and 31st December 2018 was performed. Patient demography, diagnosis, operative details and post-operative course were analyzed.

Results: A total of 90 MIS procedures were performed. These included 58 laparoscopic (64%) and 32 thoracoscopic (36%) procedures. Mean age was 9 years [range:1 month-17 years]. Thirty-four procedures (38%) were performed for diagnosis/evaluation and 56 (62%) were therapeutic (resection of tumors). Thirty-two cases (36%) were malignancies. Laparoscopic surgery is performed significantly more often for therapeutic procedures than thoracoscopic surgery ($p=0.025$).

The most common MIS procedure performed was oophorectomy (19 cases, 21%), followed by adrenalectomy (14 cases, 16%). However, the frequency of MIS adrenalectomy for malignant adrenal tumors was significantly higher than MIS oophorectomy for non-benign condition ($P=0.003$). The mean operative time was 72 minutes [range:25-147] for diagnostic procedures, and 117 minutes [range:30-519] for therapeutic procedures. There were eight intra-operative complications (9%), with majority being intra-operative bleedings. Hemostasis were achieved in all cases. Sixteen cases (18%) required conversion to thoracotomy/laparotomy due to intra-operative complications (25%) or technically challenging tumor dissections (75%). Post-operatively seventy-four patients (82%) were discharged home within 5 days, and all patients who required adjuvant therapy were able to commence their treatment within 3 days. There were no significant long-term complications.

Conclusions: With the advance of MIS instruments and techniques, MIS procedures can be safely performed in pediatric

oncology patients. While MIS has been established as a useful diagnostic tool in childhood cancer, it has also proven to be a safe approach for therapeutic resection of solid tumors in selected cases, with the potential benefit of rapid postoperative recovery and early commencement of adjuvant therapy.

IPSO02 SIOP19-0086 | Reliability of Ultrasound-Guided Core Needle Biopsy in Diagnostics of Pediatric Solid Tumors: A Retrospective Study

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Background/Objectives: Ultrasound-guided percutaneous core needle biopsy (PCNB) has been used more and more frequently in diagnostics of pediatric solid tumors in our center as it's less invasive than an incisional biopsy. However, reports relating to its reliability in clinical practice are limited. Therefore, we aim to investigate the reliability of ultrasound-guided PCNB in the pediatric population.

Design/Methods: A 7-year retrospective study including patients ≤ 18 years who underwent ultrasound-guided PCNB in our center was conducted. Initial clinical diagnoses, pathological diagnoses, diagnostic yield, accuracy, anesthetic requirements, and complications were assessed.

Results: From August 2012 to January 2019, PCNB under ultrasound guidance was performed on 435 patients. In 95 patients (21.8%), the initial clinical diagnoses were not consistent with pathology and management was changed according to PCNB reports. Local anesthesia was used in 344 cases and general anesthesia in 91. The diagnostic yield was 94.5%. Among them, 169 patients received operations and postoperative pathology was consistent with PCNB in 143 patients. The overall accuracy was 84.6%, with 99.2% in diagnosing malignancies and 68.8% in benign diseases. In 5 cases, the quality of the specimens was too poor for analysis. And in another 7 cases, there was not enough tumor tissue for a confident diagnosis. Severe complications occurred in 6 patients, whose tumors ruptured within 2 weeks after PCNB.

Conclusions: Ultrasound-guided PCNB is safe and effective in diagnosing pediatric solid tumors, especially in malignancies.

IPSO03 SIOP19-0527 | Preoperative 3D Reconstruction Images for Paediatric Tumours: Reliability, Advantages and Drawbacks

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Background/Objectives: Three-dimension (3D) reconstruction of preoperative CT or MRI images has recently emerged and has shown to improve the post-surgical morbidity of adult tumours. We aimed to analyse the advantages and drawbacks of preoperative images 3D reconstruction in paediatric tumours in order to determine its reliability.

Design/Methods: We conducted a prospective observational study from 2016 to 2019 of patients with solid thoraco-abdominal tumours having predictable surgical risks (difficulties due to vascular risks for resection of the whole tumour, i.e. neuroblastic and soft tissue tumours or for parenchyma preservation of the invaded organ, i.e; liver and kidney) on preoperative CT-scan or MRI. A comparison of 2D/3D and surgical findings was performed.

Results: Twenty-nine patients had a 3D reconstruction but three were not operated due to tumour progression or change in management and the reconstruction was performed after surgery for two. Twenty-four patients were finally included, with a median age at surgery of 68.2 months [13d-203m]. The tumour aetiology was neuroblastoma (n=7), renal tumour (n=7), hepatic tumour (n=4) and others (n=6, bone sarcoma of the iliac branch, abdominal lymph nodes of a recurrent testicular germ cell tumour, pseudo-inflammatory tumour of the omentum, thoracic lipoblastoma, desmoplastic tumour, solid and pseudopapillary tumour of the pancreas). Reconstruction was of poor quality in 2 patients with renal tumours because CT had no urological time. Discrepancies between 3D and surgical findings occurred in one patient with renal nodules infiltrating calices that was seen during the nephron sparing surgery but was not modeled by 3D. For all the other tumours, 3D improved the visualization and precise location of vessels during surgery.

Conclusions: High-quality CT-scan and MRI are mandatory to provide the best 3D reconstruction. 3D preoperative images are of significant help during surgery to better identify vascular structures within tumours and preserve parenchyma.

IPSO04 SIOP19-0582 | Robotic Surgery for Pediatric Tumors: Preliminary Results

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Background/Objectives: Whereas the use of robotics in adult oncology has become commonplace, it remains rarely used in pediatric oncology. We report our preliminary results of robotic surgery for pediatric tumors in the frame of the first prospective multidisciplinary robotic program dedicated to children.

Design/Methods: Procedures were performed between October 2016 - March 2019. Indications were submitted and approved by the tumor board. Patients treated according to SIOP/SIOPEN running protocols.

Results: 60 pediatric tumors were resected during 55 procedures in 51 patients at a median age of 8.5 years (0.5-17.9), representing 26% of the complete series of robotic surgery (n=208) and 25% of all the tumors operated during this time-frame. The series comprised:

- 10 nephrectomies (Wilms tumor n=9; renal sarcoma n=1)
- 4 partial nephrectomies (Wilms tumor n=3; tubulopapillary carcinoma n=1)
- 12 thoracic, abdominal or pelvic neuroectodermic tumors: four neuroblastoma, three ganglioneuroblastoma, five ganglioneuroma·
- 1 presacral neurofibroma (NF1)
- 4 bilateral adrenalectomies for Cushing in Carney (n=2) and McCune-Albright (n=2)
- 3 paraganglioma (aortocaval, lateroaortic and prerenal) and three pheochromocytoma
- 8 benign and 6 malignant thyroid tumors
- 2 mature teratoma (paravaginal and mediastinal)
- 1 total gastrectomy for inflammatory myofibroblastic tumor
- 1 thymoma

Three cases were converted for renal vein injury, sliding clip on the renal vein and major infiltration of the renal hilum (sarcoma). One emergency undocking was needed for bleeding. No injury of adjacent organ occurred. Resection was R0 in all cases. Median length of stay was 3 days (2-4). With a FU of 1 to 28 months, one patient presented a local recurrence and one died of CNS metastasis.

Conclusions: Robotic surgery for tumors in children is feasible and may be an option in highly selected cases. Indications have to be discussed in tumor boards with medical oncologists and radiologists in order to avoid widespread and uncontrolled application of the robotic approach.

IPSO05 SIOP19-1755 | An Orthotopic Pleural-based Tumor Xenograft Model to Test Novel Therapeutics for Pleuropulmonary Blastoma

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Background/Objectives: Preclinical models of pleural-based malignancy are hampered by technical limitations and cardiorespiratory tolerance of laboratory animals. Development of new treatment options for pleuropulmonary blastoma (PPB) have thus been limited by lack of representative disease models and known targets in *DICER1* loss-of-function-mediated tumors. We developed a novel method to generate orthotopic intra-thoracic patient-derived xenografts (PDXs), and used it to evaluate the effect of RNA Pol I inhibition in PPB.

Design/Methods: Fresh tumor tissue from a 4 year-old patient with type III PPB were engrafted in NSG (NOD.Cg-Prkdc^{scid}Il2rg^{tm1Wjl}/SzJ) mice. Subsequently, minced tumor slurry was serially passaged in NOD-SCID (NOD.CB17-Prkdc^{scid}/J) mice using a tunneled intra-thoracic injection method that avoided pneumothorax and respiratory embarrassment. Histopathological, radiographic and molecular characteristics of PDX and patient tumors were compared. Survival, respiratory rate and histopathology were compared between PDXs treated with oral CX-5461 versus controls.

Results: Only pre- and not post-chemotherapy tumor specimens engrafted. Orthotopic PDX models developed pleural-based tumors that recapitulated original disease features on micro-MRI and histopathology. The original germline *DICER1* frameshift deletion remained unchanged and no new hotspot mutations were detected on targeted next-generation sequencing over 6 serial passages. Median respiratory rate peaked at 212 breaths/min (32.5% over baseline) at limits of humane end-points at median 47.5 days (range: 37–64). Respiration also correlated with increase in tumor weight and time from injection and served as a surrogate marker of disease burden. Despite serial passaging, spontaneous metastases to brain and viscera did not develop. CX-5461 was well tolerated at test doses.

Conclusions: Intra-thoracic implantation of pleural-based tumors via a tunneled injection method was well tolerated in rodents, and facilitated the creation of a novel PDX model of

localized PPB. Radiographic, histopathological, and molecular tumor features were accurately recapitulated and maintained through serial passaging. RNA Pol I inhibition is a potential novel treatment strategy for PPB that warrants further study.

IPSO06 SIOP19-1715 | Microrna Expression Profiles in the Esophagus of Children with Caustic Stenosis: Is There A Pathway Towards Esophageal Cancer?

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Background/Objectives: Eighty percent of caustic ingestions occur in children; esophageal neoplasms may develop as a late complication of such injury. Thus, a comprehensive knowledge of the biological relationship between caustic ingestions and esophageal cancer is of major importance for identifying biomarkers that could facilitate early diagnosis and treatment. This study aimed to identify global microRNA expression changes in cells of the esophageal mucosa from children with caustic stenosis.

Design/Methods: Samples were divided into two groups according to the time elapsed after injury (Groups A and B, less and more than five years, respectively), compared with paired samples of normal esophageal tissue. miRNA expression profiles of tissues were determined and bioinformatic algorithms were applied to identify predicted miRNA target genes. Protein-protein interaction networks and molecular pathways involving genes and miRNAs were constructed.

Results: Thirteen miRNAs were significantly deregulated in Group A, of which nine were overexpressed and four under-expressed. In Group B, two miRNAs were over- and two were under-expressed. Of these deregulated miRNA in group B, miR-374 and miR-574 are strongly linked to esophageal cancer. Protein-protein interaction network analysis of both groups showed a number of miRNA-mRNAs in various signal transduction and transcription factor networks with genes strongly related to esophageal tumorigenesis.

Conclusions: There is no literature regarding microRNA expression following caustic ingestion in children. Thus, the miRNAs identified herein may help clarify the pathway of malignant transformation from caustic stenosis to esophageal cancer and could lead to the development of novel molecular markers of malignancy progression.

IPSO: FPS-GCT and Miscellaneous

IPSO07 SIOP19-0365 | Sacrococcygeal Teratomas: Midline Incisions Improve Cosmesis Without Compromising Outcomes

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Background/Objectives: Several studies have addressed the long-term functional, psychosexual & psychosocial outcomes following sacrococcygeal teratoma (SCT) excision. Although well reported that the classical chevron incision leaves a cosmetically unsatisfactory result, there is little in the literature focused on improving this outcome. In our institution the preference is to perform a midline incision, it is felt to improve appearance without compromising the oncological or functional outcome.

The aim of this study was to evaluate patient perceived cosmetic outcomes of the midline incision & compare the functional/oncological outcomes with those in the literature.

Design/Methods: All patients undergoing surgery for SCT between 1995-2016 were identified. Patient demographics, operation type, functional outcome and recurrence were all recorded. The primary outcome measure was patient/parent satisfaction with the cosmetic appearance. This was assessed using both qualitative/quantitative methodology. Following ethical approval parents were asked questions from two existing validated patient outcome questionnaires: "Patient and Observer Scar Assessment Scale" (POSAS) v2.0 and "Patient Scar Assessment Questionnaire"

Results: 43 patients underwent surgery for SCT during the study period. 25 had a midline incision (20 females/5 males). Median follow up was 10 years (range 2-23). 4/25 (16%) had a recurrence, 4/25 (16%) had persistent urological symptoms, and 6/25 (24%) had constipation requiring treatment. These outcomes are comparable or better than reported in the literature (recurrence 12.5–15%, urological symptoms 24–60%, Bowel dysfunction 25–36%). 14/25 (56%) returned the POSAS. Median score was 13 (range 7–43) on a 70 point scale (1=best, 70=worst). 13/14 (93%) reported the scar never affects the child's activities & 11/14 (79%) said they are not conscious of the scar.

Conclusions: Reducing the impact of scars is important. A midline incision should be considered for SCTs. This approach conveys comparable functional outcomes to the traditional chevron whilst improving the life-long cosmetic outcome for the child.

IPSO08 SIOP19-0449 | Surgery in Perforated Pediatric Intestinal Lymphoma

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Background/Objectives: Perforation is the most common surgical complication in pediatric intestinal lymphoma. During operation, many surgical decisions are debatable.

To address the location, timing, surgical management and outcome of perforation in the course of the disease of pediatric patients with intestinal lymphoma. The ultimate goal is to improve the multidisciplinary management of these cases

Design/Methods: This is a retrospective analysis of all pediatric patients (<18 years old) with intestinal lymphoma treated in our hospital between July 2007 and June 2017. Risk factors for perforation, type of management and outcome in cases of intestinal perforation were analyzed.

Results: The study included 240 patients with intestinal lymphoma. Perforation developed in 16 patients (6.7%) with a median age of 5.3 (range: 2.8e15.7) years. Most of the patients (92.5%) had Burkitt lymphoma. The ileum was the most common site of perforation (n = 10). Wall thickness initially ranged from 1.9 to 5.8 cm (median 3.9 cm). Perforation occurred at presentation (n = 2), during induction (n = 10), during maintenance chemotherapy (n = 2), or at relapse (n = 2). the median time of perforation was 26 days (range: 4e36 days) after chemotherapy initiation. Thirteen patients (81.3%) had free air and fluid in the peritoneal cavity, and two cases had localized air loculi at the site with perforation. One case had air in the bowel wall with necrosis denoting gangrene. Primary resection anastomosis was done in 12 patients. The resected specimen showed a viable tumor in ten patients. Wound infection (25%) and dehiscence (12.5%) were the most common postoperative complications. The 5-year overall and event-free survivals of patients with perforation were 78.6% and 71.4%, respectively, compared with 85.5% and 81.2% in non-perforated patients; the difference was not significant (p = 0.374 and p = 0.270, respectively).

Conclusions: Perforation is not an adverse prognostic factor for survival in pediatric intestinal lymphoma patients. Primary resection anastomosis seems to be a safe option if complete tumor resection is feasible.

IPSO09 SIOP19-0216 | Surgical Treatment of Castleman's Disease in Children: A Report of 10 Cases

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Background/Objectives: Castleman's disease is a rare reactive lymphadenopathy. The purpose of this article is to explore the surgical diagnosis and clinical features of Castleman's disease in children.

Design/Methods: The symptoms, examinations, treatment, prognosis and follow-up data of Castleman's disease confirmed by postoperative pathology in our hospital from July 2009 to July 2017 were retrospectively analyzed.

Results: A total of 10 patients were collected, including 4 males and 6 females, with an average age of 8.42 years (1.5 ~ 12.5 years). Local mass was found in 6 cases, including 1 of low back pain, 1 of vomiting and 2 of cough. Among the systemic symptoms, there were 3 cases with microcytic hypochromic anemia, including 1 with growth retardation and 1 with low fever. The lesions were single site, including 4 cases of neck or supraclavicular, 1 of mesocolon, 1 of ileum and 1 of posterior peritoneum, 2 of mediastinal origin and 1 of left axillary origin. Ultrasound showed that most tumors were hypoechoic, the cortex and medulla could not be distinguished clearly, the shape was not regular, the blood supply was abundant, some showed dendritic blood flow signals. MRI suggests isotonic or slightly longer T1/T2 signal shadows, which show the compressive effect on surrounding tissues. All were treated surgically. Generally, there are complete capsules, pink or dark purple. Postoperative pathology revealed 9 cases of hyaline vascular type and 1 case of plasma cell type. Immunohistochemistry showed that CD3 was positive (10/10), CD20 was positive (10/10), CD21 was positive (10/10), CD138 was positive (2/8), CD30 was negative (7/7), Ki-67 was positive (15-95%). The symptoms disappeared without recurrence or complications after following for 11 ~ 102 months.

Conclusions: Surgical treatment is effective for patients with hyaline vascular type and plasma cell type, the overall prognosis of the disease is favorable.

IPSO10 SIOP19-1682 | Counting the Cost of Premature Central Venous Access Device Removal

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Background/Objectives: Central venous access devices (CVADs) are important for the management of many

oncological and non-oncological conditions. CVAD dysfunction is financially and emotionally costly to the patient, family and healthcare system. It is an independent predictor of poor survival in children with cancer.

We hypothesised that there would be identifiable risk factors for premature CVAD removal, allowing targeted intervention.

Design/Methods: We retrospectively reviewed the records of all patients undergoing CVAD insertion between October 2014 and December 2018.

Results: CVADs were inserted 651 times in 475 children with a total of 18,495 catheter days (median 211). Childhood cancer was the indication for insertion in 503 (77.3%) devices. Premature removal occurred in 238 (36.6%).

CVADs were not more likely to be removed prematurely in children with cancer (32% vs 37% $p=0.766$). Removal for infection occurred more commonly in children with leukaemia than another oncological diagnosis (29.7% vs 18.0% $p=0.002$) or a non-oncological diagnosis (29.7% vs 16.2% $p=0.002$). Hickman lines failed 3 times earlier than portacaths (time to failure 651 ± 29 days vs 1990 ± 10 days (95% confidence limits), $p < 0.001$). Younger age at insertion was associated with increasing rates of line failure in children with a hickman line ($p < 0.001$) but not a portacath ($p = 0.86$). 128 patients (27%) underwent multiple line insertions (range 1-6, median 1) at an approximate procedural cost of £541,400.

Conclusions: Over the course of treatment CVADs in children with cancer are not at increased risk of dysfunction. However, leukemic children are at higher risk of infection and may benefit from focused prevention measures. A portacath should be considered in preference to a hickman line especially in younger patients requiring a shorter duration of treatment.

IPSO11 SIOP19-1229 | Percutaneous Trans-Thoracic Procedures in Children With Tumors of Thoracic Wall, Mediastinum and Lung. The Experience of a Single Institution

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Background/Objectives: While percutaneous trans-thoracic procedures (PTTP) are commonly performed in adults with tumors of thoracic wall, mediastinum and lung, the experience is limited in children, in whom however less invasive methods should be the choice for the diagnosis or the identification of small pulmonary nodules that need to be removed, sparing lung tissue. The results of the PTTP performed by the

interventional radiologists in our Pediatric Surgery Department are analyzed.

Design/Methods: CT-guided biopsies, utilizing a 64-slice CT scanner, with low-radiation dose, were performed applying the coaxial technique with 16-18G needles with a single tissue path. For localization of lung nodules before surgery, two 20G-hook wires were positioned beyond the nodule. CT images after each manipulation of the needles were obtained. US-guided biopsies were performed either with or without coaxial technique through a needle bracket. Younger patients required sedation. All patients underwent a chest radiogram two hours after the procedure and remained under observation for 24 hours.

Results: From January 2015 to March 2019, 23 procedures were performed in 22 patients (Age:16M-19Y): 6 patients underwent CT-guided biopsy (4 lung nodules, 2 mediastinal mass); 3 underwent 4 CT-guided hook-wire localization of pulmonary nodules, just before surgery; 13 underwent US-guided biopsy (posterior mediastinum 2; anterior mediastinum 5, thoracic/intrathoracic mass 5). Adequate core biopsies were obtained in all patients, except three, who underwent thoracoscopy/thoracotomy. The hook-wires were successfully positioned in all cases, as confirmed by histology. After the procedure, two patients presented perilesional hemorrhage and one pneumothorax, but they did not require treatment.

Conclusions: PTPP were successful in most patients, without significant complications. These techniques should be encouraged to avoid diagnostic aggressive surgical approaches in children with cancer. For all cases a multidisciplinary team is essential to discuss the indications and planning the procedures.

IPSO: FPS-LIVER AND PANCREAS

IPSO12 SIOP19-0816 | The Benefit of Indocyanine Green (ICG) Fluorescence Imaging to Treat Hepatoblastoma from Hepatectomy to Liver Transplantation in Pediatrics

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Background/Objectives: Currently, fluorescent imaging using indocyanine green fluorescence (ICG) that enables radical surgical resection in hepatoblastoma (HB) have beneficial uses, although its usage for young children is still limited. The purpose of this study is to examine the feasibility and safety by exploring a variety of cases.

Design/Methods: From 2015 to March 2019, fluorescence-guided surgery using ICG was performed for 11 cases of ten

hepatoblastoma patients. ICG (0.3mg/kg) was injected intravenously 24-48 h before the operation. With 805nm excitation spectrum and peak wavelength of the 835nm emission signal, intraoperative identification of biologic structures and demarcation of mass was conducted.

Results: ICG fluorescence-guided surgery was performed for hepatoblastoma (11 cases). Among these, there were 8 cases of anatomic resection, 2 cases of partial hepatectomy, and 1 case of liver transplantation. Three patients accompanied lung metastasis during, and one patient underwent lung surgery using ICG. The blood vessel invasion as well as the margin of the metastatic tumor was more sharply demarcated by ICG fluorescence, which also enabled successful transplantation. The median for Interval from ICG injection to surgery was 27 h (range, 20.5 – 45.7 h). The median for tumor size was 4.4 cm (range, 0.5 – 13.2 cm). All of the primary tumors had less than 2 mm of depth in the liver surface. According to the pathologic finding, the median for safety margin was secured for 1.5 mm (range, 0 – 1.5 mm), and there was no residual finding for the follow-up computed tomography (CT).

Conclusions: ICG fluorescence imaging for patients with HB was feasible and safe for tumor demarcation and enhancing the accuracy of radical tumor resection.

IPSO13 SIOP19-0056 | Clinical Application of Hisense Computer Assisted Surgery System (CAS) in Pediatric Patients with Giant Liver Tumors

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Background/Objectives: To evaluate the usefulness of a 3D visualization technology for diagnosis and preoperative surgical planning in precise hepatectomy for pediatric patients with giant liver tumors, Hisense Computer Assisted Surgery (CAS) System was studied.

Design/Methods: 68 pediatric patients, aged 2 months to 12 years old, with giant liver tumors involving the hepatic hilum underwent precise hepatectomy from April 2010 to December 2018 were enrolled. All patients received upper abdominal contrast-enhanced CT scanning before surgery. We used Hisense CAS (Hisense Computer Assisted Surgery System, Invented by Dong Qian' Group) System to reconstruct 3D liver, intrahepatic vascular system and gallbladder from the original enhanced CT Dicom files. The 3D reconstruction of liver and intrahepatic blood vessels of 48 patients was generated using the Hisense CAS system, while 20 patients using the CT Workstation as the control group. The Hisense CAS system presents image or video of digital liver model, assisted

diagnosis, preoperative planning and intra-operative navigation. The clinical outcomes were compared between the two groups.

Results: Hepatectomy of all 68 patients went well. The 3D reconstructing models clearly demonstrated the anatomic relationship of liver tumors and the intrahepatic vascular system, providing a better preoperative assessment and assisting surgeons in preoperative procedural planning. Anatomic hepatectomy was accomplished for all patients in the reconstruction group. The mean operation time was shorter in the reconstruction group (136.8 ± 20.8 min) than that in the control group (190.3 ± 33.6 min) ($p < 0.01$). The mean intraoperative blood loss was less in the reconstruction group (20.8 ± 18.4 ml) than that in the control group (53.5 ± 18.3 ml) ($p < 0.01$).

Conclusions: 3D visualization technology provides better preoperative assessment and allows individualized surgical planning, assisting precise hepatectomy in pediatric patients with giant liver tumors.

IPSO14 SIOP19-1225 | Feasibility and Outcomes After Non-Anatomical Resection in Diligently Selected Patients with Hepatoblastoma

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Background/Objectives: Complete surgical excision of hepatoblastoma is a prerequisite for better outcomes in hepatoblastoma. Hitherto, non-anatomical resections (NAR) have been dissuaded due to the high risk of residual disease and relapse. With refinement in radiological staging, preoperative chemotherapy and availability of various energy sources for parenchymal transection it may be feasible in judiciously selected patients to have complete clearance without residual disease. With a complete resection following NAR will the outcomes be similar to anatomical resection?

Design/Methods: The analysis included 131 consecutive patients diagnosed with liver tumors from January 2007 to October 2018, treated at a tertiary cancer center. Feasibility of NAR was based on the preoperative radiological evaluation of the location, size, relations to vessels and careful intraoperative assessment.

Results: Hemilobectomy was performed in 70 patients, extended resection in 25 and median hepatectomy were performed in three patients. A composite resection including partial hepatectomy and wedge excision for multifocal

disease was performed in five patients. NAR was performed in 28 patients. None of the patients with NAR had a positive parenchymal cut margin. The median duration of surgery was 4.50 hrs. for anatomical resection and 3.45 hrs. for NAR ($p = 0.0001$), the median blood loss was also less (150 ml vs. 250 ml) with NAR, although it did not reach statistical significance. Except for one transient biliary leak, there were no complications attributed to NAR. There were no local recurrences in patients with NAR, while one developed recurrence in the contralateral liver lobe and one had distant metastases. The 5-year overall and relapse-free survival for hepatoblastoma were 84.2% and 81.5% for anatomical resection while the NAR had 79.5% and 81.1% respectively ($p = \text{NS}$).

Conclusions: NAR is feasible with clear margins in carefully selected patients based on radiological and intraoperative assessment. It is not associated with added complications and outcomes are not inferior to anatomical resection.

IPSO15 SIOP19-0513 | Liver Transplantation and Liver Resection for Treatment of Hepatoblastoma

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Background/Objectives: Radical resection of hepatoblastoma can be obtained either conventionally by partial hepatectomy or by total hepatectomy with orthotopic liver transplantation thereafter. Liver transplantation has been increasingly performed for unresectable hepatoblastoma with acceptable results. Overall, outcomes have greatly improved because of advances in chemotherapy and innovations of surgical technologies, including the liver transplantation.

Design/Methods: The aim of this study was to study results of surgical treatment patients with hepatoblastoma in our center in period 2005 to 2018 years and compare outcome between liver resection group and liver transplantation group. Eighty six children with hepatoblastoma have entered the study. The age range at surgery was 8 months to 5.6 years (median 28 months). Five patients (5.8%) were PRETEXT group I, 30 (34.9%) group II, 42 (48.8%) group III and 9 (10.5%) group IV. Patients with PRETEXT IV tumors, multifocal tumors and tumors invading major vessels of the liver underwent liver transplantation.

Results: The overall 1-,3- and 5-year survival rate for 77 patients after liver resection and for 9 patients after liver transplantation in the study was 91.2%, 84.2%, 73.7% and 100%, 88.8%, 77.8%, respectively. Recurrence-free 1-,3- and 5-year survival rate for liver resection group and for liver transplantation group in the study was 87.7%, 78.9%, 71.9%

and 100%, 88.8%, 77.8%, respectively. Operative morbidity and mortality after liver resection and after liver transplantation were 13% and 11.1%, 10.4%, and 0%, respectively. Five patients died after extended hepatectomies. After a median follow-up of 3.8 years (range 1.5–5.3 years), 65 (75.6%) of the patients were tumor-free in remission.

Conclusions: Resection and transplantation technology in combination with chemotherapy allows to obtain a good long-term outcome. We did not find any difference in the long-term results between resection and transplantation groups although in transplantation group patients liver tumor lesion was more extensive.

IPSO16 SIOP19-0194 | Surgical Resection of Hepatoblastoma in the Unavailability of Liver Transplantation: Factors Affecting Local Recurrence

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Background/Objectives: To investigate the potential factors that contribute to local relapse after surgical resection of hepatoblastoma (HB).

Design/Methods: A retrospective study contained all patients with HB presented to our hospital and underwent non-transplant surgery between July 2007 and July 2018. Data were retrieved and analyzed regarding microscopic surgical resection margin, multifocality and extra-capsular tumor extension in correlation with local recurrence. These univariate factors were assessed by logistic regression.

Results: The study included 133 patients (75 males and 58 females) with a median age of 1.3 years (0.5 – 12.8). There were 99 (74.44%) cases standard risk and 34 (25.56%) cases high risk. Sixty seven patients (50.4%) underwent hemihepatectomy (41 right, 26 left), 39 (29.3%) segmentectomy, 17 (12.8%) extended hepatic resection and 10 (7.5%) mesohepatectomy. Follow up till the end of February 2019 revealed that 23 patients (23/133, 17.3%) had local recurrence, whereas the remaining 110 were locally disease free. Microscopic positive margin (R1) was observed in 29 patients, 8 of them had local relapse with p value= 0.097. Out of the 29 patients

with R1, 23 had tumor adherence to major vessels (11 on vena cava, 7 on portal vein and 5 on both). Regarding tumor multifocality, there were 12 cases with multifocal lesions, of them only 3 developed local recurrence with p value=0.459. Forty four patients had extra-capsular tumor extension on their postoperative pathological reports (12 cases had local relapse and 32 did not) with p value= 0.032.

Conclusions: Extra-capsular tumor extension was a significant prognostic factor of local relapse after resection of HB, and such observation requires evaluation in further studies. Multifocality and R1 had no significant impact on local recurrence. Resection with R1 in combination with systemic chemotherapy could be accepted as an alternative approach in the management of HB when transplantation is unavailable.

IPSO17 SIOP19-0862 | Pancreatectomies for Pediatric Pancreatic Tumors: A Single Institute Experience from 2007 to 2018

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Background/Objectives: To investigate the safety, feasibility, and complications of pancreatectomies for pediatric pancreatic tumors.

Design/Methods: A retrospective analysis of medical records of patients received pancreatectomies from January 2007 to January 2018 was conducted. Patients were retrospectively divided into the pancreatic head (n = 43), body (n = 18) and tail (n = 43) groups, among which perioperative factors and complications were compared.

Results: Seventy-two girls and 32 boys, with a median age of 119 months at diagnosis were enrolled. Diagnosis included solid pseudopapillary tumor (SPT, n = 73), pancreatoblastoma (PB, n = 19), neuroendocrine tumor (n = 9), and others. The main surgical procedures included pylorus preserving pancreaticoduodenectomy (n = 10), duodenum-preserving pancreas head resection (n = 25), middle segmental pancreatic resection (n = 15), distal pancreatectomy with splenectomy (DPS, n = 4), spleen-preserving distal pancreatectomy (SPDP, n = 37) and local enucleation (n = 13), with a median blood loss of 50 cm³ for the entire cohort. After comparison, no statistical significance was found in the incidences of short- and long-term complications between the three groups. There were eight patients with tumor thrombus in this study and all of the tumors were located in pancreatic tail, with the diagnosis of SPT (n = 1), PB (n = 6), and neuroendocrine tumor (n = 1). Two patients received DPS and six patients received SPDP procedure. After the follow-up, all of the eight patients were alive without disease.

Conclusions: PB was more frequent in young children, while SPT was more frequent during adolescence. Patients with PB could obtain long-term survival after chemotherapy and surgery. Pancreatectomies for pediatric pancreatic tumors were relatively difficult, and perioperative management might be challenging for surgeons. Organ-sparing resection procedure should be proposed as a treatment option for pediatric patients, and SPDP might be safe for patients with tumor thrombus.

IPSO18 SIOP19-1347 | Spleen Preserving Distal Pancreatectomy to Treat Pancreas Tumors in Children: Clinical Comparison of Splenic Vessel Preservation and Warshaw Technique

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Background/Objectives: Spleen preservation during distal pancreatectomy for benign or low-grade malignancy tumors in children has been proposed to decrease post splenectomy infection and hematologic disorders. The purpose of this study is to compare perioperative outcomes of two different techniques of spleen preserving distal pancreatectomy in children

Design/Methods: We retrospectively reviewed patients under 18 years of age with solid pseudopapillary neoplasm of pancreas who underwent spleen preserving distal pancreatectomy between November, 2002 and November, 2018 at a single center.

Results: There were 28 patients in total, of whom 17 patients (60.7%) underwent spleen preserving distal pancreatectomy with splenic vessel preservation (SVP) and 11 patients (39.3%) underwent Warshaw technique (WT). In the SVP and WT groups, the median size of mass were 4.2 cm (range, 1.8-12.5), 5.0 cm (range, 3.0-7.6); the median operation times were 217 minute (range, 120-540), 200 minute (range, 120-440); the median length of the postoperative hospital day were 9 days (range, 6-22), 10 days (range, 5-28) respectively. No significant difference was observed in postoperative pancreatic fistulas between two groups ($P=0.336$). Asymptomatic partial splenic infarctions were observed from computed tomography in 1 case (5.8%) in the SVP group, and 3 cases (27.3%) in the WT group. However, the splenic infarction was relieved without any invasive procedure.

Conclusions: Comparison of surgical outcome for WT to SVP was not inferior. Although SVP appears to be preferable techniques, WT can be performed safely and may be a feasible option for technically challenging cases.

IPSO: FPS-NEUROBLASTOMA AND SARCOMA

IPSO19 SIOP19-0776 | The Evaluation of the New Guideline for Assessing Image-Defined Risk Factors in the Low-Risk Protocol (JN-L-10) from the Japan Children's Cancer Group Neuroblastoma Committee

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Background/Objectives: The Japan Children's Cancer Group (JCCG) Neuroblastoma Committee (JNBSG) conducted the JN-L-10 study for low-risk patients using image-defined risk factors (IDRFs) as the main factor for determining treatment. According to the new guideline (NG) for assessing IDRFs (Brisse HJ, et al. Radiology, 2011), "even if the tumor is in contact with renal vessels only," this situation should be considered "IDRF present," despite being previously diagnosed as "IDRF not present." In this study, we re-evaluated the IDRF results in JN-L-10 in order to clarify the predictive capability of IDRFs for surgical complications before and after applying the NG.

Design/Methods: Of the 60 patients enrolled in JN-L-10, the 34 who underwent surgery rather than a biopsy were selected. We analyzed IDRFs (before and after applying the NG) in association with surgical complications.

Results: Of the 34 patients, 6 had been diagnosed with IDRFs before the NG. According to the NG, 19 patients were classified as IDRF present (IDRF could not be determined in 1 patient). Thirteen patients were therefore reassigned from IDRF not present to present by the NG. Surgical complications were observed in five patients. Of these, two and three patients with surgical complication were diagnosed with and without IDRFs before the NG, respectively. According to the NG, five and no patients were diagnosed with and without IDRFs, respectively.

Conclusions: The NG increased the ratio of patients with IDRFs from 18% to 58%. In addition, the NG improved the sensitivity of IDRFs for predicting surgical complications (40% to 100%) but reduced the specificity (86.2% to 50%). Thirteen patients would have been treated with chemotherapy instead of primary resection after applying the NG. Of these, 10 patients were actually safely cured by surgery alone.

IPSO20 SIOP19-0209 | Correlational Research Between Image Defined Risk Factor and INRG Staging and Surgical Complications of Retroperitoneal Neuroblastoma in Children

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Background/Objectives: To investigate the correlation and clinical significance of image defined risk factor (IDRF) and international neuroblastoma risk group (INRG) staging of neuroblastoma with operative complications in children undergoing retroperitoneal neuroblastoma resection.

Design/Methods: The clinical and imaging data of children with retroperitoneal neuroblastoma who underwent surgical resection from June 2016 to June 2017 in Beijing Children's Hospital were retrospectively analyzed. IDRF and stage were defined according to INRG standard. The correlation between the number of preoperative IDRF and the number of surgical complications was analyzed by Spearman correlation coefficient method (P value < 0.05 was statistically significant).

Results: A total of 68 cases were collected, including 32 boys and 36 girls. The age of onset ranged from 0 to 148 months, with an average of 38.3 ± 30.1 months. The number of preoperative IDRFs in each case ranged from 0 to 10, with a median of 2. There were 132 complications in 49 children; each case has 0 to 6 complications, with a median of 1.5. The number of operative complications was significantly correlated with the number of IDRF in each patient ($r = 0.775$, $P < 0.05$). Among the focal tumors, 9 cases were in L1 stage and 22 cases were in L2 stage. The total number of operative complications in L2 stage (44 items) was much larger than that in L1 stage (0 item).

Conclusions: IDRF has an important correlation with the occurrence of operative complications. INRG staging has a risk assessment value for the surgical treatment of focal lesions.

IPSO21 SIOP19-0674 | The "Delayed Local Treatment" Strategy is a Feasible and Effective Option for Multimodal Treatment of High-Risk Neuroblastoma – A Single Institution Experience

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Background/Objectives: The delayed local treatment approach (DL) is a unique strategy for high-risk neuroblastoma (HR-NB) in which tumor resection takes place after completing all chemotherapy courses including

myeloablative high-dose chemotherapy (HDC). In contrast to the conventional local treatment approach (CL) in which tumor resection is performed during induction chemotherapy, DL aims to increase the intensity of chemotherapy by minimizing the intervals of each course without being interrupted the surgery, and thereby improve the control of metastatic lesions, which is critical for the prolonged survival of the patient. We conducted an institutional review of HR-NB cases to assess the surgical outcome of patients treated with CL and DL.

Design/Methods: Data of forty-seven consecutive patients newly diagnosed of abdominal HR-NB that underwent resection of the primary tumor within the period 2002 to 2018 were retrospectively collected. Patients that never underwent tumor resection or those not treated with HDC were excluded. The timing of surgery was determined in a case-by-case manner based on the consensus of the multidisciplinary team, although cases that were enrolled in clinical trials were basically given surgery at the timing recommended in the protocol. We compared the surgical outcome of each approach.

Results: There were 25 patients in the DL group and 22 in CL. The mean value of operation time and blood loss were smaller in the DL group, although not significant. Immediate surgical complications and concurrent nephrectomies were significantly more frequent in the CL group. Recovery from surgery was quicker in patients in the DL group, assessed by the timing of postoperative oral feeding. 3 year EFS was 50.0% in DL and 53.9% in CL.

Conclusions: Surgery after HDC was safely managed with less frequent complications, without affecting the extent of resection, local control rate, EFS and OS of patients with abdominal HR-NB. Verification with a larger cohort is warranted.

IPSO22 SIOP19-1090 | The Prognostic Significance of Surgery and Radiotherapy for Cure in High Risk Neuroblastoma in South Africa

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Background/Objectives: Surgery is essential in the management of Neuroblastoma (NB) regardless of risk classification. In South Africa, the surgical management of NB is not standardised, especially in high-risk (HR) NB. A multicentre retrospective chart review was done to evaluate the impact of local therapies on outcomes.

Design/Methods: Patients treated between January 2000 and December 2014 in nine paediatric oncology units were included. Demographic data, disease stage, risk stratification, extent of surgery, administration of radiotherapy and outcomes were analysed.

Results: Data from 295 HR patients were included with a median age of 39.9 months. Only 35.6% of all HR patients underwent surgery and 16.3% received radiotherapy. Post-induction metastatic complete remission was achieved in 25.4%, of whom 82.6% (n=62) had surgical excision. Metastatic incomplete remission was achieved in 71.5%, but only 18.5% (n=39) had excisions. Patients with completely resected tumours had a 2-year OS of 46.4%, in contrast with those with incompletely resected tumours (51.4%) and inoperable tumours (16.2%) ($p < 0.001$). Two patients (0.6%) died from surgery related complications. In patients with HR disease who received tumour bed radiotherapy, the 2-year OS was 42.3% versus 24.1% without radiotherapy. Radiotherapy without surgery, in palliative setting, conferred a 2 year survival advantage (25.8% vs 17.3%, $p < 0.001$) in patients with HR disease. On multivariate analysis stage ($p < 0.0001$), INSS risk classification ($p < 0.0001$), post-induction complete remission rate ($p < 0.001$), degree of surgical resection ($p < 0.01$) and radiotherapy administration ($p < 0.001$) were identified as significant prognostic factors.

Conclusions: Surgery, whether complete or incomplete excision, confers a significant survival benefit in children with HR NB who have achieved metastatic complete remission. Radiotherapy alone improved local control and survival. Both treatment modalities should be implemented systematically in settings without access to autologous transplant or targeted therapy.

IPSO23 SIOP19-1448 | The Impact of Chemo-Sensitivity on Surgical Resection in MYCN-Amplified Neuroblastoma

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Background/Objectives: Considering neuroblastoma's heterogeneity, it is difficult to predict its response to neoadjuvant chemotherapy and its impact on surgery. We aimed to evaluate the chemo-sensitivity of a relatively homogenous group of MYCN-amplified (MYCNA) neuroblastoma and its impact on surgical resection.

Design/Methods: Patients with MYCNA neuroblastoma who received neoadjuvant chemotherapy followed by surgical resection performed at our centre were included. The tools of response evaluated included tumor volume (tVol) reduction and resolution of image-defined risk factor (IDRF) s based on radiological imaging, percentage tumor necrosis (tNec) on pathological scoring, and postoperative complications.

Results: Among 62 patients evaluated, mean age was 3.0 (range 0.9-11.8) years, primary tumors were distributed in the abdomen (n=59), pelvis (n=2) and thorax (n=1). Fourteen (22.6%) were stage L2, while 48 were stage M (6 had no IDRFs). Surgery was performed after median 4 (range 2-10) cycles of chemotherapy. Upon completion of neoadjuvant chemotherapy, 39 (62.9%) patients had >65% tVol reduction, 14 (22.6%) had 50-65% tVol reduction and 9 (14.5%) had <50% tVol reduction. Only 24 (42.9%) responded with fewer IDRFs, of these, 4 had complete resolution of IDRFs. Majority (83.9%) of patients still had IDRFs at surgery-time. IDRFs commonly encountered were encasement of renal pedicles (n=50), superior mesenteric artery (SMA)(n=46), celiac axis (n=45), and aorta/vena cava (n=44) and they remained refractory to resolution. Percentage tNec after chemotherapy was classified as >90%(n=27), 50-90%(n=20), and <50%(n=15). Patients with tVol reduction >65% had higher percentage tNec while those with <50% tVol reduction experienced poorer percentage tNec ($p = 0.007$). Surgical complications including nephrectomy (n=5), renal atrophy (n=3), chyle ascites (n=12), intestinal obstruction (n=5) and biliary stenosis (n=2) developed.

Conclusions: MYCN-amplified neuroblastomas are usually chemosensitive. Majority are good responders who experience high tumor volume reduction and percentage tumor necrosis. Persistent IDRFs such as encasement of renal pedicles, aorta/vena cava, SMA and celiac axis are commonly refractory to chemotherapy and remain a surgical challenge.

IPSO24 SIOP19-0541 | Correlation Between Imaging and Operative Findings in Children with Pulmonary Metastatic Osteosarcoma Undergoing Thoracotomy or Thoracoscopy: A Pediatric Surgical Oncology Research Collaborative Study

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Background/Objectives: Complete surgical resection of pulmonary disease is believed to be crucial to long-term survival in patients with metastatic osteosarcoma. In a multi-institutional review, we previously reported comparable outcomes in children with osteosarcoma who underwent metastasectomy by thoracoscopy and thoracotomy. The objective of this study was to correlate preoperative imaging results with surgical and histologic findings.

Design/Methods: A multi-institutional review was performed on 202 patients who underwent surgery between 1996-2018 at 13 North American hospitals participating in The Pediatric Surgical Oncology Research Collaborative.

Results: The median age was 13 years (range 2-28), and 60% were male. Bilateral surgery was performed in 20.8% (10/48) of patients who underwent thoracoscopy and 49.4% (76/154) who underwent thoracotomy. 5-year EFS after thoracotomy and thoracoscopy was similar in the entire cohort (34.2% vs 32.9, $p=0.81$) and in the subset of patients with 4 or fewer nodules per side (49.4% vs 42.5%, $p=0.91$). The median number of nodules (5 vs 1), viable malignant nodules (2 vs 1), and benign nodules (1 vs 0) removed by thoracotomy was greater than by thoracoscopy. In 27% of thoracotomy patients and 2% of thoracoscopy patients, the number of malignant nodules resected exceeded the number seen on pre-operative CT ($p<0.01$). The maximum lesion diameter ranged from 1-106 mm. 93% (125 of 134) of patients with maximum nodule size > 5 mm had viable metastatic disease, compared to 58% (7/12), 86% (12/14), 80% (8/10), and 50% (2/4) for those with nodule size of 4 mm, 3 mm, 2 mm and 1 mm respectively.

Conclusions: In patients with osteosarcoma, even small nodules may represent viable metastatic disease and should be resected. Unlike thoracoscopy, thoracotomy allows for removal of more viable nodules than seen on imaging, but this is not associated with a demonstrable improvement in event-free survival, and future prospective study is required.

IPSO25 SIOP19-1064 | Bilateral Anterior Thoracotomy: An Alternative for Bilateral Pulmonary Metastasectomy in Pediatric Patients with Osteosarcoma

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Background/Objectives: Osteosarcoma is the most common malignant bone tumor in children and adolescents. Up to 70% of patients will develop lung metastases. Techniques for resection include staged posterolateral thoracotomy (sPLT) and median sternotomy.

We present experience with bilateral pulmonary metastasectomy in 30 pediatric patients with osteosarcoma, using bilateral anterior thoracotomy (BAT). Describe advantages, drawbacks, and outcomes.

Design/Methods: Retrospective review: files from patients with metastatic OS at our Institution (2000-2018)

Results: Found 198 patients with OS, 83 had bilateral lung metastases. 43 underwent sPTL, 10 sternotomy, and 30 had BAT. Twenty boys, 10 girls, median age: 13 years (7-18). Most common primary site: distal femur (37%), histologic type: osteoblastic (66%), 69% of patients were limb-salvaged. All received neo and adjuvant chemotherapy. BAT without sternal transection was sufficient in >80% of cases. Surgical time: 2 - 6 hours. Average blood loss: 365 ml. Hospital length of stay: <7 days (77% of patients).

Interestingly, the number of metastases resected, significantly correlated with those identified by HR-CT-Scan (Spearman $R_s=0.99$, $p<0.001$, Kappa Index 96.3%).

There were no perioperative deaths. One patient required reoperation for bleeding control. Most common postoperative issues: pain ($n=15$), atelectasis ($n=5$), pneumothorax requiring longer drainage ($n=3$), and one case of chylothorax resolved with medical treatment. All lesions removed had histologic confirmation. All initiated chemo 7 - 10 days post-operatively. Necrosis did not correlate with survival (35% - Kaplan-Meier).

Conclusions: BAT is a safe alternative for bilateral metastasectomy in pediatric patients with osteosarcoma. Accuracy of preoperative diagnosis has increased. In this cohort, lesions at surgery correlated with image-defined. "Clamshell" thoracotomy is required in selected cases. Procedure is well tolerated, allows for simultaneous exploration of both lungs, and shortens the time needed to resume chemotherapy. Re-do thoracotomies are feasible. Anterior chest-wall lesions are technically difficult. Surgical prognostic factors in children with OS and lung metastases may be redefined.

IPSO26 SIOP19-0825 | Isolated Lung/Pleura Perfusion as a Treatment Option for Childhood Metastatic Bone Tumors

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Background/Objectives: To improve outcomes in patients with isolated lung metastases, it seems promising to use local chemotherapy administered by intraoperative isolated lung/pleura perfusion.

Aim: Determination of the effectiveness of metastasectomy, combined with isolated lung/pleura chemoperfusion under conditions of hyperoxia in children with malignant bone tumors.

Design/Methods: From March 2008 to January 2018, 30 patients underwent isolated lung/pleura perfusion with melphalan and cisplatin. The method of isolated chemoperfusion itself is a surgical procedure, during which the lung is temporarily turned off from the circulation and perfused with modified saline containing high concentrations of anticancer drug, which allows delivery of high doses of cytostatics. Antitumor drugs - melphalan and cisplatin are used for chemoperfusion (37 degrees C) of lungs and pleura, and cisplatin for hyperthermic (42 degrees C) chemoperfusion of pleura. Children aged 15-18 years old accounted for 46.7%. The primary tumor was osteogenic sarcoma in 67%, Ewing's sarcoma in 27%, primitive neuroectodermal tumors and undifferentiated sarcoma in 3% of each.

Results: Pulmonary, hematologic, and nonhematologic toxicities were recorded. Forty-five isolated lung/pleura perfusions were performed in 30 patients. The number of removed metastases was from 1 to 56 (average value of 9). Operative and postoperative mortality was 0%, and no systemic toxicity was encountered. The mean follow-up was 45 months; 3-year overall survival was $65.5 \pm 9.4\%$; progressive free survival was $40.5 \pm 10.5\%$. The median time to progression was 24 months (range 1 – 51 months). The median time to progression in lungs was 23 ± 14 months.

Conclusions: Chemoperfusion of lungs and pleura with cytostatics is a local method of treatment and can only be considered as a possible component of complex therapy that can improve the quality and increase the life expectancy of patients, especially with the exhausted possibility of other therapy methods.

IPSO: FPS-Renal Tumours

IPSO27 SIOP19-0110 | Open versus Minimally-Invasive Surgical Techniques in Pediatric Renal Tumors: A Population-Level Analysis

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Background/Objectives: Minimally invasive surgery (MIS) for adult tumor resections is widely performed. However, the use of MIS in pediatric cancer cases has been adopted more slowly. We hypothesized that adolescents are more likely than younger children to undergo MIS. We further hypothesized that there may be regional differences in surgical technique and that there may be differences in perioperative outcomes between techniques.

Design/Methods: We queried the 1998-2014 National Inpatient Sample (NIS), an all-payor database which consists of a 20% stratified probability sample of US hospitals based upon specific hospital demographics. Inclusion criteria were age < 18y, ICD-9 diagnostic code for renal tumor, and procedure code for open or laparoscopic (MIS) partial or radical nephrectomy. The primary outcome was surgical technique (open or MIS); secondary outcomes were in-hospital postoperative complications, length of stay, and inpatient costs. Primary predictor was age, grouped as younger children (0-9y) vs. adolescents (10-18y).

Results: 9,259 pediatric encounters were included: 91% 0-9y and 9% 10-18y. 50.7% were female. Adolescents underwent MIS more than young children (9.9 v. 1%; $p < 0.001$). The proportion of MIS was similar across region within age groups. Perioperative complications occurred in 13.3% of encounters; mean length of stay was 8.9 days and mean cost was \$34,457.68. The proportion of post-operative complications, mean hospital length of stay and mean cost were similar between the procedure types.

Conclusions: We observed that children and adolescents had overall MIS rates of 1% and 9.9%, respectively; these rates were stable across US census regions. We did not find an association between surgery type and inpatient length of stay

(LOS) on in-hospital surgical outcomes, including perioperative complications or mortality.

IPSO28 SIOP19-0349 | Adherence to Lymph Node Sampling Recommendations in Wilms Tumours Registered in the SIOP WT 2001 and Import Studies in the UK and Ireland

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Background/Objectives: Lymph node (LN) sampling is important for accurate staging in Wilms tumour (WT). Patients without LN sampling have an increased risk of relapse. The surgical guidelines of the SIOPWT2001 trial and the IMproving Population Outcomes for Renal Tumours of childhood (IMPORT) study mandate LN sampling, with IMPORT recommending sampling seven LNs. This study aims to describe adherence to protocol recommendations for LN sampling.

Design/Methods: Retrospective analysis of all surgical F3 case report forms received for UK/Irish patients registered in the SIOPWT2001 (2002-11) & IMPORT (2012-18) studies by 20 Principal Treatment Centres (PTCs) for childhood cancer that serve the UK/Ireland's population: ~12.4million children aged 0-14yrs. Eligible patients for this analysis were 1,091 unilateral WTs from a total of 1,186 registered WTs in two consecutive clinical studies spanning 16yrs enrolment.

Results: Median caseload/centre for all WTs was 3 patients/yr (range 1-10) in SIOPWT2001 and 4 pts/yr (range 1-11) in IMPORT. The surgical F3 form was available in 831 (76%) of unilateral cases, 746 (90%) had at least one LN sampled. 12% (62/520) patients had zero LNs sampled in SIOPWT2001, falling to 7% (23/311) in IMPORT ($p=0.03$, Fisher's exact test). Seven centres sampled LNs in all SIOPWT2001 patients and nine in IMPORT, with four centres achieving this in both studies. The mean and median number (with interquartile

range (IQR)) of LNs taken per patient were 3 and 3 (IQR 2-4) in SIOPWT2001 and 4 and 3 (IQR 2-5) in IMPORT. Only 11% of patients had 7 or more LNs sampled, 7%(36/520) in SIOP increasing to 18%(56/311) in IMPORT ($p<0.0001$)

Conclusions: Most patients (90%) with unilateral WT had at least one LN sampled but only 11% adhered to the current recommended number of seven. Surgical protocol adherence rates for LN sampling in the UK/Ireland are in line with international reported levels. This study demonstrates that further improvement is required.

IPSO29 SIOP19-1747 | Bilateral Wilms' Tumor: A Single Institution Experience

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Background/Objectives: Wilms tumor (WT) is the most common extracranial malignancy in Mexican children. It is considered a curable disease. However, distinct features make for a worse prognosis, one being bilateral renal involvement (stage V/BWT), which occurs in 5-8% of cases. These carry a higher risk of relapse, and end stage renal disease (ESRD). International treatment protocols have been designed aiming to improve life expectancy and manage comorbidities in these patients. We present herein our experience regarding the surgical and perioperative management of nine patients with BWT over a 10-year time frame, at a single Institution.

Design/Methods: The files of patients treated for BWT at the National Institute of Pediatrics (Mexico) between 2005 and 2015 were retrospectively reviewed.

Results: During the study time (10 years), 94 patients were treated for Wilms tumors, nine of which had BWT (9.5%). There were three boys and six girls, with a median age of 2 years (6 to 90 months). All patients received neoadjuvant chemotherapy and nephron sparing surgery (NSS) according to individual patient characteristics. Procedures included bilateral NSS (n=3), radical nephrectomy and contralateral NSS (n=4), and two patients underwent NSS on one side with radical nephrectomy, bench surgery, ex-vivo resection and auto-transplantation. Mean operating time was four hours, average blood loss was 250d cc, ICU stay was 3 days, and average hospital length of stay was 6 days. All patients had nephroblastomatosis. One patient relapsed, subsequently developed renal failure, and was transplanted. At present, all patients are disease free with normal renal function.

Conclusions: BWT is a relatively rare disease. Long-term survival can be achieved in up to 80% of patients with adequate multidisciplinary management. Incidence of relapse and renal failure is higher when compared to unilateral cases.

A robust surgical armamentarium is paramount for survival as to preserve enough healthy renal tissue to prevent renal failure.

IPSO30 SIOP19-0774 | Clinical Features and Prognosis of the Clear Cell Sarcoma of Kidney in Children - A Single Institute Experience of 43 Cases in 10 Years

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Background/Objectives: To expand the current knowledge about the clear cell sarcoma of kidney (CCSK), a rare but highly malignant tumor that commonly occurs in infants and young children.

Design/Methods: A retrospective review was conducted on medical records of 43 patients with CCSK, which were confirmed by pathology in Beijing Children's Hospital through March 2007 to October 2017.

Results: Forty-three patients were diagnosed with CCSK at a median age of 27 months, in which 7 patients suffered from the distant disease and the most common site of metastasis was the bone. For treatment, 43 patients underwent radical nephrectomy, 23 patients received preoperative chemotherapy, 31 patients received abdominal radiotherapy, and 40 patients received postoperative chemotherapy. After a median follow-up of 42 months, 9 patients died, 32 patients survived without disease, and 2 patients were undergoing treatment due to recurrence. Among the 9 dead patients, 7 died of tumor progression or recurrence and 2 died of severe complications after chemotherapy or surgery. The overall survival rate (OS) and event-free survival rate (EFS) of 3 years for the entire cohort were 80.9% and 71.1% respectively. Even for the patients with distant disease, the 3-year OS and EFS went to 71.4% and 57.1% respectively. Survival analysis revealed that the gross hematuria, tumor rupture and tumor thrombosis were related with poor outcomes.

Conclusions: CCSK is an extremely rare and highly malignant disease and there are no clear guidelines of treatment up to days. The multimodal therapy is recommended including surgery, chemotherapy and radiotherapy. Gross hematuria, tumor rupture and tumor thrombosis are adverse prognostic factors.

IPSO31 SIOP19-1687 | A Survey of Current Practices in the Management of Wilms Tumour in Africa

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Background/Objectives: Survival from Wilms tumour (WT) in sub-Saharan Africa remains dismal as a result of late presentation with advanced disease, failure to complete treatment and limited access to care. This study aims to investigate the current management of Wilms tumor by the members of Pan African Paediatric Surgical Association (PAPSA).

Design/Methods: After approval of the PAPSA executive board, a questionnaire was distributed individually to all paediatric surgeons attending the Biennial conference of PAPSA 2016 in Lagos, Nigeria.

Results: Forty-seven paediatric surgeons from 6 countries completed the questionnaire giving a response rate of 62%. Thirty-seven (78.8%) respondents managed less than 10 new cases of Wilms tumour yearly. Sixty-eight percentage (n=32) of the respondents see less than 25% of the cases in early stage. About 70%(n=33) of the respondents follow International Society of Paediatric Oncology (SIOP) protocol. Thirty-two respondents have computerised tomogram in their hospital but 32 (42%) of them still do routine intravenous urography. Only 6 (12.8%) of the respondents reported having radiotherapy in their institutions. There were only 10 (21.3%) respondents with tumour board in their hospital. Five-year survival of less than 50% was reported by almost half of the respondents. Only 5 (10.6%) of the respondent reported 5-year survival of greater than 75%. Some of the challenges reported by the respondent were delay presentation 22 (46.8%), lack of fund 18 (38.3%) and lack of radiotherapy 4 (8.5%).

Conclusions: This survey indicated that most patient with Wilm tumours presented late in Africa. Although SIOP protocol is use by most respondents, the 5-year survival is less than 50%. Earlier referral of patients to a tertiary care setting, and financial coverage of treatment may contribute to improve outcome and minimize over-staging of such patients.

IPSO32 SIOP19-0531 | Oncologic and Nephrologic Prognosis Impact of The Nephron Sparing Surgery Formula for Wilms Tumours in the Umbrella Protocol: A Single-Center Experience

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Background/Objectives: Definitions of nephron sparing surgery (NSS) procedures in Wilms tumor (WT) are not clear. The new UMBRELLA protocol offers a formula (NSS (X)-SRM (n)-PRM (n)-RRP (n%)) to better define the different

NSS parameters. We aimed to assess the advantages and limits of this new formula.

Design/Methods: This retrospective monocentric study included patients operated by NSS for WT from 1975 to 2018. We reviewed the medical records and applied the NSS formula to all included patients.

Results: Eighty kidneys were operated on 56 patients at a mean age of 19.2 months [4d-7.5y], with 49 partial nephrectomies (NSSA) and 31 tumorectomies (NSSB). The assessment of the surgical resection margins (SRM) showed a doubt in six cases (SRM1) but no tumour breach (SRM2). An intact pseudo-capsule along the resection margin with no renal parenchyma was found in four cases at pathological resection margins (PRM) assessment (PRM1) while a tumour breach (PRM2) was described in eight cases. Among the six patients with SRM1, only one was PRM2 with a pathological stage III. There were neither SRM1 nor SRM2 in seven PRM2 patients. At a mean follow-up of 96.8 months [15d-28.6y], eight patients had elevated blood pressure levels, and 10 had proteinuria. These two parameters were significantly increased in patients with a renal remaining parenchyma (RRP) of less than half of the initial total renal parenchyma. The serum creatinin level was normal for all except one patient.

Conclusions: The new NSS formula described all the crucial elements of NSS. RRP seemed essential for the evaluation of long-term renal function.

IPSO: FPS- The Robert Arceci Best of IPSO

IPSO33 SIOP19-0533 | Number of Lymph Nodes Sampled in SFCE/SIOP 2001 Nephroblastoma Patients: Is the Objective of More Than 6 Achievable?

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Background/Objectives: The number of lymph nodes (LN) that should be sampled during nephrectomy for Wilms tumour (WT) remains controversial but of utmost importance for staging purposes. We do know that the rate of LN invaded by tumour cells increase with the number of sampled LN. A cut-off of more than six LN has been proposed in the surgical

guidelines of SIOP-RTSG UMBRELLA protocol. The aim of this French national retrospective study of patients enrolled in SIOPWT2001 trial was to analyze the number of LN sampled according to their site and to determine the achievable number of LN sampling.

Design/Methods: We reviewed the data collected on central pathology review (CPR) forms from 2002 to 2014 for only unilateral WT. LN were divided whether they were clearly identified by surgeons at nephrectomy or discovered on the pathological nephrectomy specimen by pathologists.

Results: Among 594 patients with available data, 552 patients (253 male, 299 female) were finally included (467 localized, 85 metastatic). Median age at surgery (540 total and 12 partial nephrectomies) was 3.5 years [0-16]. The number of LN sampled was 0, 1-6, ≥ 7 and uncountable in 70 (12.7%), 280 (50.7%), 161 (29.2%) and 41 (7.4%) respectively. The mean number of LN sampled was ≥ 7 only for stage III and IV. The mean number of LN sampled by surgeons and pathologists was 2.8 [0-46] and 3.0 [0-35] for localized WT, 3.1 [0-20] and 4.5 [0-32] for metastatic WT, respectively. Overall, 71 (12.9%) patients had metastatic LN, 28 (39.4%) patients with metastatic LN only sampled by surgeons, 33 (46.5%) patients with metastatic LN only sampled by pathologists and 10 (14.1%) patients with metastatic LN sampled by both.

Conclusions: Exceeding six LN sampled may be achievable but only with the active collaboration of both surgeons and pathologists.

IPSO34 SIOP19-0094 | Relationship Between Tumor Response at Therapy Completion and Prognosis in Group III Rhabdomyosarcoma: A Report from the Children's Oncology Group

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Background/Objectives: Some patients with rhabdomyosarcoma (RMS) achieve less than a complete response despite protocol therapy. This study compares outcomes based upon tumor response at therapy completion.

Design/Methods: We studied 601 Group III patients who completed all protocol therapy without progressive disease in Children's Oncology Group studies ARST0531 (n=285) and D9803 (n=316). Response was determined by imaging; complete response (CR), partial response (PR: 50% decrease), or no response (NR: < 50% decrease and < 25% increase).

Results: Median age at diagnosis was 5.7 years (range 0.02–45.7). Common tumor sites were: parameningeal (PM) 49%, bladder/prostate 17%, and extremity 12%. CR was achieved in 60% of PM and 71% of non-PM patients ($p=0.006$). Additional factors associated with higher CR included participation in D9803 ($p<0.001$), tumor site ($p<0.001$), tumor ≤ 5 cm ($p=0.006$), T1 stage ($p=0.03$), alveolar histology ($p<0.001$) and FOXO1 fusion positive status ($p=0.003$). Participants with CR had improved 5-year FFS compared to PR/NR (75% vs 67%, $p=0.046$). This difference in FFS was restricted to PM sites (FFS of 75% with CR vs 63% with PR/NR, $p=0.04$), with no impact on FFS for non-PM sites ($p=0.56$). Tumor response had no impact on OS regardless of tumor site ($p=0.12$). Resection of end-of-therapy mass was performed in 26 patients with PR/NR but was not associated with FFS ($p=0.13$) or OS ($p=0.38$).

Conclusions: While 5-year FFS is improved in patients with PM RMS who achieve CR at the end of therapy, there was no similar benefit for patients with tumors in other primary sites, no improvement in OS, and no evidence of benefit to end-of-therapy mass excision.

IPSO35 SIOP19-1567 | Incidence, Pattern and Predictors of Cervical Lymph Node Metastases in Differentiated Thyroid Cancer in Children: A Longitudinal Study at a Single Centre

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Background/Objectives: Differentiated thyroid cancer (DTC) being rare in children, the emphasis justifiably has been on the primary tumor while the role of lymph node metastases is rather moderately described. This prospective data from a tertiary cancer centre appraises the incidence, pattern of spread and the predictors of cervical lymph node metastases in DTC.

Design/Methods: Between February 2007 & November 2018, 114 children underwent surgery for thyroid lesions of which 86 patients with DTC treated by a multidisciplinary team were evaluated.

Results: The median age of presentation was 12 years (4–17 years) with 57% female patients. Palpable cervical lymphadenopathy was present in 62.8% children. The median tumor size was 2.5cm (0.1 – 8.3 cm). 38.4% showed multifocal disease and 61.6% exhibited extrathyroid extension. 68 patients (79.1%) had metastases to the lymph nodes and 91.1% of involved nodes displayed perinodal extension. The presence of cervical lymph nodes on clinical or

radiological assessment was significantly associated with positive lymph nodes on pathology ($p<0.0001$). Metastases to the lateral nodes was significantly associated with presence of positive central compartment nodes ($p<0.0001$). The presence of multifocal disease ($p<0.0001$) and extrathyroid extension ($p=0.02$) were strongly associated with lymph node metastases while tumor size was irrelevant ($p=0.6$). Following therapy, 5 children (5.8%) developed local recurrence - 3 children had recurrence in the lymph nodes of the neck which was treated with surgery and radioactive iodine (RAI) therapy, while the other 2 were treated with RAI therapy exclusively for disease in the thyroid bed. With a median follow up of 50 months, all patients were alive at follow up.

Conclusions: Cervical lymph node metastases are seen in three-fourth patients with DTC and usually both lateral and central compartment lymph nodes are involved. Clinical or radiologically involved nodes harbour metastatic disease. Multifocal disease and extrathyroid extension portend cervical lymph node metastases.

IPSO36 SIOP19-0643 | LOCO-Regional Treatment of Para-Testicular Rhabdomyosarcoma (PRMS) A Report from the European Pediatric Soft-Tissue Sarcoma Group (EPSSG)

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Background/Objectives: PRMS is rare compared to benign scrotal pathology. Inappropriate first surgery (InFS) requires salvage treatments to maintain excellent outcomes but can add to morbidity. This study aims to determine the quality of loco-regional treatment and its implications for patient morbidity and survival.

Design/Methods: Analysis was performed on all non-metastatic PRMS patients enrolled in EpSSG RMS 2005 protocol. Aspects assessed: adherence to surgical guidelines and

impact of protocol violations, relapse analysis and survival outcomes.

Results: Analysis was performed on 237 patients. Median age was 9.0 years (range 0.4 – 22.6). InFS occurred in 74/237 (31.2%). These included tumorectomy without orchidectomy (38), trans-scrotal orchidectomy (17), and inappropriate initial biopsy (19). InFS resulted in the need to intensify chemotherapy (13) and local therapy to obtain similar over-all survival (OS) and event-free survival (EFS) as patients with appropriate initial surgery. Seventy-seven patients underwent pre-treatment re-excision, 59 after InFS, and 18 after appropriate surgery with residual tumour. Delayed surgery was required in 15 patients, 4 after InFS and 11 after appropriate surgery. Of 48 patients undergoing local radiotherapy 16 were in association with InFS. Risk of relapse was higher in ≥ 10 yr (21/25) especially tumours > 5 cm (18/21). Relapses were mainly loco-regional 16/25 (+/- metastatic), and 9/25 were metastatic only. One patient developed a second tumour. Relapse resulted in poor salvage (15/ 25 died) with almost all deaths in ≥ 10 yr (14/15). Nodal relapse did not occur when N1 nodes were identified at diagnosis. Five-year OS at age < 10 yr vs ≥ 10 yr was 99.0% and 86.6% ($p=0.0003$). EFS at age < 10 yr vs ≥ 10 yr was 95.8% and 79.5% ($p=0.0004$). After therapy, OS and EFS was similar for patients undergoing appropriate vs InFS.

Conclusions: Inappropriate first surgery results in the need to intensify therapy to maintain excellent OS and EFS, so better anticipation of malignancy is required.

IPSO37 SIOP19-1753 | Microscopic Positive Resection Margin after Hepatoblastoma Resection and Outcome of the Patients: The Japanese Study Group for Pediatric Liver Tumor (JPLT)-2 Study Report

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Background: Survival of patients with hepatoblastoma (HB) improved due to results of clinical JPLT trials that evaluated a combination of cisplatin/pirarubicin-based chemotherapy and surgical resection. In this study, we aimed to clarify whether complete surgical resection was correlated with prognosis of the HBL patients in the JPLT-2 study (1999-2012).

Methods: Out of the 361 JPLT-2 patients, 4 died before surgery, 14 were inoperative after preoperative chemotherapy and 6 were macroscopic positive resection. In this study, local recurrence and survival rates were analysed in 338 cases who underwent primary resection including liver transplantation.

Results: The 5-year EFS and OS of the patients ($n = 312$) with complete resection of primary tumor were 75.9% and 87.0%, respectively, and of those ($n = 25$) with microscopic marginal positive resection (microMPR) including microscopically positive resection were 59.1% and 83.0%, respectively. In the patients without distant metastasis, the 5-year EFS and OS of those ($n = 264$) with complete resection were 81.1% and 90.4%, whereas of those ($n = 22$) with microMPR were 62.5% and 90.9%, respectively. The EFS of patients with microMPR was significantly lower ($P < 0.05$), while OS was not. The local recurrence of the two groups were significantly difference (chi-square 8.323, $P < 0.01$).

Conclusion: In the context of cisplatin/pirarubicin-based chemotherapy, the presence of microMPR did influence the local recurrence but did not outcome. Although the complete resection of primary tumor should be aimed in the patients with HB, but microMPR does not necessitate mandatory second look surgery. The outcome of the patients with microMPR might be depend on postsurgical treatment or biology of the tumors.

IPSO38 SIOP19-1207 | Cavectomy without Reconstruction for Wilms' Tumor with Inferior Vena Cava Involvement

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Background/Objectives: We sought to determine the clinical profile of Wilms' tumor (WT) patients undergoing circumferential resection of inferior vena cava (IVC) without its replacement, and to evaluate their oncologic outcomes and procedure-related morbidity.

Design/Methods: Extensive literature review (1971-2018) and personal experience on WT patients receiving cavectomy without reconstruction as part of their surgical treatment for

IVC involvement. Data collected included patient demographics, stage of disease, laterality of renal primary, level of IVC extension, histopathology, treatment received, morbidity and mortality. We attempted to contact the study authors to obtain additional data and provide long-term outcomes.

Results: A total of 15 patients were identified (13 from 6 publications and 2 new cases from our own institution). Renal primary was right-sided in 13 and left-sided in 2 cases. Indications for cavectomy included complete IVC occlusion from tumor invasion (13) or adherence (2). IVC resection was performed en bloc with nephrectomy (12) or as second-look intervention (3). Type of cavectomy included resection of the infrarenal portion (4), and resection of the infrahepatic portion with ligation of left (9) or right renal vein (2). Four stage IV patients died, including 1 perioperative death. Of the remaining 11 survivors (1 stage II, 6 stage III, 3 stage IV, 1 stage V) aged 10-39 years at last follow-up (median, 21), 2 experienced an episode of lower extremity deep vein thrombosis (DVT) successfully managed with anticoagulation and compressive stockings.

Conclusions: In WT patients with IVC involvement and complete luminal occlusion, cavectomy without reconstruction is well tolerated because these patients have well-developed collaterals secondary to pre-existing IVC occlusion. Such procedure may allow for complete tumor clearance, thus obviating the need for postoperative radiation therapy. However, long-term follow-up is highly recommended, with special emphasis on prevention of, screening for, and treatment of these patients at risk of lower extremity DVT.

NURSES

Nurses: FPS 01-Support and education of nurses

N01 SIOP19-1285 | Situations Important to Capture Moral Distress in Paediatric Oncology – A National Cross-Sectional Survey

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Background/Objectives: The paediatric Moral Distress Scale-Revised (MDS-R) has been translated and culturally adapted to Swedish paediatric oncology. Cognitive interviews revealed five not captured situations: 1) Lack of time for conversations with patients/families, 2) Parents unrealistic expectations, 3) Not talk about death with a dying child, 4) Perform painful procedures, 5) Deciding on treatment/care when uncertain. The latter especially directed to medical doctors (MDs). The aim was to explore experiences of moral distress in five added situations, in the Swedish MDS-R, among healthcare professionals (HCPs) in paediatric oncology.

Design/Methods: In this national cross-sectional survey, HCPs at all paediatric oncology centres in Sweden were invited to answer the Swedish MDS-R. Focusing on the added situations (items), the analysis included descriptive statistics and non-parametric analysis of differences between professions. A MDS score for each item was calculated, i.e. intensity and frequency was multiplied.

Results: Participants included 278 HCPs (> 89%) of which 157 were registered nurses (RNs), 55 MDs, and 66 nursing assistants (NAs). NAs reported significantly lower frequency and higher intensity than RNs and MDs on all added items. RNs reported significantly higher frequency than the others on situations 1-4. MDs reported higher MDS-score than RNs and NAs in situation 5. In situation 1, both the intensity and frequency scores were high among all, with RNs rating the highest MDS-score. Item 1 had the second highest MDS-score of all 26 for all professional groups. Regarding situation 2, the level of disturbance was low but it occurred often, with RNs rating the highest MDS-score.

Conclusions: It is clear that RNs experience the situations more often while NAs find them more disturbing. The situation specifically directed towards MDs was experienced more frequently by MDs, thus also relevant for them. The results indicate that the added items are important to capture moral distress in paediatric oncology.

N02 SIOP19-0631 | The Lived Experience of Pediatric Oncology Nurses Caring for Terminally Ill Children: A Qualitative Study at the Uganda Cancer Institute

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Background/Objectives: Globally, more than 300,000 children are diagnosed with cancer annually. Majority of these children with cancer live in low- and middle-income countries (LMICs), and their chances of survival are often less than 20%. Due to this high acuity of terminally ill pediatric patients, nurses in LMICs are faced with suffering and death daily. The Uganda Cancer Institute (UCI) registers more than 500 new pediatric cases annually. The pediatric department has 14 dedicated pediatric oncology nurses who interact with the intense suffering of children and families and may too personally experience similar feelings.

Objective: Describe the lived experience of UCI pediatric oncology nurses who care for terminally ill children.

Design/Methods: A qualitative pilot study was conducted by in-depth, unstructured individual interviews with open-ended questions to evaluate the lived experiences of five UCI pediatric oncology nurses with at least two years of experience who consented to participate. Interviews were conducted over

two months by a single interviewer and one nurse, in English, at UCI. Interviews (60-90 minutes) were tape recorded, transcribed and analyzed using content analysis.

Results: The nurses' lived experiences were categorized in four main themes: attachment, repressed feelings, feeling of helplessness, and the need to be supported.

Conclusions: Findings from the pilot study confirmed that nurses who look after children with cancer face traumatic experiences and would benefit from support. For pediatric oncology nurses to continue to deliver the highest quality care to pediatric children with cancer and their families, nurses themselves must be afforded options for mutual support, systems to manage loss and organizational staffing provisions for best care practices to be realized.

N03 SIOP19-1507 | Ethical Decision-Making in Paediatric Oncology - Do Participation in Ethics Case Reflection Rounds Increase Perceptions of Involvement, Possibility to Influence, Responsibility And Understanding?

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Background/Objectives: In paediatric oncology difficult ethical decisions have to be made in daily practice. During organised/spontaneous ethics case reflection (ECR) rounds the healthcare team can deal with ethical issues. However, the ECR rounds are usually not formal decision making forums, leading to questions about healthcare professionals (HCPs) perceptions of involvement in ethical decision making. The overall aim of this study was to describe perceptions of decision making in relation to participation/non participation in ECR rounds among HCPs caring for children with cancer.

Design/Methods: HCPs, including medical doctors (MD), registered nurses (RN) and nursing assistants (NA) at three units at a University Hospital in Sweden, were invited to answer a study-specific questionnaire. Questions concerned ethical decision-making in relation to a specific patient case in three different scenarios: A) Being present in the ECR round, B) Not being present, C) No ECR round was conducted. In each case/scenario, HCPs rated perceptions on the following items: 1) involvement, 2) possibility to influence, 3) formal responsibility, 4) shared responsibility, 5) understanding of the ethical issue /the decision.

Results: All, except item 5, were scored significantly higher when HCPs (N=89) participated in an ECR round and perceptions of formal and shared responsibility were at the same levels. HCPs understanding of the ethical issue/decision was in general high regardless of being present in the ECR round. Even if participants were not present in the performed ECR

round, the understanding of the decision made was higher than if no ECR round was conducted.

Conclusions: As the research has demonstrated participation in ECR rounds, compared to non-participation, results in greater possibilities to be involved, to influence and to have formal/shared responsibility for ethical decisions in patient care. Thus, performing and participating in ECR rounds will most likely improve teamwork and quality of care.

N04 SIOP19-0404 | Establishing Essentials Nursing Competency for Pediatric Oncology Nurses at the Indus Hospital, Karachi, Pakistan

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Background/Objectives: Nursing competency is an essential skill required to accomplish defined nursing responsibilities. It is essential to reduce morbidities and errors and also has a direct relation on job attitudes, organizational commitments and professional associations. The need to have a competency based nursing program for pediatric oncology is pertinent throughout the profession to ensure patient safety and improved outcomes.

Design/Methods: Pediatric oncology requires special set of skills to effectively deal with treatment related issues while providing support to patient and family. Pediatric nurse's education department identified need to establish competency based educational courses. Two priority courses introduced in 2018; safe handling of chemotherapeutic drugs and administration (two day course) and handling central venous access devices (One day course). Courses were presented to participants in a classroom setting with various teaching aids used such as pre reading material, videos, presentations and group discussion. Evaluation was carried out by written assessment and visual demonstration for port-a catheter care/needle insertion.

Results: Effectiveness of workshops was assessed by measuring successful completion of course. Of nurses employed (n=70), 61% (n=43) have successfully certified in chemotherapy course and 55% (n=39) have successfully achieved competency for handling of central line, out of (4) number of CVAD handling and (4) chemotherapy administration courses offered. Evaluation of courses were acquired after completion of all courses.

Conclusions: Competency is central to nursing practice and it is a critical contemporary issue to ensure high quality nursing care. After the successful results and positive feedback from students many other competency based nursing programs are under considerations such as blood and blood product administration, palliative care, potassium supplement

administration/high alert medication administration and critical thinking in oncological emergencies. Working towards building competencies in our nursing staff ensures high quality safe care to children and also results in increased staff confidence in applying skills.

N05 SIOP19-0061 | Implementing a Distance-based Learning Curriculum for Pediatric Oncology Nurses in Sub-Saharan Africa

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Background/Objectives: A constant struggle for virtual education programs is how to best create a successful distance-learning environment, especially in low resource countries. Global HOPE Nursing has created a distance-based learning model for educating nurses caring for children with cancer in Sub-Saharan Africa.

Design/Methods: The Global HOPE Nursing curriculum is a series of courses developed to teach the basic principles of nursing care for a child with cancer. Each course involves a series of modules that include short video lectures, readings, critical thinking activities and case studies. Nurses learn about common types of childhood cancer and essential components of nursing care management. Key to nursing care is an extensive understanding of chemotherapy; this is taught as a separate course in the curriculum. To promote curriculum success, each course is implemented in various ways to meet the unique needs of nurses in different countries. Courses are taken online through MOODLE, using a computer notebook where materials are already downloaded, or by uploading onto personal computers. Nurses meet together by ZOOM or WhatsApp to present case studies and discuss nursing care.

Results: Over 35 nurses involved in the care of children with cancer in Sub-Saharan Africa are currently enrolled. Key to implementation of a structured curriculum is careful evaluation to determine success. Nurses complete a knowledge assessment and self-efficacy survey of their confidence in providing care before and after completion of each course. Final written and competency examinations must be passed for successful course completion. Course evaluations are completed by each nurse to provide feedback for ongoing changes needed to ensure content is appropriate for nursing care in Sub-Saharan Africa.

Conclusions: This pediatric oncology nursing education program is designed to promote excellence in nursing care. The

Global HOPE Nursing curriculum provides key tools essential for building a specialized workforce in childhood cancer nursing across Sub-Saharan Africa.

N06 SIOP19-1086 | Analysis of Latin American Pilot Series: Association Of Pediatric Hematology/Oncology Nurses Spanish Chemotherapy/Biotherapy Course

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Background/Objectives: In response to Latin American nurses' reported lack of comprehensive Spanish chemotherapy/biotherapy education, the Association of Pediatric Hematology/Oncology Nurses (APHON) Chemotherapy/Biotherapy Provider Course was adapted and translated into Spanish. We determined the course's appropriateness for nurses' education and practice levels through 4 pilots. Research questions included: 1) Do pass rates differ by test version and pilot location, and 2) Are nurse demographics and hospital characteristics significant predictors of pass rates?

Design/Methods: Four pilot courses were held (April 2016 to May 2017), with 203 nurses from Chile; Central American Hemato/Oncology Association [AHOPCA] Congress, U.S.; Latin American Society of Pediatric Oncology [SLAOP] Congress, Argentina; and Mexico. Descriptive statistics were calculated; Fisher's exact test and Wilcoxon rank sum test were applied to study the association between pass rates and nurse demographics/hospital characteristics; multivariate logistic regression models were developed to determine predictors of pass rates with data from 108 participants across 3 pilots (SLAOP ineligible – missing demographics).

Results: Pass rates ranged from 69%-100% (adjusted mean=82.1%). No significant differences by test version were found. When Chile was removed (100% pass rate), there was no significant difference by location. In multivariate logistic regression models, pediatric oncology frontline nurses were 10 times more likely to pass (Odds Ratio [OR]=9.86; 95% Confidence Interval [CI], 2.56-65.23; p=0.004) compared to "other". A subgroup of nurses dedicated to inpatient or outpatient oncology units was 7 times more likely to pass than those rotating between inpatient and outpatient (OR=6.79; 95% CI, 1.29-51.98; p=0.033); nurses from 5-year nursing programs were 6 times more likely to pass (OR=5.92; 95% CI, 1.30-33.15; p=0.028).

Conclusions: The Spanish APHON course was deemed appropriate for Latin American nurses' education and practice levels. Although pass rates did not differ by test version, sub-specialization and 5-year nursing programs were associated with successful test outcomes. Stringent pre-screening is now required for future courses.

N07 SIOP19-0323 | Improving Pediatric Oncology Nursing Care Beyond the Borders: The Significance of Regional Collaboration

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Background/Objectives: One way to reduce the global survival gap in childhood cancer is by investing time and energy in capacity building, especially for nurses. In LMIC, subspecialty training is rare due to lack of human resources and materiel. Indus Hospital, Karachi, Pakistan, has conducted a robust pediatric oncology nursing education program since 2009 with support of a My Child Matters grant from Sanofi Espoir Foundation. Our two-week pediatric oncology nursing course has attracted international attention and participants.

Design/Methods: To date, we have trained over 350 nurses (in 18 pediatric oncology nursing courses) including 10 international nurses: Ethiopia (2), Bangladesh (2), Iraq (5), and Tanzania (1). International graduates were asked to complete a survey asking: how has this course helped your care and career, and has this course impacted the quality of care in your organization?

Results: Six responses were received (all countries included). Positive impacts included, "Open mixing antibiotic room" and "Meeting with patient's family to increase the knowledge and explain what [are] the complication[s] of chemotherapy and the disease", and "Nursing documentations became better." Each noted they had initiated teaching/learning sessions, e.g., "I was able to orient the new nurses on chemotherapy, fever management and infection control". New practice changes included, "...rotation of nurses stop, we are maintaining PPE [personal protective equipment]". All believed that pediatric oncology nurses should have more international collaborative educational programs to help them learn.

Conclusions: The Indus nursing training is the first collaboration across LMIC borders that has proven to be beneficial for LMIC nurses caring for children with cancer. The international participants relate to the patient and families' socioeconomic circumstances and late stages of diagnosis. They learn to work efficiently and effectively within an environment of limited resources, which mirrors their own setting. Recommendations and back-home training from these nurses will help improve care across LMIC.

N08 SIOP19-0300 | The Role of a Training Initiative of Primary Healthcare Nurses on Early Detection and Supportive Care for Children with Cancer in Tanzania: Improving Referral

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Background/Objectives: Tanzania-Southern Highlands face severe referral delays of children with cancer. The consequences of this issue are shown by a mortality-rate of 21.9% of children with cancer coming from this region and addressed to the Pediatric Oncology Unit (POU) of the Muhimbili National Hospital (MNH). The main reason underlying these delays is the lack of knowledge of the primary healthcare professionals on pediatric cancers. In order to provide a response to this problem, the Tanzania National Nurses Association designed a project aiming to develop capacity building on early detection and supportive care. Reported herewith is the preliminary results of this project.

Design/Methods: The project is conceived into 2 phases: planning and implementation, cut into several activities: assessment survey; stakeholders mapping; monitoring and evaluation plan; conceiving *ad hoc* training material; training the trainers; conceiving a capacity building programme for primary care nurses; launching a community awareness campaign.

Results: Fifty- six nurses from Southern-Highland Zone participated in the survey[1]. One-hundred percent needed training on early detection and supportive care. Two nurses from the POU of MNH were identified as trainers and undergone a 2-day programme on capacity building. Seventy nurses attended the training programme. One-hundred posters on childhood cancers warning signs were distributed to 18 hospitals in 3 out of the 7 regions concerned by this project. During the 3 weeks following training, 5 children from Iringa, Njombe, Ruvuma were timely referred to MNH.

[1] during the Annual General Meeting of Tanzania National Nurses Association (TANNA)

Conclusions: Even if the implementation phase is still pending, these preliminary activities show an improvement in pediatric cancer early detection of primary care nurses. The evaluation process will serve to assess the impact of a training strategy in this geographical area to improve the outcome of children with cancer.

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Nurses: FPS 02-Approaches for improving care

N09 SIOP19-0029 | A Comprehensive Approach to Improving Patient Experience

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Background/Objectives: It has been well documented that exceptional patient family experience is positively correlated with better health outcomes. The literature suggests what makes a great patient experience includes the patient feeling comforted and listened to; involved in his/her care and given clear information. The importance of improving patient experience is well understood and developing strategies to assist healthcare teams and institutions to provide optimal quality care and the finest patient experience is crucial in today's healthcare environment. The duration and complexity of care and navigation required for children with cancer and their families further signifies the importance of positive patient experience. The aim of this quality program was to improve patient experience in a large pediatric hematology/oncology service line utilizing a comprehensive approach.

Design/Methods: In addition to selecting ambulatory and inpatient highly correlated focus questions for improvement; the comprehensive approach included healthcare team didactic and interactive educational workshops and sessions; staff support; staff engagement and recognition and parent focus groups. A patient experience nurse project manager coordinated and facilitated all aspects of the program. The nurse project manager role was crucial in the program's success as a dedicated leader responsible for unifying patient experience efforts across the service line. Tactical instructions utilized in the workshops included review of acknowledge, introduce, duration, explanation, thank you (AIDET) and the Teachback method: Asking a patient or family member to explain, in their own words, what they have learned during their visit.

Results: The total yearly improvement for both questions was 5.3% surpassing the anticipated 3% annual improvements. Additionally, ongoing yearly upward trends of improvement were noted.

Conclusions: The patient experience program improvement demonstrated that a comprehensive approach to improving pediatric hematology oncology patient family experience can be successful and may be replicated in expanded healthcare settings.

N10 SIOP19-0072 | Using Nursing Quality Indicators to Improve Care for Children with Cancer

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Background/Objectives: Global HOPE nurses at Baylor-Malawi involved in the care of children with cancer have established specific nursing quality indicators to measure important changes in nursing practice. Using a quality improvement approach to change and the Plan, Do, Study, Act (PDSA) cycle, projects were organized to measure excellence in care. An example of our approach to improving care for children with cancer demonstrates how nurses can lead practice change. In Malawi, all children receive chemotherapy through peripheral intravenous catheters (PIVC); this administration method increases risk for extravasation.

Design/Methods: Pre-assessment data revealed a high incidence of extravasation in two separate prevalence assessments done prior to practice change; 32% of 37 children and 42% of 24 children had evidence of extravasation. PIVC insertion attempts in 266 children over six-weeks ranged from 0 to >9 with 19% requiring three or more attempts. Using the PDSA cycle, the plan for practice change was based on evidence from published research and established PIVC care guidelines. Change strategies were developed and nurses completed education on proper PIVC insertion, dressing placement, and ongoing PIVC assessment. Proper dressing procedures using semi-transparent dressings to allow visualization of the PIVC were implemented. Nurses learned the Touch, Look and Compare (TLC) method to assure that the PIVC was intact.

Results: Practice change is measured by evaluating extravasation prevalence post implementation in May 2019. Other key metrics include duration of PIVC dwell time, number of attempts for PIVC placement, and percentage of PIVCs with phlebitis; these indicators are assessed during the post implementation period.

Conclusions: Using an organized approach to nursing practice change and establishing specific quality indicators to evaluate improved care are essentials aspects of the pediatric oncology nursing role. This project provides evidence that nursing quality indicators can be used in any setting including countries with limited resources.

N11 SIOP19-0408 | Achievement, and Pitfalls in Improving Pediatric Oncology Nursing Standards: Experience of Indus Hospital in a Public Private Partnership Project Supported by my Child Matters Grant

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Background/Objectives: Discrepancies in cure rate is vast between high income countries and low income countries. Lower middle income countries like Pakistan where estimated cancer incidences are 8000/year, the approach to improving cure rates is to build capacity in subspecialty. The Indus hospital with My Child Matters grant by Sanofi Aventis initiated a public private partnership project to improve standard of care being delivered in preexisting pediatric oncology units in 5 public hospitals.

Design/Methods: In 2016 My Child Matter's grant made way to improve oncology services in 5 hospitals across Pakistan with functioning pediatric oncology units. Nursing care is one discipline which has high impact on quality care. Alliance were established with Lahore (2), Multan (1), Karachi (1) and Islamabad (1) hospitals. Improving nursing standards was primary goal for which a tool was established keeping cultural context and limitation in mind under guidance of baseline nursing standards for Pediatric Oncology nursing. Through mentorship, educational training, on-site visits, off-site training and resource improvement capacity of pediatric oncology nurses was enhanced.

Results: After three year of mentoring and collaboration few of our achievements included nurses training (58), orientation of clinical indicators and flow of Pediatric oncology unit, but the results were less than what was anticipated. Various challenges were encountered during association with government organization, mainly insufficient funds allocation, lack of subspecialty training & work opportunities, obligatory rotational duties of trained individuals & lack of administrative focus.

Conclusions: Changing health care system and influencing government is a difficult task. Yet it can be achieved with persistence and great effort. For above mentioned challenges faced to improve nursing standard of pediatric oncology, we have identified various solution to be acted upon for better results as training alone will not bring anticipated outcomes and out of the box strategies are needed to achieve goals.

N12 SIOP19-0668 | Measuring the Quality of Childhood Cancer Care and Improving Trends in Pediatric Oncology Nursing Practices Through Clinical Indicators

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Background/Objectives: Quality care is the prerequisite for the essential outcome in childhood cancer. An alteration in any care can be resulted in clinical deterioration and even death. Pediatric Oncology nursing plays an essential role to achieve the goal of the treatment. Such nursing care can be assured by implementation of evidence based practices and continues monitoring of its outcomes. Clinical nursing indicator is one way of monitoring of quality nursing care. It is

define as a set of minimum standard for care expected from health care providers. It also help to design and develop future direction and improvements plans based on the trends.

The aim of this project was to monitor quality of childhood cancer care provided through clinical nursing indicator and outline ongoing improvement strategies.

Design/Methods: After extensive review of literature and team of expert we able to introduce the specialized nursing indicators for each oncology units i.e. Peads Oncology ward, Oncology day care, Peads high dependency unit and Peads intensive care unit. The project was run from Jan 2018 to Dec 2018.

Results: Eight Pediatric Oncology specific nursing indicator were established to measure the care which included extravasation, Post procedure complication, Medication error, Phlebitis, Traumatic Intrathecal, Transfusion reactions, Central Line Associated Blood Stream Infection (CLABSI) and Ventilator associated pneumonia (VAP). We analyze the result quarterly and seen marked reduction in VAP i.e. 2 to zero in last Quarter, similarly CLABSI reduced by 2 to 1, Post procedural complication decline to 3 to 1. Several multidisciplinary team approach and unit based strategies has been executed to achieve better outcome in care.

Conclusions: Clinical nursing indicators have proved to be a good measure for observing trends and identifying strategies to work on. It also enables nursing leadership to closely monitor any decline and act immediately to maintain and achieve the excellence in nursing practices.

N13 SIOP19-1758 | Improving Nursing Care in Africa: The GFAOP Nursing Group Experience

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Background/Objectives: In 2000, Pr Jean Lemerle created GFAOP (French African Pediatric Oncology Group) with the conviction that African children with cancer should be treated and cured in Africa by trained African teams. From 2000 to 2019, the group has grown from 6 units to 22 either in North or in sub-Saharan French speaking African countries.

Most of the sub-Saharan countries are facing the lake of appropriate training for health care professionals and the paucity of the organization in the healthcare system itself. This constantly challenges the care to children with cancer. So, one main concern of GFAOP is to provide caregivers in pediatric oncology with appropriate training.

Methods: The activities of the GFAOP nursing group are coordinated from Paris in collaboration with African nurses. Aims of the group are to improve nurse competence taking

into account their local working conditions and to improve collaboration between nurses and pediatricians.

Results: The GFAOP nursing group created in 2013 has initiated:

- One week intensive theoretical and practical training sessions for nurses (100 nurses from 18 countries have been trained within 3 sessions);
- 2 week session for 3 binomial (nurse and pediatrician) teams in France before opening a new unit.
- 2 month internship for 2 African nurses in France (9 nurses in 5 years)
- 1 week visit of French nurses to 5 African units
- Support to 4 twinning projects between African and French units.

In addition, following these trainings care documents were elaborated and distributed in the units.

Conclusion: Improvement in nursing care has been observed during these years especially concerning pain assessment, knowledge of the chemotherapy drugs and their management, communication and collaboration within the teams.

N14 SIOP19-0355 | Optimizing Care for High-Risk Neuroblastoma Patients Treated with Dinutuximab: Challenges for the Multidisciplinary Team

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Background/Objectives: Neuroblastoma is a rare sympathetic nervous system related cancer most frequently occurring in children younger than 5 year. Recently, the dinutuximab has been approved in Europe for treatment of patients with high-risk neuroblastoma. Dinutuximab has a unique adverse-effect profile including serious infusion reactions, pain and neurotoxicity for which premedication is required. An elastomeric pump is used for drug administration. Our multidisciplinary team was challenged to optimize treatment, develop educational programs for team members, patients and parents and to support home-infusion therapy.

To aim is to summarize keypoints in the multidisciplinary treatment of dinutuximab in neuroblastoma patients.

Design/Methods: For continuous improvement, a Plan-Do-Check-Act (PDCA) cycle is used in this care process.

Results: Several procedures were established and have been improved.

Compounding of dinutuximab

o Appropriate dilutions and additions of albumin to provide maximum stability

o Preparation of elastomeric pumps to allow continuous administration (at home).

Patient Care

o Assisting patients/parents in understanding immunotherapy and its side effects

o Information on the adverse effects of dinutuximab

o Prevention serious infusion reactions: hydration and pre-medication

o Prevention of neuropathic pain and peripheral neuropathy: opioids and gabapentin.

Team support:

o Guidelines with instructions on administration and monitoring, prevention and treatment of adverse events

o Bedside teaching on the use of elastomeric pumps.

Homecare support:

o Drug information sheets with instructions for premedication and handling side effects

o Written guide with information on how to use the pouch (including bathing and sleeping), temperature influences, pump height and monitoring of infusion progress

Conclusions: Complexity of therapeutic regimens with dinutuximab has expanded the role of pharmacists, oncologists, nurse educators, bedside- and homecare nurses.

Their collaboration and the development of appropriate treatment guidelines and educational programs is crucial in this high level treatment. Continuous improvement has led to clear and complete guidelines for team members, patients and parents.

Nurses: FPS 03-Tools for symptom reporting

N15 SIOP19-0967 | Acceptability of a Newly Developed Symptom Reporting App: Perspectives of Children and Parents

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Background/Objectives: Children receiving cancer treatment suffer multiple symptoms, yet often struggle to describe these symptoms. mHealth resources, including apps, offer developmentally meaningful, multi-sensory approaches to support symptom reporting. This study investigated the acceptability of an investigator-developed symptom-reporting app from perspectives of children receiving chemotherapy and their parents. This game-based app features a personalizable avatar to guide children to report symptoms using brief

checklists, drawing features, and short-answers. It also includes a drawing page, diary, and daily goals checklist.

Design/Methods: Children received a tablet computer containing the app to use between two clinical visits for chemotherapy. After using the app, children and parents participated in semi-structured interviews addressing the app's acceptability. Interview questions included child/parent perceptions about the app itself (positive and negative) and suggestions for improvement. Analysis was guided by descriptive, qualitative content analysis. Children's and parents' responses were analyzed separately and organized into categories and subcategories.

Results: Nineteen children (7 females) (median 8 years; range: 6-12) and 19 parents (18 females) (median 35 years; range: 26-48) participated. Children used the app a median of 4.5 days (range 1-12). Children and parents endorsed the app's facilitation of choices, expression, and creativity. Parents, specifically, addressed perceived benefits of the app as a resource to facilitate the child's voice in reporting his/her symptoms. Most children (n=10) and parents (n=8) denied dislikes about the app; several identified limited interactivity, difficulty remembering to complete the app daily and navigation-related issues. Children and parents suggested increasing interactivity and incentivization and enhancing navigation as potential improvements.

Conclusions: Data support preliminary acceptability the app as a resource for symptom reporting. Parents noted that it had potential clinical utility as an option for less intimidating, more accurate self-report of the child's symptoms. Responses are guiding continued development of the app prior to evaluation of efficacy as a resource to support symptom management.

N16 SIOP19-0537 | Daily Experiences of Children with Cancer Reported Through A Game-based App

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Background/Objectives: Childhood cancer disrupts children's day-to-day experiences. The purpose of this study was to analyze children's responses to two questions included in a daily symptom reporting app: "What is the best thing about today?" and "What is bothering you the most today?" Responses were part of a larger study evaluating the feasibility and acceptability of the app. Children used the app to record daily symptoms and answer short questions about their day.

Design/Methods: Children completed a trial of the app between visits at the hospital for chemotherapy. Daily responses to each question were analyzed using descriptive

qualitative content analysis with each response serving as a unit of analysis. Coding was completed by each author and reviewed together to reach agreement. Children's responses were organized into categories and subcategories.

Results: Participants were 19 children 6-12 years of age (median 8 years) (12 boys) receiving chemotherapy who used the app for a total of 83 days (median 4.5 days/child). Children provided 72 responses about the best thing about their day that were organized into nine categories: Activities (n=22), People (n=14), Food (n=9), Well-Being (n=9), School (n=7), Nothing (n=5), Object (n=4), Going Home (n=3), and Don't Know (n=1). Children provided 60 responses about the most bothersome aspect of their day that were organized into six categories: Nothing (n=22), Symptoms (n=17), Pain (n=7), Cancer Treatment (n=5), Day-to-Day Stuff (n=5), and People (n=4).

Conclusions: Children's responses provide perspective of the impact of cancer on their daily lives. Their responses indicate the importance of maintaining developmentally normal activities and family relationships. Children's responses further indicate the pervasiveness of the cancer experience, such as symptoms, even on days when children are away from the hospital. Mobile health apps can help children not only track symptoms but also reflect on their day. Clinicians can use this information to better understand children's experiences.

N17 SIOP19-0808 | Momentary- Versus Recall-Based Pain Rating in Children with Cancer: An Examination of the Correspondence Between Measurement Method

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Background/Objectives: Cancer pain is a significant problem for children and its accurate assessment is crucial to effective management. Recall measures are commonly used to assess pediatric cancer pain. However, these measures may be vulnerable to recall bias, which calls into question their utility in both clinical and research contexts. Our aim was to examine the extent to which recall ratings reflect actual pain levels in children with cancer.

Design/Methods: A secondary analysis of data from a published study establishing the validity and reliability of the *Pain Squad*TM pain assessment app was conducted. Ninety-two children with cancer (8-18 years, all disease types) were recruited from 4 Canadian pediatric tertiary care centers. Children completed momentary reports of pain twice daily using the app for 14 days. A paper-based measure of weekly recalled pain was completed on days 7 and 14 and an

assessment of judged change in pain over the sampling period was completed on day 14. Pearson correlations, intraclass correlation coefficients and Spearman rank correlations were computed between momentary and recalled pain reports on between-person and within-person bases to examine score correspondence and the impact of last and maximum pain on recalled pain intensity.

Results: On average, children reported momentary pain episodes as moderate in intensity. Between-person correspondence between momentary and recalled reports was moderate (0.44-0.68), however within-person correspondence was low (0.30-0.36). Judged change in pain across weeks was not significantly associated with computed change from momentary reports. Recalled pain intensity was significantly associated with the last and maximum momentary pain intensity reported.

Conclusions: The poor within-person correspondence between within momentary, recalled, and judged reports suggests that there is inaccuracy in children's cancer pain memories that may be influenced by the last and maximum pain they experienced. These findings have important implications for symptom-related clinical practice and research design in pediatric oncology.

N18 SIOP19-0326 | Instruments Utilized to Measure Symptom Distress Among Adolescents with Cancer - A Systematic Review

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Background/Objectives: Cancer symptom are the major cause of symptom distress among adolescents with cancer. To reduce symptom distress and improve quality of life, it's important to assess patients' levels of symptom distress. Currently, there is no consensus on tools assessing symptom distress for adolescents with cancer. Applying knowledge generated from systematic reviews can enhance healthcare providers' care quality and patients' life quality.

Design/Methods: We searched studies measured the symptom distress for adolescent with cancer and published in database of PubMed, EMBASE, Medline, CINAHL, PsychINFO, and Web of Science between 1999 and 2018.

Results: Thirty-nine studies were found. Of these, 21 studies utilized the Memorial Symptom Assessment Scale (MSAS) and 9 studies utilized the Symptom Distress Scale (SDS) to assess symptom distress. MSAS and SDS are multisymptom cancer assessment tools with mixed-response dimensions. Nausea and pain were the most reported symptom distress for studies using MSAS, and fatigue was the most reported

symptom distress for studies using SDS. Time to complete in MSAS is around 10 minutes and that in SDS is around 5 minutes.

Conclusions: MSAS and SDS are the two instruments that are most used among adolescents with cancer to evaluate the symptom distress. It takes 10-15 minutes to complete MSAS and 5 minutes to SDS. Some items in MSAS share the similar concept, but items in SDS may be more exclusive to each type of symptom distress, which demonstrates that SDS may concentrate on patients' main concerns. MSAS consisted of 5 psychosocial aspects of items and SDS only one item, indicating that SDS is relatively a physical oriented tool and MSAS covers more psychosocial aspects. SDS may be thus regarded as an efficient tool to quickly screen physical aspect of symptom distress for adolescents with cancer.

Nurses: FPS 04-Young people and survivors' experiences and research agendas in ped onc nursing

N19 SIOP19-0721 | Developing and Sustaining a Shared Culture of Care for Young People with Cancer

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Background/Objectives: The current global landscape for the delivery of young people's cancer care is complex and varied and can impact on cancer experience and outcome. There is limited robust evidence for justifying differences on how to develop, grow and sustain a culture of care, which is age-appropriate and best meets the needs of young people with cancer.

Design/Methods: A qualitative, mixed-methods study was conducted in four networks of care, comprising: 1) a narrative review examining the culture of care; 2) a multiple-site case study involving: semi-structured interviews with young people (n=29) and healthcare professionals (n=41); and 3) a variety of observation techniques in 24 hospitals, including tours, shadowing and focussed ethnography (total number of hours=120). A combination of thematic and framework analysis techniques were used to analyse the transcripts and field notes.

Results: A model depicting the barriers and facilitators to developing an age-appropriate and young person-centred culture of care emerged from the data. Four of the key themes driving the development and sustainability of a culture was the volume of young people accessing the service, the attitude of the workforce, effective leadership and the recognition that it takes time. Additional important aspects of culture included

communication, education and the underlying values of those delivering care.

Conclusions: Our findings present an evidence-based, comprehensive structure for understanding the development of a culture dedicated to delivering care to this age group. Understanding what the components of the culture of specialist care are will help healthcare professionals optimise care for young people, irrespective of variation, in terms of the type of clinical setting, or indeed the country. This is an important step towards reducing inequalities in cancer care, through the sharing of 'best practice' that seeks to inform cancer services to improve patient experience.

N20 SIOP19-1295 | Adolescents and Young Adults with Cancer Information and Support Preferences About Body Image, Relationships and Sexuality

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Background/Objectives: Adolescence and young adulthood is a crucial time for psychosexual identity development. A cancer diagnosis disrupts this process. Given the importance of sexuality development during these years, it is crucial to understand the factors that enable the information needs of young people to be appropriately identified and met. This study expands on previous findings that young people exhibited significant unmet needs around information provision on sex, body image, and relationships. We now explore information and support preferences regarding where, how, and from whom young people want to receive information on sex, body image and relationships.

Design/Methods: Four young people aged 24-26 years, with a previous cancer diagnosis aged 14-23 years attended an in-depth four-hour workshop. Participatory activities were employed to identify the questions young people had; their support/information preferences; and, their definition of intimacy. The framework approach was used to analyse workshop transcripts.

Results: Young people's preferences of information/support provision varied. They wanted trusted sources of information and while some preferred to have face-to-face discussions with healthcare professionals, others felt embarrassed and would prefer an online platform. All acknowledged that listening to peers with cancer talk about sexuality and

relationships would 'normalise' their questions. Feeling embarrassed (professionals and young people) was a barrier to an open discussion about their needs. Triggers for information and support included: partners (pressures/expectations); lack of sexual drive (managing side effects); body image (weight gain/loss, scars); physical constraints; and fertility concerns. Young people wanted access to information tailored to their needs.

Conclusions: Knowledge of sexuality, relationships, and body image concerns has an impact on development during this transition period into adulthood. Findings from this study highlight cancer-specific relationship and body image issues faced by young people and provide important direction to the development of interventions – a balance between professional and peer support is needed.

N21 SIOP19-0700 | Relationships Among the Hope, Psychological Well-Being and Health-Related Quality of Life in Childhood Cancer Survivors

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Background/Objectives: Childhood cancer survivors are afflicted with delayed health sequelae that jeopardise their psychological well-being and health-related quality of life (HRQOL). Increasing evidence indicates that hope promotes coping with cancer and enhances positive well-being of survivors. Nevertheless, no study has been conducted to examine the hope level, and investigate its relationship with the psychological well-being and HRQOL of Hong Kong Chinese childhood cancer survivors. This study aimed to (1) examine the hope level of Hong Kong Chinese childhood cancer survivors; and (2) investigate the interrelationships among hope, depressive symptoms, self-esteem and HRQOL of these survivors.

Design/Methods: A cross-sectional study was conducted. A total of 176 childhood cancer survivors aged 10–16 years who had their medical follow-up in a paediatric oncology outpatient clinic were recruited. Participants' hope level, HRQOL, depressive symptoms and self-esteem were assessed.

Results: The findings indicated that lower level of hope was associated with more depressive symptoms, lower self-esteem and HRQOL. The results of the study also showed that hope, depressive symptoms and self-esteem are the significant contributing factors of HRQOL. However, results of multiple regression analysis revealed that hope made the greatest contribution to HRQOL of these survivors.

Conclusions: This study showed that hope influences the psychological well-being and quality of life among childhood

cancer survivors. It is crucial for healthcare professionals to develop and evaluate hope-enhancing interventions for childhood cancer survivors so as to promote their psychological well-being and enhance their quality of life.

N22 SIOP19-0302 | Ten Years of Pediatric Oncology Nursing Research in Low- and Middle-Income Countries: A Literature Review

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Background/Objectives: The majority of children with cancer reside in low- and middle-income countries (L&MIC) where there is a lack of nursing research to generate culturally appropriate standards of care. This study reviewed ten years of pediatric oncology nursing research from L&MIC.

Design/Methods: A search was performed for grey literature and published research conducted in L&MIC (2008-2018) using five electronic databases (CINAHL, PubMed, Science Direct, EMBASE and Google Scholar). Articles in any of six languages were eligible for inclusion. Included studies were evaluated using the *Johns Hopkins Nursing Evidence-Based Practice Research Evidence Appraisal* (2017) for strength and quality of evidence. The study framework was precision health as defined by the US National Institutes of Health as a strategy to identify the evidence to inform (nursing practice) in consideration of child/family biological, environmental and cultural circumstances.

Results: Initially, 4,457 studies were identified; after eligibility review and removal of duplicates, 156 studies from 17 L&MIC were included. Studies were grouped according to WHO regions: Americas (n=57), Western Pacific (n=55), Eastern Mediterranean (n=20), Europe (n=17), South- Africa (n=6), and East Asia (n=1). Articles were published in English (n=84), Portuguese (n=38), Chinese (n=26), Spanish (n=7), and French (n=1), (none in Arabic). Evidence strength was generally level III—quantitative non-experimental (54/156) or qualitative (46/156) and most evidence quality was B (good). Participants and subjects included children/adolescents (e.g., fatigue, quality of life), or parents (e.g., stress, coping), or nurses (e.g., nursing practice, burnout).

Conclusions: Our findings highlight significant research efforts by L&MIC nurses, although a paucity of research from South-East Asia and Africa. Using a precision health framework and local research findings, L&MIC nurses can tailor care according to child/family circumstances in recognition of the challenges of complex cancer care in settings with poor

health care infrastructure, limited resources and unreliable access to childhood cancer care.

N23 SIOP19-0859 | Research Priorities in Paediatric Oncology Nursing: An African Perspective

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Background/Objectives: SIOP PODC baseline standards for paediatric oncology nursing in low- and middle-income countries (LMIC) recommend evidence-based policies/procedures to guide quality nursing care. LMICs often lack nursing policies/procedures for vital care including managing chemotherapy, clinical emergencies, and end-of-life care. Rigorous research is required for the development of evidence-based policies. The aim of this survey was to identify research priorities that are important to paediatric oncology nurses in Africa.

Design/Methods: Using a recognized approach to scope expertise of conference participants, a convenience sample of nurse attendees from Egypt, Tanzania, Morocco, Uganda, and Cameroon, completed an exercise at the 13th African continental SIOP conference in Cairo, Egypt, March 2019. They were asked to discuss their priorities for research in small groups, and using post-it notes, submit two research priorities to share with the larger group. All submissions were collected, collated and duplicates removed. A thematic analysis was conducted to first, group by research priorities, and second, by target stakeholders.

Results: Participants submitted 54 research priorities, 46 were retained after eliminating duplicates. Themes were: psychosocial support and counselling (n=30); professional practice (n=30); clinical care (n=5); education (n=7); access to care (n=6); end-of-life care (n=2); research funding (n=1); and cancer prevention (1). The target stakeholders included: nurses (41.3%), parents (37%), or children and parents (13.4%).

Conclusions: African paediatric oncology nurses identified 8 research priority themes, targeted towards key stakeholders. These research priorities go beyond the scope of hospital care to include advocacy and sustainability. Identifying questions that matter the most is taking the first step in revealing gaps in knowledge yet to be filled. African nurses caring for children and adolescents with cancer have significant interest in conducting research, however, they require capacity building,

mentoring and funding to engage in research and create guidelines for practice based on best evidence in consideration of local, resource-limited healthcare environments.

Nurses: FPS 05-Care settings and infection control

N24 SIOP19-0415 | Anesthesia for Short Procedures in Familiar Settings

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Background/Objectives: Anesthesia is one of the most stressful medical procedures a child can undergo during sickness and treatment. Research show that 50% experience a high level of anxiety and fear under induction of anesthesia. Anxiety and fear is influenced by the context with parents and healthcare professionals behavior, indicating that sensitivity and flexibility towards the child is essential. Assuming that a feeling of comfort and safety is more likely experienced in familiar settings with continuity in care supported by already known pediatric nurses, the pediatric oncology ward changed practice. Anesthesia for short procedures as bonemarrow aspiration followed by awakening in the unit is now performed in the pediatric oncology ward with reduced number of healthcare professionals instead of in the operation unit. Sparse knowledge exists on the meaning of a known context for the child, parents and healthcare professionals.

Aim: To explore children, parents and healthcare professionals experiences with anesthesia performed on the pediatric oncology ward Aalborg University hospital.

Design/Methods: Qualitative studydesign with 11 semistructured interviews with children aged 2-21 together with parents were conducted. Furthermore two focusgroup interviews with respectively pediatric oncology nurses, doctors and anaesthetist. All had experiences both from former and present practise.

Results: Overall finding is that children and parents are more at ease and feel more comfortable. They experience anesthesia as less traumatic when performed by few familiar healthcare professionals in a familiar setting that is not so clinical with high-technology equipment. Parents emphasize the importance of not leaving their child in an operating room, and the value of being close to their child during the procedure. The staff experience a flexible smooth team corporation and the time consumption is significantly reduced. Finally results indicate an improvement in the awakening from anesthesia with less agitated children.

Conclusions: Familiar settings seem to play an important role in reducing anxiety during anesthesia.

N25 SIOP19-0417 | Evaluation of Outreach Nurse Educator Roles; Supporting None Specialist Professionals Caring for Children with Cancer Closer to Home in England (United Kingdom, UK)

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Background/Objectives: Children with cancer should be cared for 'closer to home' when appropriate; however "Children's Key Worker Service Evaluation Project" (CLIC Sargent, 2015) found that families experience anxiety when community services and local hospitals appear to have limited knowledge of the needs of children with cancer. The role of the outreach Nurse Educator (NE) has been developed to work alongside Principal Treatment Centres (PTC) to deliver ongoing education to those professionals who do not regularly look after children with cancer.

Design/Methods: The role of the NE was developed by CLIC Sargent, reviewed by National Health Service (NHS) staff. One PTC in a region 'host' the NE role, offering an honorary contract; important for ongoing partnerships and credibility of the role. The first NE was employed by CLIC Sargent in March 2017, with funding from Stavros Niarchos Foundation. Since then 4 more NE posts have been established in England.

Results: 'Research-Partners' were appointed to evaluate the NE role. To date evaluation activity has focused on establishing robust monitoring systems of NE activity and consulting stakeholders online. The interim report indicates that NE roles are becoming established in regions of England, working locally with none specialist professionals. Professionals are highly satisfied with the service received from NE and see the activities they provide as effective and meeting their needs; associated with increased clinical knowledge, skills and confidence.

Conclusions: The NE role was developed to deliver ongoing education to those professionals who do not regularly look after children with cancer. This role has flexibility to offer appropriate, timely and relevant training and/or education at a convenient location. Evaluation thus far is positive although impact and outcomes for families and children is hard to measure; this will be addressed more thoroughly as the evaluation progresses.

N26 SIOP19-0789 | Feasibility of Outpatient Parenteral Antibiotic Therapy to Children with Cancer by a Portable Pump at Home

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Background/Objectives: Children with cancer suffer from numerous infections during the intensive treatment trajectory requiring intravenous antibiotics. In Denmark, we implemented a new pathway for children to be treated with outpatient intravenous antibiotics with a portable pump at home. Evidence is limited, and our objective was to describe the characteristics of patients and to evaluate the feasibility.

Design/Methods: This is a prospective, observational intervention study in February 2018–January 2019 at the Paediatric Haematology Oncology Department. Inclusion criteria were children cancer 0 months–18 years of age with uncomplicated infection and resided within 2 hours travel time. Patients received intravenous antibiotic treatment at home continuously by a portable pump, which was connected to the child and refilled with medication daily by a nurse at the inpatient ward and continued at home. Outcomes were adverse events and the families' experience with the outpatient therapy. Quantitative data were analysed with descriptive statistics. Qualitative data was collected by interviews and analysed with thematic method.

Results: The observation period included 323 days and 83 children, of which 76% had leukemia. The mean age was 6.5 years. There were 561 treatments with the pump in total, and mean number 1.7 children/daily (range 0–7). There were no adverse events. In the interviews, 21 children and their parents participated. All families described improved quality of life e.g. better sleep and appetite, more normal family life, and experience of freedom. Disadvantages described were that the pump was too heavy, difficulties finding a suitable bag for the pump, and time of transport.

Conclusions: Outpatient intravenous antibiotics at home was feasible and the families were highly satisfied despite the disadvantages. The pathway had an extensive effect on the department's organisation and staff resources, which was challenging. Changes in organisation and resource allocation should be considered to create an optimal setting for outpatient therapy.

N27 SIOP19-1114 | Administration Time for the First Dose of Antimicrobials in Episodes of Fever and Neutropenia in Children with Cancer, Before the Implementation of a New Protocol

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Background/Objectives: Early administration of antimicrobial (AM) is believed to be relevant in children with cancer, fever and neutropenia (FN). The recommendation is to administer the first dose of AM within the first hour since admission. The aim of this study is to determine the time from the moment that a child with FN is admitted to the hospital until they receive their first dose of AM and its relationship with clinical outcome before and after the implementation of a new protocol.

Design/Methods: Experimental, prospective and multicenter study to evaluate the time elapsed from the admission to the first dose of AM, comparing this variable by hospital and presentation location (Emergency Department/ Oncology Units) and evaluate the clinical outcomes by the following variables: days of fever, days of hospitalization, hypotension, transfer to intensive care unit, sepsis and mortality.

Results: A total of 156 episodes of FN were enrolled from 9 hospitals in Chile (April 2018–Feb 2019). The median time between admission and administration of the first dose of AM was 84 minutes (interquartile range: 60–138 minutes). The median time to AM administration was different between hospitals (60 vs. 205 minutes) and between presentation locations (Emergency Department vs. Oncology Units, median: 110 vs. 70 minutes, $P=0.0027$). Twenty-six percent of children received AM within 1 hour of admission. The administration of AM after 60 minutes was not associated with negative outcomes.

Conclusions: Time to AM administration was longer than the recommendation. The second phase of this study will be to prove the effects of the implementation of a new protocol to improve the equality and excellence of care in children with cancer and FN. Once these educational actions have been implemented, we will carry out a new assessment.

N29 SIOP19-0327 | Effectiveness of Implementing Strategies to Reduce Asparaginase Related Adverse Effects at Pediatric Oncology Daycare at the Indus Hospital Karachi Pakistan

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Background/Objectives: Asparaginase is an essential chemotherapeutic agent for the treatment of Acute Lymphoblastic Leukemia which can induce several adverse effects including pain and cellulitis. The increase incidences of cellulitis result in repeated hospitalization, increased cost

and delay in treatment. At our setup an average of three hundred patients are being administered asparaginase per month. In a period of six months sixteen patients reported with asparaginase induced cellulitis which doubled the cost of treatment from 14.98 USD to 28.53 USD. The objective of this study was to identify the cause of increased incidences and implement strategies to reduce incidences

Design/Methods: A Multidisciplinary team of trained professionals carried out root cause analysis which included Doctors and Nurses of Peads Oncology Daycare, Pharmacy, Supply Chain and Nursing Administration. Several rectifiable potential causes were identified and strategies were planned. Monthly data was recorded for every administration and complain to tract the reduction.

Results: Major potential causes identified were technique of administration, drug quality and reusable icepacks which were essential to ease pain associated with administration. All nurses who were assigned for administration were evaluated for their competency and intense training was provided, few nurses with satisfactory skills were allowed to administer. Visual aid was designed to reinforce proper technique and process of administration. Product analysis and preparation technique was analyzed and asepsis was emphasized. Reusable icepacks were replaced by low cost disposable individual gel icepacks.

Conclusions: The implementation of all strategies resulted in significant reduction in the incidences. There was a gross reduction from sixteen to eight in six months (2% to 0.6%). We also achieved great deal of pain reduction as pain scores reduced from 6/10 to 2/10. Overall good results were achieved to reduce the incidences and also aided in pain management. However, factors like hypersensitivities cannot be addressed as patient's response to drugs can be varied.

Nurses: FPS 06-Parent's perspectives and education of parents

N30 SIOP19-0286 | Nurse's Role on Managing Chemotherapy Side Effects to Children with Cancer at Muhimbili National Hospital, Tanzania: Parent Perspective

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Background/Objectives: **Background:** Nurses play a vital role in caring for children with cancer and are critical for chemotherapy preparation and administration in low-income countries like Tanzania. Nurses administering chemotherapy assume responsibility for teaching parents about and managing chemotherapy side effects.

Objective: Determine parent perspectives of nurse's role managing chemotherapy side effects for children with cancer at Muhimbili National Hospital (MNH).

Design/Methods: A cross-sectional survey was given to a convenient sample of parents/guardians with consent. The locally developed questionnaire included sections items on demographics, chemotherapy general information, management of side effects and health education. Data collection, entry (in real time with REDCap mobile application) and analysis were done with REDCap.

Results: Fifty parents/guardians participated (female 66.0%), and for 62.0%, this was their child's first admission. A majority (72.0%) were given general information about chemotherapy by doctor (52.8%), social worker (25.0%) and nurse (22.2%). Some parents (20%) reported they had not received information about potential side effects. Common side effects included nausea (86.0%), vomit (84.0%), loss of appetite (58.0%), fever (54.0%) and mucositis (24.0%). A majority (88.0%) reported that the side effects were adequately managed by nurses, although 18.0% reported the side effects were not managed on time because the nurses were always busy (44.4%), tended to ignore the complaint (33.3%), were few (22.2%) or chemo-nurse was not available at the moment (11.1%). Three quarters of participants agreed that they would like to be educated on chemotherapy side effects through group health education sessions (45.9%), leaflets (43.2%) and one-to-one talks before giving the child chemotherapy (24.3%)

Conclusions: The survey findings suggest that nurses have an effective role managing chemotherapy side effects of children with cancer at MNH. However, identified gaps needing improvement include managing side effects in a timely manner, increasing nursing staff, and improving consistent health education to parents/guardians on chemotherapy side effects.

N31 SIOP19-0142 | Parents Transitional Experience when Caretaking their Child with Cancer. A Secondary Analysis

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Background/Objectives: **Background:** The experience of caring for a child with cancer triggers profound and enduring changes for the parent living under this situation. As a result of these experiences, parents tend to reshape personal values, redefine goals, mobilize personal resources, develop skills, and even adapting personal identity.

Aim: To analyse the experience of parents who take care of a child with cancer considering the Theory of Transitions of Meleis.

Design/Methods: Considering the Transition Theory of Meleis, a qualitative secondary analysis was performed with data retrieved from a previous study using content analysis. A total of 17 parents of children with cancer in the active phase of treatment participated in this study. Data were collected through semi-structured interviews. NVivo 10 software was used for data processing.

Results: The parent who takes care of a child with cancer undergoes a transitional experience during parenthood. A child diagnosed with cancer prompts additional and increased responsibilities, leading to a change and extension of the parenting role. These study results enable to identify circumstances (personal, social and community) very likely to influence the transition process. Over time, parents were able to develop responses to meet the child's needs and provide complex caretaking activities. They develop complex skills and become a health professionals partner with a relevant expertise.

Conclusions: The produced knowledge confirms the transitional character and the complex nature of the experience and the imperative for regular follow-up by nurses, in order to provide effective professional help. It should be noted that this transition is particularly relevant for nursing regarding the exercise of parenting in the context of chronic disease in childhood.

N32 SIOP19-0097 | Initiation of Patient/Family Education Program for Pediatric Oncology Patients in the Indus Hospital Pediatric Complex Karachi Pakistan

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Background/Objectives: High rate of mortality and morbidity from cancer treatment, in LMIC is very common and a real challenge to manage. The reasons behind are inadequate parental education, knowledge regarding disease and treatment, availability and accessibility of pediatric oncology centers, affordability and locally available treatment. As it is well recognized that Patient/Family Education, is an essential part of comprehensive care concept. Many organizations in the higher income countries have designated patient/family education programs. Thus, The Indus Hospital pediatric complex Nursing services Karachi Pakistan initiated on developing a pediatric oncology patient education program for patients and their families.

Design/Methods: Strategies for Patient/Family Education in various hospitals of higher income countries was observed and a comprehensive plan was made according to our

domestic resources and circumstances using multidisciplinary approach involving different departments (Nursing services, psycho-social, Safety and security, infection prevention and control, Food and nutrition department). Lectures and interactive learning sessions in local language (group and individual) was implemented to teach the basics about cancer, chemotherapy, ways to prevent and control infection at home, facility orientation, social services available for patients and families and counseling services.

Results: Patient/Family Education (PFE) would be effective in reducing the rate of mortality and morbidity as it helps teach families about pediatric cancer and its treatment, and it lead to a reduction in patients' and families' anxieties. As it teaches patients and families about the significance of complying with cancer treatment, leading to decreased anxiety level and enhanced compliance.

Conclusions: Patient/Family Education is an essential way of enhancing Patient/Family knowledge regarding cancer and significance of complying with cancer treatment. Better patient understanding of health issues will improve compliance with treatments, help improve anxiety, and enable patients and their families to participate actively in their care and overall leading to improve quality of life.

N33 SIOP19-0673 | Raising the Bar: An Educational Handbook for Pediatric Patients, Parents and Nurses in Vietnam

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Background/Objectives: The Vietnam Nursing Project funded by My Child Matters Sanofi-Esper focuses on the development of a patient/parent educational handbook for newly diagnosed children. With limited evidence-based educational materials, it was imperative to create a written handbook to be used across thirteen pediatric oncology centers. Utilizing Orem's theory of self-care, parents and nurses were empowered to take a more active role. The Vietnamese nurses partnered with international nurse mentors for the project and their professional development.

Design/Methods: Nurse leaders from pediatric oncology centers across Vietnam met in August 2018 and February 2019. The project team identified the group's leader, established roles/responsibilities and set deadlines while working on content and artwork. The handbook focuses on three main areas:

cancer diagnosis and treatment, care of the child undergoing treatment, and psychosocial coping. Physicians, parents and other healthcare members critiqued the handbook. Prior to implementing the handbook at each center, nurses were required to attend training on how to teach caregivers the material.

Results: The standardized handbook provides every child with cancer and their parents the basic information to support their cancer journeys. Educational posters and a bedside teaching flipchart enhance the teaching by the nurses and health care team. Translation of the handbook into Vietnamese and English allows use outside of Vietnam. The nurse leadership team faced several challenges including a change in leadership, lack of networking between centers and overwhelming work commitments. Incorporating teamwork strategies such as in-person workshops, physician partnerships and a design to individualize the handbooks for each center led to a successful outcome.

Conclusions: The project has established best practices for patient/parent education and serves as a valuable platform for pediatric oncology nurses in Vietnam to gain additional knowledge and leadership skills. The project objectives were achieved through the collaborative relationships built between nurse leaders with the support of international nurse mentors.

N34 SIOP19-1328 | Effect of Video Based Education on Knowledge of Caregivers of Children with Acute Leukemia Regarding Prevention of Infection During Chemotherapy

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Background/Objectives: Background: Leukemia is the most common childhood cancer in India and largest contributor of cancer-related mortality. The use of chemotherapy has significantly improved survival rates but the associated myelosuppression and resultant infection remains major burden. Periodic counselling and teaching is provided to caregivers in relation to healthy habits but challenge lies in retention of information.

Objective: To compare the knowledge of caregivers of children with acute leukemia who received video based education in addition to routine care on prevention of infection during chemotherapy with those who received only routine care.

Design/Methods: This randomized controlled trial included 53 subjects attending pediatric daycare and out-patient department of a Tertiary care hospital, India. Subjects were randomized in experimental and control group using sequentially numbered opaque sealed envelopes. A self-structured knowledge questionnaire and video was used. Data was collected

at baseline, immediately after intervention and at 1 month. Telephonic assessment was done at 15 days and feedback of the video was obtained from experimental group immediately after the intervention.

Results: Statistically non-significant difference was found in baseline knowledge scores of both the groups. A significant difference was found in experimental group between baseline knowledge score (mean of 14.26) and scores immediately after intervention (mean of 23.56) and at 1 month (mean of 22.48) with p value <0.001. When compared the improvement was significantly better in experimental than control group (p<0.001 at both time intervals).

Usefulness of intervention was assessed, out of 27 participants in experimental group, 81% were extremely satisfied with the video, 41% preferred video as a mode of information when compared to written and verbal, 70% caregivers felt that watching video helped them to remember the information better and 92% participants gave the opinion that all topics were useful in the video.

Conclusions: The addition of video based education to routine chemotherapy care significantly improves the knowledge of caregivers and help them to retain information regarding the prevention of infections during chemotherapy.

N35 SIOP19-1260 | Prevalence of Oral Health Problems Among Children Undergoing Chemotherapy and Caregivers' Knowledge on Oral Health at Tertiary Care Hospital, New Delhi, India: A Survey

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Background/Objectives: Oral health is a vital component of general health and well-being of an individual. An important concern in childhood is to keep the oral cavity healthy in order to enhance the absorption of food and promote the sense of well-being. Children undergoing chemotherapy are more vulnerable to oral complications related to chemotherapy drugs. Their well-being is directly related to the nature and quality of the care provided by the caregivers.

Objectives: To identify the prevalence of oral health problems in children undergoing chemotherapy and caregivers' knowledge regarding oral health problems related to chemotherapy with a view to develop an informational booklet.

Design/Methods: A cross-sectional study was conducted among 120 children, aged 2-16 years visiting a tertiary care hospital, New Delhi, India. The children along with the caregivers were selected through convenient sampling technique. Data was collected during July-December 2018, using

validated screening examination sheet for oral cavity and self-developed knowledge questionnaire ($\alpha = 0.96$) regarding oral health problem related to chemotherapy for caregivers. Finally, oral health education booklet was prepared for the caregivers.

Results: Out of total children, 42% had one or more oral health problems namely; dental caries (21.6%), oral ulcers (15.8%) and grade III mucositis (5%). The mean knowledge scores of the caregivers was 13.7 ± 1.97 (8-18). More than half of the caregivers (53.4%) had good knowledge, 40.8% had satisfactory, while 3.3% had excellent and 2.5% had poor knowledge about oral health. Highly significant association of oral ulcer and mucositis with oral pain ($p=0.001$), child's ability to eat ($p=0.001$) and caregivers' education with prevalence of mucositis ($p=0.008$) was observed.

Conclusions: This study has strengthened the need for having frequent counselling session on oral health for caregivers and provision for oral health care consultation for the affected children.

Nurses: FPS 07-Complimentary care

N36 SIOP19-0301 | A Systematic Review of Questionnaires Assessing Complementary Health Approaches Use in Pediatric Oncology

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Background/Objectives: Complementary health approaches (CHA) can be defined as products and practices that are deemed to be outside the mainstream of healthcare. CHA are commonly used among children with cancer (CWC). Thus, it is critical that clinicians assess and discuss CHA use with children and their parents to ensure that the use of CHA is safe and helpful. However, a 2012 systematic review of measurement properties of CHA questionnaires in pediatrics found no questionnaire had been thoroughly validated. We updated that systematic review aiming to determine if an adequately validated CHA questionnaire that could be used in CWC exists.

Design/Methods: The search strategy was implemented in seven major electronic databases. The search period was from March 1, 2011 to May 31, 2018. Studies of all designs that reported on CHA questionnaires in pediatrics were included. Two researchers independently screened study titles, abstracts and full-texts. The methodological quality of studies and

measurement properties of the questionnaires were appraised using the Consensus-based Standards for the selection of health Measurement Instruments (COSMIN).

Results: Twenty-six studies were included. From these studies, 24 different CHA questionnaires were identified. Only two studies aimed to test measurement properties of two CHA questionnaires. One questionnaire was a generic self-administered (self- and proxy-reports) and the other was a CWC-specific interviewer-administered questionnaire. The COSMIN-rated methodological quality of both studies was 'inadequate' or 'doubtful' and both questionnaires were not thoroughly validated. However, both questionnaires are promising for adaptation and further validation.

Conclusions: The findings of this systematic review highlight the need for further research related to the development of a valid CHA questionnaire for use by CWC and their parents in clinical settings and for research. Next steps include the adaptation and validation of a current self- and proxy-report CHA questionnaire for use by CWC and their parents.

N37 SIOP19-0694 | Using a Musical Training to Promote Psychological Well-Being and Quality of Life Among Paediatric Survivors of Brain Tumours: A Qualitative Study

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Background/Objectives: Brain tumour and its treatment pose long-lasting adverse effects on the psychological well-being of paediatric survivors and consequently compromise their overall quality of life. This study aimed to explore the feasibility and acceptability of a musical training program in promoting the psychological well-being and quality of life for Hong Kong Chinese paediatric brain tumours survivors from the perspectives of survivors, their parents and interventionists. The intervention consisted of a weekly 45-minute musical training session for 52 weeks delivered by professional orchestral performers at the participants' homes.

Design/Methods: A phenomenological approach was employed. A total of 18 paediatric brain tumour survivors who received musical training and their parents (11 mothers and 7 fathers), and 6 interventionists were successfully interviewed. The attendance rate and retention rate were reported.

Results: Four main themes emerged from the results of the interviews, including overall satisfaction towards the training program, perceived benefits, acceptability of the training program, and recommendations for improvement. In general, all interviewed children, their parents, and interventionists were highly satisfied with the intervention. Many children found musical training to be helpful for inducing positive mood,

improving abilities in managing and expressing emotions, and eliciting a sense of achievement. Recommendations included an increase in frequency and duration of the intervention, and conducting a mini-concert after the completion of the program to offer an opportunity for the children to show their musical achievements to the public. In addition, a high attendance rate was reported, with about 80% of participants had attended all musical training sessions. Moreover, the retention rate was high, with 93.3% of participants completed the study.

Conclusions: Musical training was feasible to be conducted in the Hong Kong context. Additionally, musical training was well accepted by the paediatric brain tumour survivors as an intervention to promote their psychological well-being and quality of life.

N38 SIOP19-0018 | Effect of Recorded Maternal Voice on Child's Cooperation and Pain Perception During Bone Marrow Examination- A Double Blinded Randomized Controlled Trial

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Background/Objectives: To assess the effectiveness of recorded maternal voice on the child's cooperation and pain perception during bone marrow examination.

Design/Methods: This double-blinded randomized controlled trial included 46 children between 4 to 12 years of age with hematological malignancy, scheduled for bone marrow examination at tertiary care hospital of India. Clinical Trial Registry-India (CTRI) no. is CTRI/2018/09/015597. Subjects were enrolled into two groups (23 each) by stratified random sampling on the basis of the type of procedure scheduled to them. Maternal voice was recorded for 3 minutes before the procedure and headset was placed during the procedure, for all children but maternal voice was played only to intervention group by another person to blind the researcher. Child's cooperation for the entire procedure was recorded as video by researcher and later on, video was rated using Face Leg Activity Cry Consolability (FLACC) behavioral scale. Pain perception was rated by children using Wong-Baker faces pain rating scale.

Results: The results showed a significant difference in the level of child's cooperation with mean (SD) distress score of 7 (2) in control group and 4.52 (2.15) in the intervention group ($p=0.0002$). There was no significant difference in pain perception of control and intervention groups. Significant moderate positive correlation (0.31) was found in the child's distress and pain perception levels ($p=0.03$). There was significant negative association of age was found with the

child's distress (-0.30) and pain perception level (-0.33) at ($p=0.04, 0.02$) respectively.

Conclusions: Recorded maternal voice can significantly decrease the child's distress level thus improve the child's cooperation during bone marrow examination along with local anesthesia. As the child's cooperation increased, the child perceived less pain during the procedure. Older children were more cooperative and perceived less pain as compared to younger ones. Nurses are at an ideal position to implement this cost-effective, non-pharmacological intervention for children undergoing bone marrow examination.

PODC

PODC: BEST OF THE CONTINENTS

PODC01 SIOP19-1583 | Aiming for Zero Errors -Creating a Novel Open-Source Simple Platform for Highly Automated Patient-Specific Chemotherapy Prescriptions at Tumaini La Maisha/Muhimbili National Hospital, Tanzania

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Background/Objectives: Background: Manual prescription of chemotherapy is inherently error prone, requiring sub-specialist input. Errors increase toxicity and decrease treatment efficacy. Existing chemotherapy automation software is underdeveloped and prohibitively expensive for resource-limited countries.

Objective: To assess the viability of a comprehensive, cost-effective, open-source automated solution to minimize human error in chemotherapy prescription.

Design/Methods: Local protocols and a random sample of handwritten prescriptions were reviewed to classify prescribing errors. Questionnaires assessing automated options were sent to international pediatric oncology centres. We created a Microsoft ExcelTM software solution using embedded formulas to automate almost all complex protocol decisions, which included daily error log-assessment. All identified mistakes were neutralised by appropriate modifications. A structured questionnaire-based interview of key stakeholders was conducted to evaluate satisfaction.

Results: Twelve replies from international centres confirmed automated chemotherapy prescribing is neither universal nor comprehensive. Reviewing 124 randomly selected manual

chemotherapy sheets revealed over 200 errors, including, dosage, quantity, frequency, timing, modification errors, missing clinical information and protocol directed response-to-treatment (RTT) actions. Sixteen protocols required automation. Nine protocols were fully automated, along with a generic automation sheet for the 7 remaining protocols. These were created to replace all manual chemotherapy prescribing, automatically updating all recurring fields including name, diagnosis, stage, etc. Automation resulted in elimination of the following errors: upfront regimen, RTT choice, dose omission and drug modification related to clinical status. Since implementation in October 2018, 26 errors were logged and subsequently resolved. Active, daily error reporting and code modification removed this risk permanently. Other 'human' errors were reduced through training and user checklists. All 10 participants in our key stakeholder survey found chemotherapy prescribing safer for patients after implementation of our automated protocols.

Conclusions: Open-source automated sheets, with continual error surveillance, have the potential for zero-error chemotherapy prescribing for all.

PODC02 SIOP19-0538 | HIV Prevalence and Disease Outcome Among Patients with Childhood Cancer in Mbingo, Bango, and Mutengene Baptist Hospitals, Cameroon

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Background/Objectives: Cameroon has a population of 23.3 million, with 42.2% below 15 years. The Human Immunodeficiency Virus (HIV) prevalence amongst children aged 0-14 years is 0.4%. HIV is routinely tested for every child with cancer treated in the Cameroon Baptist Convention Health Services (CBCHS) Childhood Cancer Programme at Mutengene, Mbingo and Bango Baptist Hospitals in the Southwest and Northwest regions. Childhood cancer patients with HIV are treated with the same protocol as HIV negative cases. Our aim is to evaluate the prevalence of HIV among children diagnosed with cancer and the outcome.

Design/Methods: Retrospective review of patients records from 2003-2016 on our database (POND). We analyzed all HIV positive cases for cancer type, and length of survival. Records review was conducted for information on antiretroviral therapy (ART). Data was analyzed on SPSS Version 25. An alpha level of 0.05 was considered for statistical significance.

Results: A total of 1,513 patients were registered, 1,204 (79.6%) were tested for HIV. Twenty two (1.8%) patients were positive for HIV, with a female to male ratio of 1:1.2 and the median age of 7 years. The HIV prevalence by cancer type was as follows: Burkitt lymphoma (1.3%), Kaposi sarcoma (38.9%) and Retinoblastoma (0.9%). The distribution of childhood cancer patients with HIV by stage was: stage I (9.1%), stage II (13.6%), stage III (45.5%) and stage IV (9.1%). There was record of ART for 68.8% of HIV positive cases. Fifty percent were alive with a follow up range of 1-120 months (median 16 months). Survival was better amongst patients on ART (Fisher's exact = 0.006).

Conclusions: The prevalence of HIV (1.8%) was 4.5 times higher in cancer patients than in the general population (0.4%). Outcome is better amongst patients who receive ART.

PODC03 SIOP19-0080 | Pediatric Classical Hodgkin Lymphoma- A PET/CT Based Study from Tertiary Care Center of Pakistan

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Background/Objectives: To determine the efficacy of COP-Dac/ABVD regimen for pediatric Classical Hodgkin Lymphoma (CHL) based on PET/CT for staging and interim reassessment and their event free (EFS) and overall survival (OS).

Design/Methods: Patients of genders both, aged 1-17 years diagnosed as Classical Hodgkin Lymphoma from September 2013 till July 2017 were enrolled and retrospectively analyzed. Patients who either died or abandoned before treatment were excluded. Ann Arbor staging was used using PET/CT as imaging modality. Stage IA/B, IIA were grouped in Treatment Group (TG)-1, Stage IIB, IIIB in TG-2 and Stage IIIBS, IVA/BS in TG-3. An outpatient based chemotherapy regimen- COPDac alternating with ABVD was given. TG-1 received 3 cycles, TG-2 received 5 cycles and TG-3 got 7 cycles of chemotherapy. Reassessment PET/CT was done in all three groups after 3 cycles (COPDac/ABVD/COPDac) and classified as adequate, inadequate response or progression. Patients with inadequate response received radiation at the end of chemotherapy. Progressive patients were off protocol. Deaths, abandonment during treatment, progression or relapses were events for EFS.

Results: Total 209 patients included. M:F ratio was 5:1. Median age was 7 years. 21% were included in TG-1 (44/209) and TG-2 (43/209) whereas 58% in TG-3 (122/209). Stage 1A/B were 10 and IIA -32. Stage IIB were 12 and IIIB - 31. Stage IIIB were 55 and IVA/B - 67. Adequate response was 90% (40/44) in TG1, 86% (37/43) in TG2 and 60% (73/122) in TG3. Radiation was given in 7% of TG-1 (3/44) and

TG-2 (3/43). TG-3 required radiation in 28%(34/122). Relapse rate was 5% in TG1 and TG-2.10% (12/122) of TG-3 showed progression or relapse. OS is 89% (TG1-93%, TG2-95% and TG3-85%). EFS is 85% (TG1-89%, TG2-93% and TG3-81%).

Conclusions: COPDac/ ABVD regimen is an effective and comparable chemotherapy regimen with less short term toxicity and excellent event free and overall survival.

PODC04 SIOP19-0131 | Intravascular Extension of Renal Tumours in Children: Influence of Contemporary Treatment on Outcomes

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Background/Objectives: The aim of this study was to review the contemporary management of children with renal tumors especially Wilms' tumour who had intravascular tumor extension.

Design/Methods: The data regarding presentation, treatment received, surgical management, complications and outcomes were evaluated. All patients received neoadjuvant chemotherapy except in three.

Results: The study cohort included 51 patients with intravascular thrombus treated from October 2005 to November 2018. The thrombus extent at presentation was: renal vein – 8, Infrahepatic inferior vena cava (IVC) -22, retrohepatic IVC -9, suprahepatic IVC -1, atrium -9 and ventricle-2. The histological tumor type was Wilms (48), clear cell sarcoma of kidney (1), primitive neuroectodermal tumor (1) and renal cell carcinoma (1). There was complete clearance of IVC in 10/48 patients with neoadjuvant chemotherapy. Regression of the thrombus occurred in 26/48 patients while it was stable in 21 and progression occurred in one. Due to regression of the tumor thrombus from the atrium, cardiopulmonary bypass could be avoided in 4 patients. In all patients the thrombus had to be dissected off from the tunica intima due to dense fibrosis around it. The postoperative complication included blood loss in five patients and intestinal obstruction in two. There was a postoperative mortality secondary to abdominal compartment syndrome. There were seven disease relapses, local alone in five and distant alone in two. The 4-year OS and EFS for Wilms tumor was 89.3% and 82.3% respectively.

Conclusions: Intravascular tumor thrombus extension has favourable outcomes after contemporary multidisciplinary

treatment. Chemotherapy aids in surgery, with tumor regression and thus may obviate the need of cardiopulmonary bypass in atrial thrombus.

PODC05 SIOP19-1778 | Oncopeds: Early Diagnosis of Childhood Cancer Using a Mobile Application: A Multicenter Pilot Study

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Background: The diagnostic delay in children and adolescents with cancer is a public health problem in Peru leading to high rates of advanced disease and mortality. ONCOpeds® is a mobile application that provides consultations for the timely diagnosis and referral of children and adolescents with suspected cancer.

Objective: To evaluate the implementation and utility of ONCOpeds in reducing the time to diagnosis (TD) and referral time (RT) in children and adolescents diagnosed with cancer in Peru.

Material and Methods: A multicenter pilot study was conducted in the region of Callao between November 2017 and April 2018. Attending primary care physician were trained in the use of ONCOpeds in 5 educational sessions. Patients younger than 18 years living in Callao and diagnosed with cancer from all the pediatric cancer units were analyzed in two groups: referred by the mobile application or by the conventional referral. The TD and RT of both groups were compared using descriptive statistics and the Mann-Whitney U-test. A p-value < 0.05 was considered statistically significant.

Results: ONCOpeds was successfully installed in the smart-phone devices of 78 attending physicians of Callao (pediatricians and general practitioners). During this period, 23 new cases of cancer in children and adolescents from Callao were collected (median age, 11 years). Ten patients were referred through the application and 13 in a conventional manner. The TD and RT were reduced in the group referred by ONCOpeds by 53% and 61%, respectively; however, only the RT reached statistical significance (U-Mann-Whitney, p = 0.008).

Conclusions: The implementation of the use of ONCOpeds was feasible in this pilot study, having a potential util-

ity in improving the diagnosis and referral in children and adolescents with suspected cancer. A larger study at the national level is required to demonstrate the effectiveness of this telemedicine tool.

PODC06 SIOP19-1779 | Re-Irradiation in Recurrent Ependymoma: Experience of an Institution

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Introduction: Neoplasms of ependymal cells constitute the third central nervous system tumor (CNS) in the pediatric age group. Treatment includes complete surgical resection, whenever possible, and focal radiotherapy. The improvement of the techniques of both provides an increase of 5-year overall survival close to 70%. However, despite intensive treatment, one-third of patients recur.

In this context, the re-irradiation has been employed as a possible alternative treatment.

Objective: Evaluate the overall survival (OS) of patients with a confirmed diagnosis of ependymoma submitted to re-irradiation.

Materials and Methods: Retrospective observational study obtained through consultation of the database of patients with ependymoma treated with and without re-irradiation after relapse.

Results: Between 1993 and 2018, 93 patients diagnosed with ependymoma were admitted to the IOP / GRAACC / UNIFESP. Of these 46 (49.4%) patients relapsed. The average age at the diagnosis was 75.9 ± 61.5 months, 98.7 ± 42.8 months in the 1st relapse, and 136.1 ± 79.6 months in the second relapse, with 68.8% of the patients being male.

Up to 2009, 44 patients were treated after relapse with surgical resection and / or chemotherapy. After this period, 24 patients underwent re-irradiation, doses between 50.0 to 59.0 Gy, 96% of cases in the posterior fossa.

All patients tolerated well the re-irradiation, without significant side effects. The mean follow-up time for the group of re-irradiated patients was 101.6 ± 14.6 months, and the 3 years overall survival was $35.7\% \pm 12.8\%$ in the group not submitted to re-irradiation, versus $86.3\% \pm 7.4\%$ in the group of patients submitted to re-irradiation ($p < 0.0001$).

Conclusion: Re-irradiation is a therapeutic option to consider in cases of ependymoma of child-juvenile recurrence due to low toxicity and significant improvement in global survival. Further studies are necessary to define the late effects of re-irradiation as well as late motor deficit and increased risk of second neoplasms.

PPO

PPO: ADOLESCENTS AND YOUNG ADULTS

PPO01 SIOP19-0459 | Perceived Centrality of Cancer and Symptoms of Posttraumatic Stress and Growth in Adolescent and Young Adult Pediatric Cancer Survivors

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Background/Objectives: The degree to which a traumatic event is perceived as central to one's sense of identity has been associated with both posttraumatic stress (PTS) and positive outcomes such as posttraumatic growth or benefit finding (PTG). We examined the perceived centrality of cancer in the lives of adolescent and young adult survivors (AYA), and how this relates to cancer-related PTS, PTG, and resilience.

Design/Methods: Participants included 217 AYA (M age=17.5, SD=2.96, range 12-23, 52.5% male) who were 8.65 (SD 3.9) years post-diagnosis, predominantly white (76.5%), with diagnostic representation: Leukemia/Lymphoma=46.5%, Solid Tumor=39.1%, and Brain Tumor=14.4%. Survivors spontaneously identified their most traumatic life event (whether or not cancer-related) and completed the Centrality of Event Scale (CES), along with measures of PTS (UCLA PTSDI), PTG (Benefit Finding Scale, BFSC), and resilience (Social Emotional Assets for Resilience Scale, SEARS). Survivors who initially completed the CES in reference to a non-cancer event, were asked to complete it again specifically in reference to cancer.

Results: A cancer-related event was identified as most traumatic by 57% of survivors. Centrality scores were significantly higher when referencing cancer than non-cancer events ($p < .001$). Centrality scores were associated with age and gender (older, and females higher, p 's $< .01$), but not to diagnosis or time since diagnosis. Perceived centrality of cancer was significantly and positively associated with PTS ($r = .27$, $p < .01$), PTG ($r = .50$, $p < .001$), and perception of cancer-related burden ($r = .30$, $p < .01$). There was no relationship with measures of resilience.

Conclusions: Perceived centrality of cancer is an important predictor of both positive and negative psychological outcomes in cancer survivors. Further research is needed on this construct to better understand how it might be utilized in the psychosocial care of pediatric cancer survivors.

PPO02 SIOP19-0814 | Psychosocial Difficulties in Dutch Young Adult Survivors of Childhood Cancer

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Background/Objectives: The developmental stage of young adulthood comes with many age-specific challenges that can be further complicated by a history of childhood cancer and late-effects of treatment. We aimed to increase our understanding of the psychosocial well-being of young adult survivors of childhood cancer.

Design/Methods: In a cross-sectional study on well-being and need for psychosocial care, young adults (aged 18-30) who were diagnosed with cancer before the age of 18 and at least five years since diagnosis, filled out the 'Pediatric Quality of Life' (PedsQL-young adult version), the 'Hospital Anxiety and Depression Scale' (HADS), and the survivor-specific 'Impact of Cancer – Childhood Survivors' (IOC-CS). The IOC-CS measures long-term impact in life domains having relevance to young adult survivors. Outcomes were analyzed with descriptive statistics (IOC-CS) or compared to scores of reference groups of young adults (PedsQL, HADS), using logistic regression, ANOVA and Cohen's *d*.

Results: A total of 151 survivors (61.6% female, mean age 24.4 years) with mixed diagnoses participated (40% response rate). Survivors scored significantly lower than the reference group in all PedsQL domains (*d* 0.35-0.47, $p \leq 0.001$). Survivors had significantly higher mean levels of anxiety and depression than the reference group (*d* 0.32-0.43, $p \leq 0.01$). Regarding anxiety, a significantly larger percentage of the survivors than the reference group scored within the (sub) clinical range (29.9% vs 18.8%, OR 1.8, $p = 0.02$) and in the clinical range (15.9% vs 6.3%, OR 3.0, $p = 0.002$). Survivors reported greater positive than negative impact of cancer according to the IOC-CS scales. Most positive perceived impact was attributed to socializing and most negative to thinking/memory problems.

Conclusions: Although survivors reported worse psychosocial outcomes than reference groups, they also experienced positive long-term impact of the childhood cancer. Systematic attention for the psychosocial outcomes is necessary to provide timely interventions in this vulnerable age group.

PPO03 SIOP19-0731 | Identity Formation in Adolescent and Emerging Adult Cancer Survivors: Associations with Illness Characteristics and Psychological Functioning

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Background/Objectives: Identity formation constitutes a key developmental task in adolescence and emerging adulthood. The LInC-study, a longitudinal questionnaire study in childhood cancer survivors, investigates whether and how surviving a life-threatening disease may impact identity formation. The present abstract focuses on first results using data obtained at baseline.

Design/Methods: At baseline, 435 cancer survivors (14-25y) were eligible for participation, of which 91 participated at the time of submitting this abstract. Correlations and MANOVAs were used to test the potential role of clinical and demographic variables for identity exploration and commitment dimensions. Linear regressions examined associations between these identity dimensions and psychosocial functioning.

Results: The current preliminary sample consisted of 91 participants (40% male). Mean age was 19.87 ($SD=2.70$), mean time since diagnosis was 11.17 years ($SD=5.63$), and 61% reported physical complaints or disabilities. Type of diagnosis was classified as blood cancer (24%), brain tumor (20%), bone or soft tissue tumor (20%), lymphoma (11%), or 'other' (24%). No significant differences in identity functioning were found for type of diagnosis, physical disabilities, or gender. Age correlated positively with a pro-active exploration of identity alternatives ($r=0.23$, $p=0.030$). Time since diagnosis was unrelated to the identity dimensions. Regressions showed significant results for a ruminative or maladaptive type of exploration, being related to more depressive symptoms ($\beta=0.54$, $p<0.001$), lower satisfaction with life ($\beta=-0.47$, $p=0.001$), and a more central place of the illness in one's self-concept ($\beta=0.51$, $p=0.013$).

Conclusions: These preliminary findings seem to suggest that clinical variables may be unrelated to identity formation in cancer survivors. Ruminative exploration, characterized by repeated and indecisive overthinking of identity issues, may hinder adaptive functioning. At the conference, we will present results for the complete dataset obtained at baseline, and the results for this complete baseline sample will be compared to results from a non-clinical control sample.

PPO04 SIOP19-0442 | Perception of the Announcement of Diagnosis of Cancer in Adolescents and Young Adults Patients

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Background/Objectives: The announcement of a cancer diagnosis often causes an emotional shock for the patient. The initial consultation is crucial to establish a relationship of trust between the doctor and the patient. It is even more delicate at Adolescents and Young Adults (AYA) age, when psychological and social transitions occur. The objective of this study is to evaluate the experience of the medical announcement of diagnosis of cancer by the AYA and, in a second time, by their relatives.

Design/Methods: This is a prospective cohort, semi-quantitative and multicentric study carried out in the three units supporting AYA cancer patients in Rennes (medical oncology, hematology and pediatric hemato-oncology). The "patient" and "relative" questionnaires have been proposed within one month of the announcement by the doctor or a nurse.

Results: Between January 1, 2016 and June 30, 2018, we included 31 patient questionnaires and 26 "relative" questionnaires. Patients and their relatives expressed a favorable feeling about the announcement as well as a great satisfaction concerning the help and support provided by the doctors. AYAs seem particularly concerned about the following topics: sexuality, drug and alcohol use during treatment, side effects including alopecia and infertility and support for the whole family.

Conclusions: The medical cancer announcement must be personalized and tailored to the needs of AYAs and their relatives. The knowledge of these vulnerable patients remains to be improved in order to harmonize our practices and offer optimal care.

PPO05 SIOP19-1368 | Caregiver Disclosure of Oncofertility Risks Among Adolescent Cancer Patients

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Background/Objectives: Open discussion with adolescent cancer patients about fertility and preservation options is

associated with better long-term quality of life and psychological well-being. Although rates of disclosure about oncofertility risks to adolescents have not been well-characterized, extant research suggests significant unmet informational needs among survivors. The current analyses, representing a subset of data from a larger study on parent-child communication, sought to describe the prevalence of disclosure of oncofertility risks, and identify associated demographic and medical factors.

Design/Methods: Primary caregivers of male (N=59) and female (N=45) cancer patients ages 12–17 years (M=14.8) were recruited at outpatient infusion appointments and through international online support groups to complete an anonymous online survey. Adolescents were on or within one year of active treatment comprising chemotherapy (96.2%), surgery (43.3%), radiation (29.8%), and/or stem cell transplant (19.2%). Data were analyzed in SPSS via cross-tabulations, bivariate/partial correlations, and independent sample t-tests.

Results: Most caregivers (62.5%) endorsed having disclosed potential oncofertility risks to their children. Adolescents told about risks were older (M=15.1 years, SD=1.5) than those not told (M=14.3, SD=1.7; $t(102)=-2.68$, $p<.01$). Disclosure did not differ by child gender, age at diagnosis, time since diagnosis, prognosis, or treatment history. Adolescents in remission at time of survey were less likely to have been told about risks ($\chi^2=5.66$, $p<.05$): 51.9% of adolescents in remission had been told, versus 76.3% of those not in remission. Caregivers who disclosed oncofertility risks to their adolescents also reported poorer child physical functioning on the PedsQL ($t(67)=2.05$, $p<.05$).

Conclusions: Caregivers appear more likely to disclose potential oncofertility risks to adolescents who are sicker (i.e., poorer physical functioning, not having achieved remission) and who thus may have undergone more intensive treatment compounding oncofertility risks. This indicates a substantial portion of future survivors may be unaware of these complications, potentially impacting their long-term psychological well-being.

PPO: DECISION MAKING

PPO06 SIOP19-0505 | A Comparison of Attitudes Towards Clinical Trials and Decision Regret Among Survivors of Childhood Leukemias Treated On-Trial Versus Off-Trial on Standard Therapy and Their Caregivers

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Background/Objectives: Cancer clinical trials are a critical component in development of curative treatments in pediatric oncology, but rates of cancer clinical trial enrollment vary. Multiple factors contribute to clinical trials decision-making process; however, perspectives on these decisions are rarely examined. This study examined whether treatment on a cancer clinical trial is associated with more positive attitudes towards trials and less decision regret among survivors of childhood cancer.

Design/Methods: Self-report from 30 leukemia survivors ages 18 and older and proxy-report from 54 caregivers of leukemia survivors under 17 (age 19 or younger when diagnosed, diagnosed between 2000-2010) (Mage at diagnosis=6.24 years; 58.3% treated on trial) was obtained on the Pediatric Research Participation Questionnaire-AYA, a measure of attitudes to clinical trials, and the Decision Regret Scale as part of a study on economic impact of treatment on cancer clinical trials. ANCOVAs compared those treated on-trial to those treated off-trial on standard therapy on perceived barriers, perceived benefits, decision balance (z score of benefits-barriers), and decision regret, covarying for age at diagnosis, cancer risk, and overall health.

Results: There were no significant differences between self-report and caregiver-report; therefore, combined survey responses are presented. Participants were more likely ($p=.000$) to endorse perceived benefits ($M=4.01$; $SD=0.42$; range=2.70-4.72) than perceived barriers ($M=2.89$; $SD=2.89$; range=1.69-4.23) with balanced decisions ($M=-0.01$; $SD=0.73$; range=-1.83-1.82) and low regret ($M=1.40$; $SD=1.40$; range=1-5). ANCOVAs identified no significant differences between groups. As covariates, older age at diagnosis ($p=.019$) and better overall health ($p=.085$) were associated with more perceived barriers, and higher leukemia risk was associated with more perceived benefits ($p=.043$).

Conclusions: Patient/disease characteristics are more relevant to cancer clinical trials decision-making process than trial participation and can be attended to during informed consent. Cognitive bias to affirm prior decisions may contribute to retrospective ratings, and evaluation of attitudes at the time of trial decision-making is needed.

PPO07 SIOP19-0377 | Role of Health Literacy on Perception of Voluntariness During Informed Consent for Pediatric Cancer Clinical Trials

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Background/Objectives: Valid consent for research requires that the decision for participation be informed and voluntary. Parents often do not understand the many components of informed consent, including voluntariness of participation. There is limited research on the effects of health literacy (HL) on perception of voluntariness in pediatric cancer clinical trials. HL is the ability to process health-related information to function effectively in healthcare environments. We examined the role of HL and other contextual factors on the perception of voluntariness during informed consent for cancer clinical trials, focused on differences between non-Hispanics and Hispanics.

Design/Methods: Parents/guardians ($n=97$) of children aged 0-17 years with newly diagnosed cancer, who had consented to participation of their child in a clinical trial for treatment at Rady Children's Hospital-San Diego were prospectively recruited. Participants completed questionnaires assessing socio-demographics, HL, perception of voluntariness, decisional regret, satisfaction, and acculturation level, if Hispanic. Outcomes and contextual correlates were analyzed using logistic regression.

Results: Fifty participants (51.5%) were Hispanic and 47 (48.5%) non-Hispanic. Hispanics, Spanish-speaking participants and those with lower health literacy reported lower perception of voluntariness ($p<0.001$, $p=0.048$ and $p<0.001$, respectively). Decisional regret was overall low and satisfaction was overall high across all subgroups and neither was significantly impacted by HL, socio-demographics, or acculturation.

Conclusions: In this study, with equivalent numbers of Hispanics and non-Hispanics, we found that Hispanic parents of children with newly diagnosed cancer, and particularly Spanish-speakers and those with low HL, had inadequate perception of voluntariness, despite overall high rates of satisfaction with the informed consent process. True voluntariness of participation is essential to the ethical practice of informed consent, and our results suggest that many participants with low HL, particularly Spanish-speakers and Hispanics (the fastest growing ethnic group in the U.S) are not making informed decisions. Tailored interventions are needed to reduce clinical trial participation inequities in underserved populations.

PPO08 SIOP19-0024 | Parents' and Young Adults' Perspectives on Undertaking Cancer-Related Genetic Testing in Childhood: A Mixed-Methods Study

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Background/Objectives: Recent estimates indicate that up to 10% of childhood cancers may be caused by germline mutations in cancer predisposition genes. Genetic testing for these genes has the potential to precipitate cancer surveillance procedures from childhood, manage family-wide cancer risk, and inform treatment. However, little is known about families' experiences. We conducted a mixed-methods investigation of families' experiences of genetic counselling/testing for childhood hereditary cancer predisposition, the psychosocial impact of testing, and their information and support needs.

Design/Methods: We recruited families from two hospital sites in Sydney, Australia who had considered genetic testing for a child (≤ 18 years) within the family. All family members ≥ 16 years were eligible to participate. We conducted semi-structured interviews and quantitatively assessed emotional distress, quality of life, and genetic service-related satisfaction. We analysed the interviews thematically. We also analysed participants' demographic/clinical characteristics and psychosocial outcomes.

Results: We interviewed 35 participants ($n=26$ parents; $n=9$ young adults) from 26 families (*Mchildage* at referral=9.3 years, *SD*=4.4). Families expressed high satisfaction with genetic services and reported benefits to receiving a genetic diagnosis. Both parents and young adults rated high quality of life and reported low impact of cancer risk information on their personal relationships. Many parents described high distress related to their child's cancer treatment as inhibiting their capacity to understand important family risk information at the time of genetic testing. Participants commonly desired further information and follow-up concerning their family's cancer risk.

Conclusions: Families have largely positive experiences of genetic testing. Our results provide further support for families' acceptance of cancer-related genetic testing in childhood, where there is clinical benefit to knowing a child's genetic cancer risk. However, some parents and young people had unmet information and support needs. We will discuss how these findings will inform news models of genetic counselling in the paediatric cancer setting.

PPO09 SIOP19-0087 | Delta: A Parent and Patient Decision Aid to Support Clinical Trial Decision-Making in Childhood Cancer

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Background/Objectives: Clinical trials are the bedrock of cancer medicine. However, families of a child with cancer can find the decision to enrol challenging, and often misunderstand key concepts. To address the International Society of Pediatric Oncology (SIOP) guidelines for valid informed consent and participative decision-making, we developed and evaluated 'Delta'. Delta is an online and booklet decision aid for parents with a child with cancer, and adolescents with cancer, deciding whether or not to enrol in a clinical trial. We assessed acceptability of Delta and clinical trial knowledge acquisition.

Design/Methods: We conducted a pre-post pilot with parents with a child ($n=37$), and adolescents ($n=3$), who had enrolled in a pediatric Phase III clinical trial for newly diagnosed Acute Lymphoblastic Leukaemia. Parents and adolescents chose which version of Delta they preferred to review.

Results: 23 parents (62.2%) and three adolescents (100%) reviewed the website. Overall, parents rated Delta as highly acceptable in regards to being clearly presented (100%), informative (97.3%), easy to read (97.3%), useful (91.2%), visually appealing (78.4%) and easy to use (78.4%). Most parents reported that the amount of content was 'just right' (73.0%) and that content was 'balanced' (83.8%). All participants reported that they would recommend Delta to others. Parents' subjective ($M_{diff}=10.8$, $SD_{diff}=15.69$, $p<.001$) and objective (odds ratio=2.25, 95% CI:1.66-3.04; $p<.001$) clinical trial knowledge increased significantly after reviewing Delta.

Conclusions: To our knowledge, Delta is the first reported decision aid for parents and adolescents deciding whether or not to enrol in a pediatric oncology clinical trial. Delta has the potential to address families' unmet information needs and improve the quality of informed consent. Our findings indicate that Delta is acceptable, feasible and significantly improves clinical trial knowledge. We are currently preparing for a multi-site stepped wedge cluster randomised controlled trial using an Implementation-Effectiveness Hybrid Type 1 design.

PPO: SCHOOL AND EDUCATION

PPO10 SIOP19-0315 | Perceptions and Gaps Regarding Patient-Provider Communication of Educationally-Relevant Late-Effects After Pediatric Cancer –For Educational Series: Gaps And Models of Care for Schooling After Cancer

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Background/Objectives: Pediatric cancer survivorship rates are increasing, with neurocognitive late-effects a critical concern for a substantial proportion of survivors; access to relevant educational and legal supports is inconsistent. We report on parent and provider perceptions and gaps about knowledge, communication, and practices related to schooling after the diagnosis of childhood cancer.

Design/Methods: Two national U.S. surveys assessed gaps in practices related to patient-provider communication surrounding educationally-relevant late-effects of pediatric cancer treatment. Providers (N=287; 39.7% male) at COG-member institutions responded regarding perspectives and practices surrounding patient education and supports post-diagnosis; parents (N=259) of pediatric survivors (87% returned to school; Mage=12.4y; 53% male) described information received and post-treatment schooling experiences.

Results: Most providers (82.6%) report that patients/caregivers are routinely informed of potential for educationally-relevant late effects, but significantly fewer parents (52.8%; $p<.001$) reported receiving information about such impacts. Notably, the majority (74%) provide this information at diagnosis, although few providers (21%) or parents (18%) believe this is the most helpful point at which to communicate this information.

Few providers (28%) endorsed a good understanding of the issues patients face related to post-treatment schooling; they reported only moderate confidence in identifying (57.5%) and managing (46.8%) treatment-related problems relevant to schooling. Although most providers are confident (90%) in their ability to refer to neuropsychological services, and indicated they typically (81.2%) make such referrals, significantly fewer parents (35.4%; $p<.001$) of survivors reported receiving these referrals. Also concerning, fewer than half of providers (42.4%) were aware of any institutional guidelines regarding referrals, with few (19.3%) using specific screening tools to guide needed referrals.

Conclusions: Findings highlight gaps and areas for improvement in parent-provider communication regarding educationally-relevant late-effects of cancer treatment. Dissemination of specific guidance and provider- and patient-focused informational materials has potential to ameliorate

these gaps; the planned educational series addresses options for materials and dissemination.

PPO11 SIOP19-0921 | Kids with Cancer Still Need School' Roadmaps for Schooling After Cancer Diagnosis (For Consideration-Educational Day Series: Gaps and Models of Care for Schooling After Cancer)

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Background/Objectives: Gaps exist in parents' knowledge of and parent-provider communication about educationally-relevant late-effects of pediatric cancer treatment. The objective of this project was to use information from a national survey and stakeholder input to develop parent roadmaps to improve communication and dissemination of pertinent information to fill gaps.

Design/Methods: The results of a national survey of affected families (N=259) identified gaps in desired information about schooling, late-effects, and timing of information provision; these formed the basis for developing understandable and actionable educational materials, as recommended by the Agency for Healthcare Research and Quality. Stakeholder families participating in a Patient Centered Outcomes Research Institute-funded Engagement Project, in conjunction with project leadership and school/cancer community stakeholders, utilized an iterative process to develop roadmaps to educate and assist parents navigating schooling after the diagnosis of childhood cancer.

Results: 'Kids with Cancer Still Need School' is a set of two-page roadmaps that provide education and information for parents at five points during the cancer trajectory: 1) Diagnosis, 2) Starting Home and Hospital Instruction, 3) Returning to school part-time during treatment, 4) Returning to school after treatment, and 5) Survivorship. Roadmaps include checklists of 'things do to or ask' when communicating with healthcare and school teams. Roadmaps also provide information to meet key gaps identified in the survey, including how cancer treatment may impact schooling, introduction to key school procedures and educationally-relevant vocabulary, neuropsychological testing, and links to vetted resources for education and support. Next steps include dissemination via automation within electronic medical records.

Conclusions: Parents have expressed the need for more information and better communication about schooling issues after childhood cancer diagnosis. This collaborative parent and stakeholder approach to developing a roadmap strategy to meet parents' needs has the potential to have wide-reaching impact to address gaps. Current implementation and evaluation of the roadmaps will be presented.

PPO12 SIOP19-0444 | Provision of School Liaison Services to Pediatric Hematology/Oncology Patients Across the US (For Educational Day Series: Gaps and Models of Care for Schooling After Cancer)

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Background/Objectives: School liaison programs across the United States address both the immediate and long-term school and learning needs of pediatric cancer patients and survivors. However, programs vary from one facility to another, and no research to date has compared how hospitals support their patients' educational needs. This project addresses this knowledge gap by delineating the functions and operations of the nation's existing school liaison programs.

Design/Methods: Hospital researchers identified appropriate personnel at 185 of the Children's Oncology Group (COG) institutions. Among those identified, 71 (38%) started the survey, of which 54 (30%) completed the questionnaire. Descriptive statistics were analyzed.

Results: Nearly all respondents supported patients' educational needs both at diagnosis and while on treatment (93%; 96%, respectively). Fewer (74%) supported patients' needs into long-term survivorship. Attendance at school meetings was more common for on-treatment patients than for those whose treatment had been completed (70%; 61%, respectively). Only 43% reported adequate program staff, and most programs indicated having staff split between pediatric oncology and other diseases (61%). Programs averaged 1.9 staff members, with larger hematology/oncology programs (greater than 25 beds) reporting a larger school liaison staff than smaller ones (mean = 2.5 and 1.3, respectively). Funding sources varied: hospital or university budget (56%); donor funding (48%), and grants (30%). None reported billing for services.

Conclusions: The challenge of school liaison clinicians in the pediatric oncology setting reflect both the variability of available services and the broader difficulty parents and practitioners encounter finding them. Continuing research is necessary to create a more comprehensive cataloging of available services across the country, and begin the discussion of devel-

oping programmatic standardization and identifying best practices.

PPO13 SIOP19-1142 | Processes of Support in Australia for Students with Cancer: Current Strengths and Weaknesses (For Educational Day: Gaps and Models of Care for Schooling After Cancer)

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Background/Objectives: Remaining engaged in school through treatment provides students with cancer with a sense of normalcy, academic progress and social connection. How healthcare professionals in Australia best support these vulnerable students is yet to be described. Therefore we conducted a multi-site evaluation of Australian school re-entry practices

Design/Methods: We recruited at least one medical (e.g., oncologist, clinical nursing consultant) and one education staff (e.g., hospital school staff, education specialists from non-government hospital-based education services) from 7 out of 8 Australian children's hospitals to participate in a semi-structured interview about the school re-entry processes for children with cancer in Australia.

Results: Our interviews identified that school re-entry support is provided but that there were inconsistencies between different Australian hospitals. Few participants reported that their hospital had a formal school re-entry process, with most believing it was an ad hoc procedure. While this allowed for a responsive and flexible approach, it did lead some participants to worry that some students may miss necessary support. All sites reported providing information about a child's diagnosis, treatment, and related educational implications to the school. Clinical nurse consultants, hospital school staff and non-government/charitable liaison staff all had a role to play in communicating with a child's school, but in some cases who led this process was variable, leading to confusion for families and schools. Few participants reported formally following up with the school, child, or parents to discuss the child's educational functioning since returning to school.

Conclusions: Variability around how to best support school re-entry for students with cancer exists in Australia. A lack of formalised return to school processes is both a strength, allowing individualised and adaptive responding, and a weakness, placing some students at risk of missing support.

Further work on developing standard models of care to support students with cancer remain engaged in their education is needed.

PPO: BREAKOUT

PPO15 SIOP19-0136 | Pediatric Cancer-Induced Financial Burden is Related to Severely Worsened Parent Stress-Related Symptoms Especially Among Parents Who Are Female, Single/Divorced or Lower Income

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Background/Objectives: Pediatric cancer-induced financial burden is a source of stress for parents, particularly female, single, and lower income parents. While studies have highlighted its effects on family quality of life (QOL), pediatric cancer-induced financial burden could also adversely influence parent QOL by heightening their stress-related symptoms (anxiety, impaired focus, impaired sleep). Our purpose was to describe the frequency of worsened parent stress-related symptoms due to pediatric cancer-induced financial burden.

Design/Methods: The local ethics board reviewed/exempted the study. Parents of children diagnosed with pediatric cancer before age 18 years were eligible and recruited through two parent-run groups - Momcology and Childhood Cancer Dads- via social media platforms. Data were collected using an anonymous, investigator-developed 142-item online survey built using Qualtrics software. Respondents used a 4-point response scale to indicate the extent to which pediatric cancer-induced financial burden worsened their symptoms. Descriptive and Chi-square statistics were used to assess bivariate relationships between symptoms and gender, marital status, and income.

Results: Within 37 days, 428 people completed the survey. Most were mothers (79.3%), white (88.6%), and married (81.15%) with at least a college degree (57.5%) Their children were mainly male (60.3%) and undergoing or had completed treatment <3 years prior (75.2%). For the majority, financial burden severely worsened their symptoms, particularly distress (64.48%) and anxiety (69.86%). Overall, parent symptoms and risk factors were not independent (p -values <0.05). Greater proportions of females versus males reported severe worsening of every symptom studied, as did greater proportions of divorced/single versus married parents. Finally, there was an inverse, stepwise association between the proportion of parents reporting severe worsening of symptoms and income.

Conclusions: Parents experience severely worsened symptoms due to pediatric cancer- induced financial burden. Further study of financial burden's influence on individual and family QOL in pediatric oncology is indicated.

PPO16 SIOP19-1006 | Predictors of Quality of Life in Caregivers of Newly Diagnosed Pediatric Patients with Cancer

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Background/Objectives: Pediatric cancer and treatment can negatively impact caregiver quality of life (QOL). As part of a larger study, this sub-study examined general distress, mental health, and family psychosocial risk concurrently and as potential predictors of caregiver QOL, shortly after the child's diagnosis and 6 months later.

Design/Methods: For the main study, families were randomly allocated to an intervention (IG, PAT summary profile provided to patient treating team) or control group (CG, no summary provided) in two pediatric cancer centers. Caregivers (N=122) of newly diagnosed children completed measures of distress, anxiety, depression, quality of life and family psychosocial risk (Caregiver Quality of Life Cancer; Hospital Anxiety and Depression Scales; Distress Thermometer; Psychosocial Assessment Tool) at 2-4 weeks (T1) and 6 months later (T2). Data from the two groups were combined for this study.

Results: Measures of distress, anxiety, depression and psychosocial risk were significantly associated with caregiver QOL at T1 and T2 (r s=0.61-0.76; p s<0.01). Concurrent regression analyses found that distress, anxiety and psychosocial risk significantly accounted for the variance in caregiver QOL at T1 (β =0.22, 0.44 and 0.26 respectively; p s<0.01); and measures of distress, depression and psychosocial risk significantly accounted for the variance in caregiver QOL at T2 (β =0.30, 0.29 and 0.25 respectively; p s<0.01). Regarding predictors of QOL at T2, regression analysis found that only psychosocial risk and depression symptoms at T1 predicted caregiver QOL at T2 (β =0.29 and 0.24 respectively; all p s<0.05).

Conclusions: Brief measures of psychosocial risk, distress and mental health may inform our understanding of caregiver QOL at different points in the pediatric cancer treatment. However, only family psychosocial risk and caregiver' depression symptoms at the child's diagnosis can predict caregiver QOL six months later. Findings have major implications for developing interventions for caregivers.

Acknowledgements: This research was funded by The Canadian Cancer Research Institute.

PPO17 SIOP19-0703 | Disentangling the Diversity of Sleeping Problems and Current Treatment-Seeking Behavior in Adolescents Who Had Childhood Cancer: Preliminary Results of the MICADO-1 Study

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Background/Objectives: Having sleep problems and childhood cancer poses a double health burden, since both are related to increased risks of adverse health outcomes. However, sleep problems are heterogeneous and each type of sleep disorder requires different treatment. Little is known about this diversity of sleep disorders and treatment-seeking behavior after childhood cancer. Therefore, our aim is to disentangle this diversity by studying sleep disorders in adolescents who had childhood cancer and determine their treatment-seeking behavior.

Design/Methods: In a cross-sectional national cohort study, adolescents (13-25 years old) diagnosed with childhood cancer between 2013–2018 and at least 6 months after treatment were invited to fill out questionnaires including: self-reported treatment-seeking behavior and the Holland Sleep Disorders Questionnaire, which distinguishes six sleep disorders and shows substantial agreement with the International Classification of Sleep Disorders-2.

Results: Thus far 201 of 500 adolescents have been invited and 58.7% (n=118) responded. General sleep disturbance was reported in 29.7%. Duration of complaints was more than 3 months in 54.3%. Criteria for a sleep disorder were met by 20% of patients, half of them met criteria for two or more disorders. Prevalence rates were: insomnia (9.3%), restless legs syndrome/limb movements of sleep (8.5%), circadian rhythm sleep disorder (7.6%), parasomnia (5.1%), hypersomnia (3.4%), sleep-related breathing disorder (2.5%). Of all adolescents, 14.4% had previously sought sleep treatment and of those with general sleep disturbance only 25.7% did so.

Conclusions: One third of adolescents after childhood cancer treatment report a diverse array of sleep problems, but only a minority seeks out treatment. Further research should investigate treatment needs and barriers to enable tailoring of sleep treatments within pediatric oncology.

PPO18 SIOP19-1183 | Barriers and Enablers for Successful Implementation of the eHealth Service Sisom for Improved Child Participation in Paediatric Care - A Multi-Centre Study

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Background/Objectives: Participation in healthcare is one of the most important components in management of children's disease. eHealth services that are adapted to the needs of children have the potential to reorganize how children and professionals work together. The digital interactive communication tool Sisom, was developed to give children in pediatric oncology care "a voice". However, the implementation of eHealth services, such as Sisom, in daily practice is rarely being investigated. The objective of this study was to explore the process and effects of implementing Sisom at four pediatric care centers in Sweden.

Design/Methods: A process and effect evaluation design was used to investigate the implementation of Sisom in a clinical context at four pediatric care centers in Sweden. In total, 46 children, age 6- 13 years, participated and most of them had a cancer diagnosis. The children used Sisom at two occasions during 6 months. Following the use of Sisom, a printed report formed the basis for a forthcoming dialogue between professionals, children and their parents.

Results: Key factors for successful implementation of Sisom was; i) alignment of the solution with values and goals of the organization, ii) professional's beliefs in the usefulness and usability of the solution, and iii) professional's willingness to apply changes in their professional roles promoted by the solution. Sisom directed healthcare communication from the parents' voices toward the child's voice and made children's needs and preferences explicitly visible in decision-making. Sisom was experienced, by the children, as a user-friendly tool through which they could find ways to express themselves and share information with their parents and healthcare professionals.

Conclusions: The results show how healthcare delivery can be reorganized towards a child-centered approach, and the importance of implementing an eHealth service to support restructuring of ways of working with children's participation to succeed with this.

PROS

PROS: FPS 1

PROS01 SIOP19-1150 | An Elegant and Robust Approach to TBI Delivery Using Modern Technology

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Background/Objectives: Total body irradiation (TBI) is an essential component of conditioning regimens for hemopoietic stem cell transplant. TBI is complex due to the large field size, variations in body separation, and need for partial transmission blocks to mitigate the risk of long-term pulmonary toxicity. There is significant variability in TBI techniques depending on available technology. In 2015 after moving to a new cancer center, we developed a sweeping overlapping beam technique which permits delivery of TBI in a safe, reproducible and efficient manner.

Design/Methods: We conducted a retrospective analysis of patients aged ≤ 18 years treated with TBI at our institution between March 2016 and April 2019. AVarian TrueBeam linac is used to deliver 14 overlapping arcs using 6 MV photon beams each with a field measuring 40x40 cm². Each arc sweeps across the patient over 10 degrees to complete a 140-degree arc with the patient in prone and supine positions. Dose attenuation is planned as needed using CT simulation in conjunction with an Eclipse Treatment Planning System (TPS). Prior to using our new technique, TPS calculations were externally validated using anthropomorphic phantoms in both pediatric and adult body types and showed high accuracy.

Results: Forty-one patients aged 3-18 years (median 10 years) were treated using the new technique. Dose range was 2 Gy in a single fraction to 13.2 Gy in 8 BID fractions. Average dose rate was 9 cGy/minute (22 minutes per fraction). All patients receiving high dose TBI (≥ 12 Gy total dose) were treated with partial blocks to reduce the prescription dose within the lung to 8-10 Gy as measured by the TPS.

Conclusions: This sweeping beam technique with multiple overlapping arcs can be reliably and efficiently delivered. Reduction in dose to organs at risk with TPS dose calculations for prescription and organ doses is feasible.

PROS02 SIOP19-0697 | Impact of Radiotherapy in Optimizing Local Control at Primary and Metastatic Sites in High Risk Neuroblastoma: A Pattern of Relapse Study

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Background/Objectives: Radiotherapy is an important part of the multimodality management of High Risk Neuroblastoma (HR-NB). We evaluate the clinico-diagnostic profile, treatment protocol, over-all outcomes and patterns of relapse (with respect to the radiotherapy portal, In-Field and Out-Field) in patients with HR-NB treated at the Tata Memorial Hospital, India.

Design/Methods: Clinical records of patients diagnosed with HR-NB, who completed the planned curative treatment were retrospectively analyzed.

Results: Between January 2011 & September 2017, 54 children (39 males;15 females) with HR-NB in the age group of 10 months to 10 years, median 3.5years (6 infantile; 48 non-infantile) were treated with multimodality treatment comprising of chemotherapy, surgery, radiation 19.8Gy-25.2Gy (primary+/-metastatic site) and differentiating agent with (9 patients;16.7%) or without autologous bone marrow transplant. At median follow up of 25 months, the 2-year and 3-year Local Control (LC) was 69.4% and 56.4%, Disease Free Survival (DFS) was 29% and 12.2% and Over-all Survival (OS) was 59.9% and 32.3% respectively. At the time of last follow up, 10 (18.5%) patients were alive and disease free. Two patients with localized relapse were salvaged with multimodality therapy. All 54 patients received radiotherapy to the primary site and 34 (63%) of them maintained local control. Out of the 8 patients who also received RT to the metastatic site as part of the primary treatment, only one patient (calvarial metastases) developed an In-Field recurrence. Of the 46 patients who relapsed, 14 (30%) were localized (In-Field only=6, Out-Field only=6, In+Out-Field=2) and 32 (70%) had disseminated disease. Of the patients with disseminated disease at relapse, 12 (38%) also had In-Field recurrences. Two patients who received definitive radiotherapy in view of inoperable disease remained controlled at the local site.

Conclusions: Radiotherapy is an effective modality for preventing local recurrences at primary and metastatic sites in HR-NB. Disseminated relapse remains a challenge and mandates aggressive systemic therapy.

PROS03 SIOP19-1179 | A Psycho-Behavioral Program to Avoid Anesthesia for Radiation Therapy in Children Under 5 Years Old

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Background/Objectives: Considering the long-term adverse effects, radiotherapy is a challenge in patients under 5 years of age, but in many neoplasms it is still part of the treatment that

provide greater local control and chance of cure. Usually to achieve the goal of treatment, it is necessary administer anesthesia or sedation to patients during the simulation and during all radiotherapy sessions to avoid movements while maintaining spontaneous breathing and cardiovascular stability. We usually use sevoflurane for deep sedation, so patients many times have an exalted awakening.

The purpose is to describe the experience of using a psycho-behavioral program to avoid sedation in radiotherapy patients.

Design/Methods: We reviewed the totality of patients under 5 years of age treated in the Radiation Therapy service of Teleton Children's Hospital of Oncology from January 2013 to December 2018 who were part of the psycho-behavioral program to avoid anesthesia.

Results: Of the 239 patients under 18 years old who were treated, 82 had less than 5 years old (34%). The most common neoplasm was lymphoblastic leukemia with CNS relapse (31%), followed by Wilms Tumor (21%), Brain Tumors (18%), Rhabdomyosarcoma (7%), Hodgkin's Disease (7%) and others (16%). The average of age was 3 years old. Patient ages were: 2 years (21), 4 years (21) and 5 years (22). We used psycho-behavioral therapy based on play, and 50% of the patients needed sedation during the simulation tomography. Patients on simulation were 82, and 88% of the patients fully cooperated during the treatment with radiation therapy, being sedation necessary only in 18 patients (22%). In total, 1231 radiation sessions were administered, 948 were administered without sedation (77%).

Conclusions: The use of a psycho-behavioral program is very helpful to avoid anesthesia or sedation procedures during treatment with radiation therapy, decreasing the total cost of treatment and avoiding complications related to sedation in patients.

PROS04 SIOP19-1185 | Multi-Modality Management of Nasopharyngeal Carcinoma in Paediatric and Adolescent Patients: Experience from a Regional Cancer Centre in North India

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Background/Objectives: Nasopharyngeal carcinoma (NPC) is a rare malignant tumour in childhood and adolescence (<1% of paediatric malignancies).

Design/Methods: Data pertaining to paediatric and adolescent patients with NPC attending our institute from 2014-18 was abstracted by retrospective chart review.

Results: We identified 33 patients with NPC. The median age at presentation was 16 years (range 8-27years). The male to female ratio was 21:12. Common symptoms included neck swelling in 84.85%, epistaxis, aural and CNS symptoms in 36.36%, nasal obstruction in 30.3% and orbital symptoms in 15.15% patients. One (3.03%), 8 (24.24%), 5 (15.15%), 16 (48.48%) and 3 (9.09%) patients had AJCC 2010 stage II, III, IVA, IVB and IVC respectively. Majority (90.91%) of the patients had undifferentiated NPC. On immunohistochemistry, 24/28 (85.71%) tumours stained positive for EBV-LMP1. All patients underwent neoadjuvant chemotherapy (NACT, median-3 cycles)-PF (Cisplatin, 5fluorouracil) in 9 (27.27%), TP (Paclitaxel, Carboplatin) in 21 (63.64%) and DCF (Docetaxel, Cisplatin, 5fluorouracil) in 3 (9.09%). Radiotherapy (RT) to locoregional disease was delivered in 32 (96.97%) patients, the techniques being 2D-conventional in 9, fixed-field IMRT in 5 and VMAT in 18 patients. The median RT dose was 65, 60, 54Gy/30fractions/6weeks (simultaneous integrated boost). Weekly concurrent Cisplatin (median-5 cycles) was added in all 32 patients. After a mean follow-up of 20.89 months, 12 patients had disease progression (PD) and 5 patients died (4 due to PD). The common patterns of failure were in the bones (12), lungs (4), distant lymph nodes (4), liver (3), and locoregional (1). At last follow-up, 15 (45.45%) and 5 (15.15%) patients had complete and partial response, 2 (6.06%) and 11 (33.33%) patients had stable and progressive disease. The median overall survival (OS) and progression free survival (PFS) had not been reached. The 2 year actuarial rates of OS and PFS were 71.8% and 54.1% respectively.

Conclusions: Majority of paediatric and adolescent patients with NPC present in advanced stage in developing nations. Multi-modality management in the form of NACT followed by CRT led to modest clinical outcome in our setting. The most common pattern of failure was distant metastases in the bones. Concerted effort is needed for increasing awareness, early detection and prompt treatment (timely conformal RT) of NPC.

PROS05 SIOP19-0579 | Comparison of Long-Term Outcomes and Sequelae Between Children and Adult Nasopharyngeal Carcinoma Treated With Intensity-Modulated Radiotherapy

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Background/Objectives: To compare long-term survival outcomes and sequelae between children and adult

nasopharyngeal carcinoma (NPC) in the era of intensity-modulated radiotherapy (IMRT).

Design/Methods: Data on 285 NPC patients aged ≤ 18 years old at diagnosis and treated with IMRT between January 2004 and November 2016 were retrospectively reviewed. Propensity score matching method was adopted to screen matched adult NPC patients at a ratio of 1:3. Survival outcomes and treatment-related toxicities between children and adult groups were compared.

Results: In total, 159 children and 477 adult NPC patients were included in this study. The 5-year overall survival (OS), distant metastasis-free survival (DMFS), locoregional relapse-free survival (LRRFS), and disease-free survival (DFS) between children and adult were 89.2% vs 83.6% ($P = 0.144$), 88.7% vs 83.5% ($P = 0.124$), 96.4% vs 89.1% ($P = 0.013$), and 86.5% vs 77.3% ($P = 0.021$), respectively. Subgroup analyses revealed that the young age was an independent prognostic factor of OS, DMFS and LRRFS in advanced N stage (N2-3) group, and DFS in advanced T stage (T3-4) group, N2-3 and stage III-IVA groups. The most common sequela was ototoxicity (68.9%) in children patients and xerostomia (70.8%) in adult patients. Adult survivors had a significantly higher incidence of grade 3-4 late toxicities in xerostomia (17.6% vs. 8.9%, $P = 0.004$), skin dystrophy (9.3% vs. 3.7%, $P = 0.022$), neck fibrosis (8.3% vs. 4.4%, $P < 0.001$) and radiation encephalopathy (0.8% vs. 0, $P = 0.006$). Children survivors were more likely to develop grade 3-4 growth retardation and endocrine insufficiency (3.0% vs. 0.3%, $P = 0.014$).

Conclusions: Children NPC patients achieved significantly better survival outcomes but less late toxicities than adult patients. However, we should pay great attention to growth problems of children survivors.

PROS06 SIOP19-1074 | Testicular Transposition in Children and Adolescent Before Scrotal External Radiotherapy: A National Retrospective Analysis

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Background/Objectives: Testicular transposition (TT) before scrotal radiotherapy (RT) is poorly reported. Surgical, RT techniques and effects on fertility and endocrine function are studied in a retrospective study.

Design/Methods: All cases of TT before external scrotal RT, reported between 01/2001 and 10/2018 in the RT departments of Société Française des Cancers de L'Enfant were included. Surgical techniques, dosimetric parameters, clinical and biological outcomes were reported. To be reliable, clinical/biological testicular evaluations were done at least one year after the last injection of alkylant and three months after the replacement of the testicle. Tanner stage, testicular volume, FSH, LH testosterone, Inhibin B and AMH plasma concentrations and if possible, semen analysis were recorded.

Results: Twelve patients, median age 14.9 years [5-17y.] with paratesticular embryonal rhabdomyosarcoma (RMS) (N=10) or pelvic Ewing Sarcoma (ES) (N=2) were identified, all treated according to RMS 2005 (except one RMS), and Euro-ewing 99 protocols respectively. Eleven patients received potential gonadotoxic chemotherapy (median alkylant dose 49.2 g/m²). Patients had TT within 2 months before RT, with no relevant acute complications. Median duration of intra-abdominal stay of the testicle was 4.5 months (< 5.7 months in 83%). Median RT prescription dose to the target volume including scrotum was 43 Gy [36-50.4]. Median maximal and average dose delivered of the transposed testis were respectively 1.2 Gy [0.02-6.3] and 0.6 Gy [0.01-1.6]. 4 pts with enough follow-up for pubertal assessment (median 94 months after testicle replacement) had normal clinical pubertal development (Tanner stage and testicular volume). In these 4 patients, sex hormones were normal in 3 patients who could be evaluated. More follow-up clinical and biological data will be presented at the congress.

Conclusions: TT should be systematically discussed in children and adolescent before scrotal RT as it is feasible, and allows a dramatically RT dose decrease to healthy testicle.

PROS07 SIOP19-0164 | Radiotherapy Practice and Quality Assurance for Paediatric CNS Tumours Across Europe: A Joint SIOPE-EORTC Quartet Initiative

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Background/Objectives: Quality assurance has become increasingly important in radiotherapy for central nervous system (CNS) tumours as this aspect of treatment becomes

ever more technical and complex. Our objective was to analyse radiotherapy quality assurance (RTQA) practice in the treatment of paediatric CNS tumours across Europe.

Design/Methods: Study protocols and publications of ten major European trials (1992-2019) for paediatric CNS tumours were reviewed to assess the RTQA aspects. To complement this work, an international survey among experts in paediatric CNS tumours was also performed.

Results: Prospective RTQA is being increasingly implemented into paediatric clinical trials, as seen in the HIT-SIOP PNET trials: PNET-3 featured retrospective RTQA; PNET-4 prospective for some groups; the ongoing PNET-5 includes mandatory, prospective RTQA, which is foreseen for PNET-6 as well. The survey was filled in by 34 experts from 21/29 contacted countries. National guidelines for paediatric CNS tumours are available in 10/21 (48%) countries. Central storage of radiotherapy data is available in 4/21 (19%) countries. Only 7/21 (33%) countries have RTQA programs for paediatric brain tumours in place; however, 12/21 (57%) have a well-established national referral network for paediatric radiotherapy, according to the experts. For one third of experts, the level of involvement of radiation oncologists in the meetings/activities of the national paediatric oncology societies is inadequate. Over 90% of the consulted experts believe that the patients would benefit to a considerable or to a great degree from a European RTQA guideline for paediatric brain tumours.

Conclusions: There is a paradigm shift from retrospective to prospective RTQA. While radiotherapy practice is heterogeneous among countries, several promising RTQA initiatives are being developed across Europe, such as QUARTET (QUALity and excellence in RadioTherapy and imaging for children and adolescents with cancer across Europe in clinical Trials).

PROS: FPS 2

PROS08 SIOP19-0939 | Proton Therapy for Ependymoma in Childhood – Experience and Results of the Kiproreg Registry Study at Westgerman Proton Center Essen

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Background/Objectives: Ependymoma are tumors of the central nervous system occurring predominantly in young

children. Radiotherapy is an important part of the interdisciplinary treatment concept and proton therapy (PT) is potentially beneficial due to its physical abilities. The aim of this analysis was to evaluate treatment outcome and feasibility of PT in pediatric patients with Ependymoma.

Design/Methods: Between June 2013 and February 2018, 75 patients (46 male /29 female) with primary, non-metastatic Ependymoma received PT at the West German Proton Center and were enrolled in the prospective registry study KiProReg. Data regarding medical history and treatment were assessed in a standardized manner. Adverse events were documented according to CTCAE V4.0.

Results: Median age was 3.0 years (range, 0.9-17.0). 47 patients underwent gross total resection, 26 subtotal resections and 2 biopsy only. Tumor grade was WHO III° (53 P), WHOII° (20 P) and WHO I° (2 P). Tumor site was infratentorial (n=58), supratentorial (n=13) or spinal (n=4). Median dose was 59.4Gy (range, 50.4-62 Gy). PT techniques were uniform scanning (n=37), Pencil beam scanning (n=33) or both (n=5). Concomitant chemotherapy (CTX) was administered in 11 patients. Median follow-up after diagnosis was 30.5 month (4.9-68.9). Estimated 3-year-overall survival and local control rate was 98.5% and 82.9%, respectively. Acute side effects $\geq$ grade 3 regarding blood cell count occurred in 13 patients and was mostly associated with chemotherapy (n=10). Two patients developed new grade 3 nervous system side effects as obstruction of liquor circulation. Three grade 3 late sequelae occurred as worsening of preexisting conditions such as hearing impairment (n=1), dysphagia (n=1) and gait disturbance (n=1). One new grade 3 psychiatric adverse event occurred after one year.

Conclusions: Results suggest good feasibility of PT in childhood Ependymoma treatment. Clinical outcome and toxicity profiles are promising. Longer follow up is necessary to assess long term side effects.

PROS09 SIOP19-0860 | Preliminary Report of Secondary Malignant Neoplasm Incidence in Pediatric Patients Receiving Proton versus Photon Craniospinal Irradiation for Medulloblastoma

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Background/Objectives: Modeling studies have predicted fewer secondary malignant neoplasms (SMN) following

treatment with proton beam therapy (PBT) compared to photon radiotherapy (XRT). However, there are concerns that secondary neutron production with passive scatter PBT (PSPT) may lead to excess SMN. We reviewed our experience treating pediatric medulloblastoma (MB) patients with craniospinal irradiation (CSI) using either XRT or PBT. We hypothesized that excess SMN would not be observed among PBT-treated patients.

Design/Methods: From 1996 to 2014, 166 MB patients received CSI and tumor bed boost using either PSPT (N=103) or XRT (N=63). Most patients had standard-risk MB (61.4%). Median follow-up was 78.5 months for the PBT cohort and 153.2 months for the XRT cohort ($p < 0.001$).

Results: The 5- and 10-year overall survival rates were 82.6% and 81.2% for standard-risk and 69.8% and 64.0% for high-risk patients, respectively. No OS difference was identified by RT modality ($p = 0.49$). The 5- and 10-year SMN rates were 2.3% and 8.1% for the full cohort (N=166). By modality, 5- and 10-year SMN rates were 2.6% and 6.0% for PBT patients, and 0.0% and 8.0% for XRT patients ($p = 0.71$). There was no difference in SMN incidence by age, gender, or CSI dose (all $p > 0.5$). Eight SMNs in total were identified (4 for each RT modality), with a median 71.2 months from RT completion to SMN diagnosis. All 4 SMNs in the PBT cohort occurred within either the target (N=2), or the entrance-dose region (N=2). For XRT patients, 3 SMNs occurred in exit-dose regions, and 1 occurred within the target.

Conclusions: Our preliminary analysis demonstrates no difference in SMN incidence between PBT-treated and XRT-treated patients. Longer-term follow-up remains necessary to better understand differential SMN patterns across RT modalities. It is notable that XRT-treated patients developed more SMNs in regions of exit dose than within the target volume.

PROS10 SIOP19-1259 | Intellectual Functioning Among Case-Matched Cohorts of Patients Treated with Proton or Photon Radiation for Standard Risk Medulloblastoma

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Background/Objectives: Initial studies suggest cognitive deficits following radiotherapy among brain tumor survivors are attenuated with proton therapy, though current data

are limited to retrospective comparison between historical cohorts. We compared intelligence quotient scores within a case control matched cohort of pediatric patients with medulloblastoma treated with either proton therapy (PRT) or contemporary photon radiation (XRT) over a similar time period.

Design/Methods: Among 88 consecutive patients with standard risk medulloblastoma treated with either PRT or XRT at two institutions between 2000-2009, 50 patients were matched 1:1 (25 PRT: 25 XRT) based on age, gender, date of diagnosis, histology, type of radiation boost, and CSI dose. One-way ANOVA test was performed to compare Full Scale IQ (FSIQ), verbal, perceptual, processing speed and working memory scores between the two cohorts.

Results: Neurocognitive data were available for 37 survivors (17 PRT; 20 XRT). Mean age was 8.5 years (SD 4.14). Median follow-up was 5.3 (range 1-11.4) and 4.6 (range 1.1-11.2) years for the PRT and XRT cohorts, respectively. Among all patients combined, mean FSIQ, verbal abilities, nonverbal abilities, and working memory were similar to population norms. However, weakness was noted in processing speed. Patients treated with PRT had significantly higher mean FSIQ, (99.6 (SD 13.4) vs. 86.2 (SD 19.0), $p = 0.021$) verbal (105.2 (SD 14.8) vs. 88.6 (SD 20.8), $p = 0.010$) and nonverbal scores (103.1 (SD 13.7) vs. 88.9 (SD 17.4), $p = 0.011$) than the XRT treated cohort. Differences in processing speed (82.9 (SD 9.7) vs. 77.2 (SD 18.8), $p = 0.331$) and working memory (97 (SD 9.9) vs. 92.7 (SD 12.5), $p = 0.388$) were not statistically significant.

Conclusions: Consistent with other recent studies, the cognitive effects associated with treatment appear to be more attenuated following proton therapy with impact primarily limited to processing speed. Comprehensive prospective studies are needed to appropriately evaluate the neurocognitive advantages of proton therapy.

PROS11 SIOP19-0917 | Patient Selection Based on Anatomical Tumour Location for Pencil Beam Scanning Proton Beam Therapy in Abdominal Neuroblastoma

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Background/Objectives: Pencil-Beam-Scanning-Proton-Beam-Therapy (PBS-PBT) may reduce dose to surrounding organs at risk (OARs) to some but not all children with abdominal neuroblastoma (NB) when compared with Intensity-Modulated-Radiation-Therapy (IMRT). This work

investigates patient selection for PBS-PBT based on tumour localisation.

Design/Methods: Twenty paediatric abdominal neuroblastoma cases were double-planned using PBS-PBT and IMRT to 21Gy in 14 fractions. Cases were divided into two major location groups; lateralized (n=9) where target volume (TV) did not extend past the contralateral vertebral body and midline (n=11). The midline group was further subdivided into midline lateralized (n=4) and midline bilateral (n=7).

Results: TV coverage was similar for both PBS-PBT and IMRT for the entire group (median D95 97.2% vs. 96.9%). For lateralised and midline lateralised tumours (n=13), PBS-PBT significantly improved contralateral kidney sparing at moderate and low doses (median Dmean 2.2Gy vs. 6.6Gy, $p=0.000$; V12Gy 1.38% vs. 5.5%, $p=0.000$; V5Gy 14.9% vs. 68.9%, $p=0.000$). For midline tumours, bilateral kidney sparing with PBS-PBT was significant at low doses only (median Dmean 8.45Gy vs. 10.6Gy, $p=0.014$; V5Gy 59.4% vs. 84.2%, $p=0.001$). Three midline cases favoured IMRT on clinical parameters. Two were midline bilateral tumours where bilateral kidney sparing was suboptimal with PBS-PBT (median V15Gy 56.8% vs. 40.5%). The other was a large midline lateralised tumour extending anteriorly, creating dosimetric robustness uncertainty with PBS-PBT due to surrounding bowel. PBS-PBT achieved sparing at moderate and low doses for the entire group at the liver (median Dmean 3.9Gy vs. 8.3Gy, $p=0.000$; V10Gy 16.8% vs. 29.8%, $p=0.000$; V5Gy 19.2% vs. 73%, $p=0.000$) and spleen (median Dmean 3.6Gy vs. 7.4Gy, $p=0.003$; V10Gy 12.4% vs. 19.8%, $p=0.002$; V5Gy 24.2% vs. 73.9%, $p=0.000$).

Conclusions: There is a clear dosimetric benefit with PBS-PBT for lateralised and midline lateralised NB tumours. A prospective clinical study to further investigate this is warranted to streamline patient selection for PBS-PBT at time of radiotherapy referral.

PROS12 SIOP19-0770 | Hypofractionated Stereotactic Ablative Radiotherapy for Recurrent or Oligometastatic Tumours in Children and Young Adults

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Background/Objectives: Cancer remains a leading cause of death in children and adolescents in the developed world. Despite advances in oncological management, rates of primary treatment failure remain significant. Radiation of recurrent or metastatic disease improves survival in adults but there is little data to support clinical decision making in the paediatric/TYA population.

Design/Methods: We present a retrospective case series of 14 patients treated with stereotactic ablative body radiotherapy (SABR) or stereotactic radiosurgery (SRS) at The Royal Marsden Hospital from September 2011 to December 2015. Eligible patients were aged <21 years, Lansky/Karnofsky performance status ≥ 60 , with confirmed relapsed or metastatic tumour in less than 3 sites. Follow-up was in accordance with standard clinical care and included regular outpatient review and radiological surveillance. Local control, progression-free survival and overall survival are presented.

Results: Data for 14 patients with 18 treated lesions were included. The median patient age was 15 years (range, 5–20 years). 9 patients were treated for local recurrence and 5 for metastatic lesions. All patients had already undergone multiple previous treatments. 11 patients had undergone prior radiotherapy. The median interval between the completion of initial radiotherapy and re-irradiation was 29.0 months (range, 0.2–49.5 months). Median follow up was 3.4 years (range, 0.28–6.4 years). The 1-year local control rate was 78.6% and the 3-year local control rate was 64.3%. Overall median survival was 58.4 months (95% CI, 33.8–82.9 months). Cumulative BED doses over 200 Gy were associated with late toxicity ($p = 0.04$).

Conclusions: Radical doses of short-course hypofractionated radiotherapy can achieve excellent local control and may contribute to the prolongation of overall survival. There is a need for prospective trials exploring the use of ablative radiotherapy in metastatic disease in the paediatric/TYA patients in order to establish safe and effective treatment schedules.

CCI

CCI: EXPLORING EDUCATION AND THERAPEUTIC EDUCATION OF CHILDREN AND ADOLESCENTS WITH CANCER

CCI01 SIOP19-1417 | Towards Inclusion: A Case of an Inclusion Educational Program in a School for Children with Cancer in Santiago, Chile

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Background/Objectives: Survival rates in children with cancer are close to 80% in developed countries. Educational trajectories are different for children who has been cancer treated. Differences relates to cognitive, psychology and other. Even, differences by gender may be presented

in youth and adulthood after cancer treatment. For that, hospital schools help to continue studies to children in treatment to reduce educational desertion and future educational gaps. However, when children completed treatments, they back to their origin schools and this can be a stressful stage if they do not have the adequate support.

Objective: To promote school continuity of children and young people with cancer in the "*Fundación Nuestros Hijos*" schools, facilitating their reintegration into school through a comprehensive approach.

Design/Methods: This project involves: 1° Prepare students and families for future school reinsertion, 2° Carry out comprehensive accompaniment to the student and his family during the student's stay in the Hospital School and after graduation, and finally 3° Know the needs that students may present and the educational establishment of origin or new. Training is given to the entire school community to avoid errors in dealing with the reintegrated student. The academic curriculum is adapted, or the school is modified when is need it.

Results: In 2018, 72% of student of this program has been included in a satisfactory way. The main problems of educational inclusion detected are psychosocial, curricular and social. Children who have not posed to insert successfully, is mainly due to parents who have not followed the guidelines and suggestions of the team, have abruptly changed schools or not enrolled in a new school.

Conclusions: It is absolute relevant to considerer support that helps children to have an inclusion process at the origin or new schools after treatments. This would have a positive future impact on their educational and labor achievements, reducing inequalities.

CCI: PROVIDING SUPPORT TO GRIEVING FAMILIES

CCI02 SIOP19-0898 | "The Mandala": Grieving Brothers and Sisters Share Their Feelings (36 Minutes Documentary)

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Background/Objectives: The death of a brother or sister when one is still a child or teenager marks one for life. Sometimes, the effects and the hurt are difficult to put into words, or even to identify. The film is intended for grieving children and parents, therapists and trainers, but also for a wider public as it speaks to anyone who has ever been remotely affected by sickness, mourning or any other form of mental distress.

Design/Methods: This film was commissioned by LOCOMOTIVE an association based in Grenoble, France, that supports and assists children suffering from leukaemia or cancer and their families.

Results: This film shows us how these children's lives are changed, how their relations with others – even with their parents – are transformed, their questions, anger and regrets, but also their strength to go on. A psychotherapist, an art therapist and a musician suggest different ways of expressing and exchanging their thoughts, helping them to observe their physical feelings and emotions and experiment with new techniques gradually to "de-identify" with their grief and try to let go of their relationship with their dead brother or sister. Making a mandala with sand brings them into contact with the ephemeral aspect of life.

Conclusions: This documentary forms part of a wide-ranging project to assist families mourning the death of a child. The association wished to offer parents and children facing such loss a film (The Mandala) and a book (Living and growing up without you) that could be used as a means of encouraging discussion and sharing in order to help bereaved brothers and sisters.

CCI: Survivorship

CCI03 SIOP19-0730 | French Nationwide Survivors Association: Les Agueris, Adults Cured from Childhood Cancer

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Background/Objectives: With medical progress made for the last thirty years, most children affected by cancer can expect to survive to adulthood. with a life ahead to fulfill.

Les Agueris was created in 2013 by motivated former patients from Gustave Roussy to improve the follow-up and quality of life of those who were cured from childhood cancer. Dealing with the « after » is a medical subject as much as a social subject.

We are working in four areas of action. To provide information to survivors about the late effects of cancer and of its treatments. To raise awareness of public authorities and other actors on the need of long-term follow-up clinics, the need of health insurance coverage, the issue of disabling sequelae. To support research about survivorship. To create a network of French survivors with close contact with other survivors associations.

Design/Methods:

Results:

Conclusions:

CCI04 SIOP19-1005 | Giving Back to Help Other Children

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Background/Objectives: As a childhood cancer survivor it has been my ardent wish to do whatever I can to give something back to society to help other children with cancer. At the age of 9, I was diagnosed with Acute Lymphoblastic Leukaemia. I completed treatment in Accra, Ghana. Two years later, I had a relapse and received more treatment. I am now 26 years old and have completed a Medical Laboratory Science degree at University. My main objective is to create awareness about childhood cancer, provide psycho-social and treatment support for children affected by cancer in Ghana.

Design/Methods: While in University, I organized symposia to create awareness about childhood leukaemia, using myself as a success story. I formed an NGO, Living Dreams Foundation in 2014, with a group of friends. We engage in activities towards awareness creation and support of children with cancer. Musical concerts, talks on radio/TV and high school educational tours have been undertaken. I organize visits to the Paediatric Oncology Unit, Korle Bu Hospital, Accra where we interact with the children and give them some edible treats. In September 2018, I organized a blood donation campaign for children with cancer in two large shopping malls in Accra.

Results: Through Living Dreams, I have helped many people nationwide now understand and have a more positive attitude towards childhood cancer. The children and parents the group interacted with have become more hopeful about a good outcome. The 34 units of blood I was able to donate to Korle Bu has helped save many children. Activities are ongoing.

Conclusions: Without much resources, it is possible, as a survivor, to give back to other children by making a huge impact in the fight to improve access to care and outcomes for children with cancer anywhere in the world.

CCI:Cancer Registries in LMIC

CCI05 SIOP19-0474 | Establishing a Pediatric Population Based Cancer Registry in a Low-Middle Income Country: Challenges and Lessons Learned

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Background/Objectives: There is limited understanding of factual pediatric cancer incidence in Mexico due to lack of population-level data. Mexico has a complex, segmented healthcare system, which constitutes a substantial challenge for implementation of a national Population-Based Cancer Registry (PBCR). Tijuana is the largest city in northwestern Mexico with 1.7 million inhabitants. We describe challenges and lessons learned during implementation of Tijuana's PBCR, one of the firsts in Mexico.

Design/Methods: In 2015, we formed an interdisciplinary working group: pediatric oncologists (1), pathologists (1), public health specialists (2), data collectors (5), informaticians (1) and external advisors (2). In 2016, the team was trained in data collection and coding through workshops (3) and web-based meetings (6). CanReg5 software was chosen for data entry/analysis. In 2017, after the Mexican National Cancer Registry bill was approved, the Tijuana team joined the National PBCR initiative, along with five additional cities.

Results: Tijuana's PBCR, BajaREG, was launched in January 2018. Twenty sources of information (hospitals, pathology laboratories and death certificates) were identified (5 public; 15 private). During BajaREG implementation, we faced the following challenges: limited local start-up funds; lack of dedicated work space; misinformation regarding PBCR's purpose and personal information use; underdeveloped hospital information systems/incomplete data; bureaucratic hurdles at public hospitals and lack of knowledge regarding mandatory reporting of cancer cases according to the Mexican Health Law. Preliminary data include 72 new pediatric cancer cases in 2017 and 84 cases in 2018, with leukemias comprising 38%, lymphomas 9.5% and brain tumors 11%.

Conclusions: Despite initial challenges, we achieved collection of accurate data in 90% of target sources. Lessons learned include to: adapt processes to local needs; optimize data collection from outdated information systems; engage and educate stakeholder regarding the need of obtaining comprehensive cancer population-level data in Mexico; and reinforce confidentiality assurances of patient information at participating institutions. BajaREG will provide a comprehensive understanding of pediatric cancer epidemiology in Tijuana.

CCI06 SIOP19-1301 | Population Based Childhood Cancer Registration in Africa

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Background/Objectives: Data on cancer incidence and outcome at the population level are sparse in Africa since existing population based registries cover rather limited populations, generally just the capital city or other major urban centres. In 2017, with the support of the My Child Matters programme, a project to develop national-level childhood cancer registries was started in 3 francophone countries.

Design/Methods: Existing cancer registries in the capital cities of Abidjan, Ouagadougou and Brazzaville were expanded to collect data on childhood cancers for the whole national population of, respectively, Cote d'Ivoire, Burkina Faso and Republic of Congo.

At the same time, laterality of renal and eye tumours, and stage of childhood cancers, using the new "Toronto consensus" staging system, was recorded for childhood cancers

Results: The results of the first year show that completeness of registration remains more complete in urban centres, but, even at this stage, registration is probably capturing more than half of the estimated incident cancers.

There were differences in the cancer profile between the three centres, with e.g. relatively high rates of Burkitt lymphoma in West Africa (Cote d'Ivoire and Burkina Faso), but not in Congo. Nephroblastomas slightly outnumber retinoblastomas in all three centres.

Staging of paediatric cancers was remarkably complete, especially for the solid (germinal cell) tumours. Only about one quarter of retinoblastomas were recorded as "localised" (intraocular).

Conclusions: It appears that, given modest extra resources, cancer registration for paediatric tumours is feasible for relatively large populations (10-12 million) in low income settings. The simple staging system of Tier 1 in the Toronto consensus system can be successfully used by cancer registrars. The availability of stage data will help greatly in evaluation of the success of early detection, and of survival statistics.

It is hoped to extend this model of national childhood cancer registration to other countries of sub Saharan Africa, starting in 2019/2020.

CCI07 SIOP19-0882 | Twelve Countries Present Their Results of a Hospital Based Childhood Cancer Register in French Speaking African. On Behalf of the GFAOP (Groupe Franco-Africain D'Oncologie Pédiatrique)

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Background/Objectives: Over the past 20 years the GFAOP, founded in 2000 have enabled over 17 hospital based cancer units to open in an effort to realize their vision: "treat effectively African children with a cancer in Africa with African teams".

Five units had previously participated in GFAOP observational feasibility studies. These studies evaluated treatment and efficacy for 5 types of cancer sharing a high chance of remission when treated early enough. The results of these studies led to the setting up of this register with the support of the Sanofi Espoir Foundation. The aims include: (1) collecting information on cancer incidence, (2) identifying material, human and training needs, (3) evaluating treatment outcome (4) encouraging consideration of paediatric cancer in both national and international health plans in participating countries.

Design/Methods: From January 2016 to December 2018, 3314 patients were registered and 2790 cases of childhood cancer identified from 13 units. Data collection was progressively performed using the online REDCap platform.

Results: Median age was 5 years (0-18 years); male/female sex ratio was 1.5. Most frequent diagnoses were cancer types for which a GFAOP protocol exists: Burkitt lymphoma (581), retinoblastoma (493) Wilm's tumors (478), Acute Lymphoblastique leukaemia (366) and Hodgkins lymphoma (72). Diagnosis could not be achieved for 344 patients.

Disease extension was higher than stage III for 748 (26%) and outcome is known for 73% of identified cancer cases. Seventeen percent of cases abandoned treatment.

Conclusions: This is the only multi center international hospital register with prospective inclusion in French speaking Africa which gives units direct access to their data. It is just the tip of the iceberg. Identified challenges are being addressed including record reporting and filing, internet stability and training of research assistants.

We acknowledge A Gagnepain-Lacheteau, medical director of the Fondation Sanofi Espoir, for her support through the My Child Matters program.

CCI:Improving Care and Quality of Life

CCI08 SIOP19-0225 | Malnutrition in Childhood Cancer Patients in Malawi: Age-Based Prevalence and Effect on Mortality

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Background/Objectives: Most children with cancer live in resource-limited countries where malnutrition is prevalent. National nutrition programs focus on children under five years, however children with cancer are at risk regardless of age. The objective of this study was to evaluate the extent of malnutrition among children with cancer in Malawi, with regard to age, disease, and mortality.

Design/Methods: This single-center retrospective cohort study enrolled 396 consecutive children (<19 years) diagnosed with cancer at Kamuzu Central Hospital in Malawi. Malnutrition was assessed by either Weight-for-Height/Body-Mass-Index or Mid-Upper-Arm-Circumference; and defined as moderate (MAM) or severe (SAM) using standardised definitions. Survival distributions were assessed using Kaplan-Meier curves and Cox Hazard analysis.

Results: The mean age was 7.2 years (SD 4.1); 66.7% of patients were ≥ 5 years and 60.1% were male. Leukemia, lymphoma, or a solid tumor was diagnosed in 17.7%, 29.6%, and 42.7% of children respectively. The majority of children (76.0%) were malnourished; 29.7% with MAM and 46.2% with SAM. Malnutrition was more common among children ≥ 5 years (215/264; 81.4%) versus <5 years (86/132; 65.2%), $p < 0.001$. Malnutrition was less common among children with a solid tumor 118/169 (69.8%) versus 56/70 (80.0%) in patients with leukemia's and 127/157 (80.1%) in those with lymphomas ($p = 0.045$). A total of 109 (27.5%) patients in this cohort died, with a median time to death 116 (IQR 20.5-267.0) days. MAM (HR 2.5 95% CI 1.3-5.0, $p = 0.009$) and SAM (HR 3.4; 95% CI 1.8-6.4, $p < 0.001$) were associated with mortality.

Conclusions: Malnutrition is highly prevalent on children with cancer in Malawi. Both MAM and SAM at diagnosis are associated with increased mortality. Hence, suggesting that all children with childhood cancer, would benefit from national nutrition support programs, regardless of age and severity of malnutrition.

CCI09 SIOP19-1583 | Aiming for Zero Errors -Creating a Novel Open-Source Simple Platform for Highly Automated Patient-Specific Chemotherapy Prescriptions at Tumaini La Maisha / Muhimbili National Hospital, Tanzania

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Background/Objectives: Background: Manual prescription of chemotherapy is inherently error prone, requiring sub-specialist input. Errors increase toxicity and decrease treatment efficacy. Existing chemotherapy automation software is underdeveloped and prohibitively expensive for resource-limited countries.

Objective: To assess the viability of a comprehensive, cost-effective, open-source automated solution to minimize human error in chemotherapy prescription.

Design/Methods: Local protocols and a random sample of handwritten prescriptions were reviewed to classify prescribing errors. Questionnaires assessing automated options were sent to international pediatric oncology centres. We created a Microsoft ExcelTM software solution using embedded formulas to automate almost all complex protocol decisions, which included daily error log-assessment. All identified mistakes were neutralised by appropriate modifications. A structured questionnaire-based interview of key stakeholders was conducted to evaluate satisfaction.

Results: Twelve replies from international centres confirmed automated chemotherapy prescribing is neither universal nor comprehensive. Reviewing 124 randomly selected manual chemotherapy sheets revealed over 200 errors, including, dosage, quantity, frequency, timing, modification errors, missing clinical information and protocol directed response-to-treatment (RTT) actions. Sixteen protocols required automation. Nine protocols were fully automated, along with a generic automation sheet for the 7 remaining protocols. These were created to replace all manual chemotherapy prescribing, automatically updating all recurring fields including name, diagnosis, stage, etc. Automation resulted in elimination of the following errors: upfront regimen, RTT choice, dose omission and drug modification related

to clinical status. Since implementation in October 2018, 26 errors were logged and subsequently resolved. Active, daily error reporting and code modification removed this risk permanently. Other 'human' errors were reduced through training and user checklists. All 10 participants in our key stakeholder survey found chemotherapy prescribing safer for patients after implementation of our automated protocols.

Conclusions: Open-source automated sheets, with continual error surveillance, have the potential for zero-error chemotherapy prescribing for all.

CCI10 SIOP19-0901 | Paediatric Oncology System Integration Tool (POSIT): A Health Systems Performance Framework for Childhood Cancer in Low- And Middle-Income Countries

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Background/Objectives: Many limitations to advancing childhood cancer care in low- and middle-income countries (LMICs) result from underlying health system constraints. To better understand how health systems intersect with and impact the performance of childhood cancer care, we developed a system-level performance framework for childhood cancer in LMICs.

Design/Methods: Framework development was informed by expert opinion from key stakeholders in global paediatric oncology, a modified scoping review of childhood cancer performance measurement and improvement in LMICs, and a structured comprehensive review of general health system literature. Literature review results were thematically analyzed and conceptually integrated with expert opinion to produce the final framework.

Results: Our findings from the childhood cancer performance literature demonstrate a current gap in efforts to strengthen the performance of childhood cancer care at a health systems-level in LMICs. Few prior studies have employed explicit performance frameworks, with none that have been applied across multiple settings. Grounded in prior literature and expert opinion, our novel framework incorporates important health system determinants of childhood cancer performance and synthesizes these with general health system frameworks. Our framework outlines the key functional domains of childhood cancer systems – *governance, financing, health workforce, infrastructure,*

health information systems, medicines and health technologies, and demand generation – and elaborates on these by articulating multiple sub-functions of specific relevance to childhood cancer in LMICs. It also delineates several performance objectives – *access, efficiency, effectiveness, and responsiveness* – and breaks these down into measurable performance dimensions. Lastly, it outlines the sociopolitical factors influencing childhood cancer system performance.

Conclusions: This is the first comprehensive framework for analyzing childhood cancer systems in LMICs. Along with an associated assessment toolkit, it has been piloted in several LMICs to date. Through future dissemination of both the framework and toolkit, we aim to facilitate comparative research to inform cross-contextual learning for strengthening childhood cancer systems.

CCI:Pain Management

CCI11 SIOP19-1511 | Management of Pain Induced in the Department of Hemato-Oncology of the Mother and Child Center of the Chantal Biya Foundation of Yaounde

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Background/Objectives: Introduction: In our context, the management of pain in children in hospital is very often sub-optimal, which constitutes an obstacle in the parent-patient and caregiver relationship.

Objective: To develop an analgesic protocol during invasive procedures.

Design/Methods: Methodology: Our prospective study focused on the management of pain induced by caregivers from December 2018 to January 2019 in the department of Hemato-oncology. A sensitization on the gesture (Bon marrow aspiration / lumbar puncture) was made, an analgesic protocol administered according to a well-defined sequence composed of: xylocaine, tramadol, midazolam; followed by an evaluation of the pain.

Results: We report data from 20 of the 47 hospitalized children in whom pain and fear were present without exception. The average age was 8 years (1.5, 16). The analgesic protocol was initiated for the first time in 15 against 5 who had already had gestures without analgesic. The presence of the free Emla cream in our service facilitated the implementation of the protocol. Injectable xylocaine was administered to 16 children during the Bon marrow aspiration. Whatever the action, a good response was found in 12 children, no response

in 4, compliance with or without protocol in 4. In addition, distraction, caresses were used to all children. An early amendment of pain was observed in 19 children versus 1 with post lumbar puncture syndrome.

Conclusions: Pain must be considered as a disease. Its management is a priority, and the positive experience in the service justifies the durability of the analgesic protocol. The absence of pain management in the past has been a barrier to the smooth running of care.

CCI12 SIOP19-1508 | The Safe Place Experience - Using Imagery to Support Children During Painful Procedures in Pediatric Oncology

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Background/Objectives: Children cancer treatment consists of repeated painful procedures. Throughout the research and clinical practice, we observed that using pharmacological support to manage the pain, does not always reassure the child. It is a challenge for the professional team to help a frightened child to drain the painful experience from anguishing content. The aim is to create a child-centered procedure environment where every procedure the child faces becomes 'just another one' and not a repeated trauma.

Design/Methods: We have developed an evidence-based method of supporting children during painful procedures that through creativity and imagery stimulation helps children face the painful experience and express their preferences for pharmacological support. Psychologist takes care of the child: *before* the procedure, creating a "listening time" where the child is stimulated to find his inner "safe place" and choose among general anesthesia, conscious sedation or no anesthesia; *during* - recalling the "safe place" image and offering support modality according to child's request and personality; *after* - helping elaborate the whole experience.

Results: We performed 247 consecutive painful procedures in 85 children. We observed that children's ability to be in tune with their needs and recall reassuring "safe place", expresses the capacity to make the most adequate choice to face procedures. Caregiver's containment modality and operators respect for child's choice is an important factor.

Conclusions: Creativity and imagery stimulation help children to face the painful experience and to express their preferences for pharmacological support. Children experiencing child-friendly procedure environment, become more compli-

ant and less anxious, which helps establish a trusting relationship among children, caregivers and multidisciplinary team. Support modality that respects child's choices/personality style prevents a perception of procedure as a repeated trauma. All we do is to give an opportunity to each child to reach his 'safe spot' through universal, powerful tool of imagery.

CCI:Research: Parents and Patients Priorities, Involvement and Support

CCI13 SIOP19-0704 | Research About Childhood Cancer: What Topics and Answers are Parent and Patient Looking For?

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Background/Objectives: Parents and young patients diagnosed with cancer have numerous questions: Why me (my child) ? What is the best possible treatment ? What long-term effect will the treatment have ? What new treatment is possible if the "standard" doesn't work ? Where could I find good, accurate and understandable information ?

But if they could choose and prioritise. What choice would they make ?

Our objective was to establish a list of question and issues expressed by families.

Once established, the Scientific Community should integrate them in their research strategy to provide answers to this questions.

Design/Methods: The French Parent and Patient Organization Union realised a survey to evaluate the needs for information and level of understanding of parent and patients.

More than 200 person (including 165 former patients and 34 parents) answered the survey. answered and the results have been analysed.

Based on this survey an informational meeting for parent and families with keynotes lectures about the may topics was organized for ICCD in the Health Ministry.

This roundtable

Both the minutes of that day and the results of the survey were used to produce a "White book" establishing the needs and questions raised.

Results: The global understanding may improve:

65% expressed that they didn't understand the word "genomic" but 80% were looking for information about this point.

Among 81 patient who took part in a clinical trial, 39% didn't understand the concept of "randomization".

Improving the treatment is a major topic:

But, the gap between what is “known” to be done and what would be needed remain important.

Especially for “Late effects” and “Environnemental causes”

Conclusions: This survey could easily be extended internationally and we propose to enlarge this study to all CCI member organization.

This could give a global and broader picture of the question addressed by young patient and there families to the scientific community.

CCI14 SIOP19-1217 | U-LINK: A PLATFORM PROVIDING INFORMATION ON PEDIATRIC ONCOLOGY CLINICAL TRIALS AVAILABLE IN FRANCE AND FINANCIAL SUPPORT FOR FAMILIES OF CHILDREN WITH CANCER

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Background/Objectives: Parents are very involved in the management and follow-up of their child's cancer and need data to understand their child's path. The idea of setting up a modern and accessible tool to meet these needs was developed through a collaboration between the National Pediatric Oncologist Society (SFCE¹) and National Parent Organization Union (UNAPECLE²).

U-Link is an Internet platform, entirely dedicated to pediatric oncology. Its purpose is to inform parents, families and health professionals about clinical trials. The availability of complete, understandable and up-to-date information on clinical studies, is a public's request.

U-Link is also a system, through which travelling and accommodation costs not covered by social health care system can be reimbursed.

Design/Methods: The U-Link clinical trial database is built from a variety of sources: information for health professionals is developed with pediatric oncology investigators - information for the families of children with cancer is written by parents volunteering for this task.

Social workers, in collaboration with an UNAPECLE U-Link committee, are responsible to resquest for family support.

Results: Since the launch of the U-Link website on April 17, 2018, 105 clinical trials have already been published for physicians, including 67 simplified for families. 90% of them are interventional studies.

For the families support system, 175 cases were processed for a total budget of €80,000, with an average of €500 per request. The rate of supports is the same between accommodation and transport.

The U-Link website is visited on average 300 times a month, 75% of which are in France. 15,000 pages are consulted including 40% for the clinical trials registry.

Conclusions: The U-Link project is useful for families and health professionals.

It is necessary to keep the published informations up to date and to ensure sustainability of the families support system.

The concept of this website can be easily shared in other countries.

CCI:RESPONDING TO THE NEEDS OF ADOLESCENTS WITH CANCER

CCI15 SIOP19-0420 | Generation Z – A New Approach is Needed

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Background/Objectives: Teens always say: “Don't tell us what you think we need, ask us what we need”. Teens, also known as Post Millennials or Generation Z, take in information instantaneously, and lose interest just as fast. CHOC needed to find out what the teens need in order to rethink our programmes of support to them.

Design/Methods: CHOC conducted focus group discussions in eight Paediatric and Oncology Units in South Africa and 41 teens participated. We prepared guidelines with questionnaires for CHOC social workers to run the Focus Group Discussions (FGD). Each participant had to sign a consent and confidentiality agreement to participate in the FGD; as well as an attendance register.

Results: The teens feels that they need their own space, need to have contact with their friends and siblings via personal contact or social media, don't want to be exposed and need to be accepted as normal. Awareness in their communities is important so that their integration back will be easy and without stigma. It is important for them to stay on par with their school friends and to receive educational assistance while in hospital. Social events different from the children and events or a symbol to celebrate completion of treatment give meaning to the journey. Most of them spoke about being bored and what CHOC could do to accommodate this. Honesty, open discussion, patience and mutual understanding play a huge role in their healing process.

Conclusions: Teens need to be kept busy, informed and needs people that they can trust. Acceptance in their communities is

very important and to give back to patients undergoing treatment was evident. Education and to learn new things came through strong. To accommodate teens, to keep their interest and to provide teen appropriate practical support CHOC will have to adapt our programmes.

CCI16 SIOP19-1502 | State of Knowledge on the Risk Factors of Childhood and Adolescent Cancers

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Background/Objectives: Cancer is a leading worldwide cause of death for children, with 300,000 new cases diagnosed each year among children aged 0-19 years. It is estimated that nearly 2,500 new cases of childhood and adolescent cancer occur each year in France, half of them in children under 5 years of age and 700 in young people aged 15 to 18 years.

Design/Methods: The research has shed light on the mechanisms of carcinogenesis, that is, the transformation steps from a normal cell to a cancer cell, but the causes are poorly understood and many uncertainties remain. The role of environmental factors in the occurrence of childhood cancer is also the subject of many studies at the national and international levels. A state of knowledge of research in this field will be proposed in this paper based on the activities carried out within the Cancer Environment Department (Lyon, France) and on a critical review of the literature published on the links between occupational exposure and rare cancers. The other possible causes of childhood cancer will also be discussed: in particular the role of genetic factors and behavioral or lifestyle factors (pollution, diet, exposure to mobile phone waves.).

Results: Current research hypotheses and issues will also be presented.

Conclusions: The many questions raised by the population about the possible causes of childhood and adolescent cancers, and in particular the attributable role of environmental, occupational and nutritional factors in increasing the risk of cancer, encourage us to strengthen our efforts in terms of evidence-based public information and recommendations for the prevention of cancers, in particular by encouraging the prevention of the risks of second cancers in this population more at risk, on preventable risk factors (tobacco, alcohol, poor diet, sedentary lifestyle).

CCI:Supporting Families

CCI17 SIOP19-0982 | Travel from One Treatment Centre to Another: Understanding the Burdens of Travel and Accommodation and the Impact of These on a Family Unit

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Background/Objectives: Informed decisions are augmented by recognition of emotional needs, social well-being, and knowledge of disease and clinical research landscape. Increasingly, more families are seeking access to clinical trials across borders when options become limited locally. Families with children affected by paediatric cancer who decide to travel for treatment must consider all potential burdens. The Family Support Service [FSS] acknowledges these issues and how specific supportive care can ease the burden families and their children may face.

Design/Methods: The FSS team is led by a Senior Family Coordinator to meet needs of individual cancer patients and families. The FSS provides trusted, experienced parent-professionals who listen, identify key needs, and provide tailored support and guidance throughout a cancer journey. Case studies are used to identify the burden for families who travel for access to novel therapies from one treatment centre to another.

Results: The childhood cancer footprint differs for families. In one year, 17 families have travelled for treatment worldwide. This includes 42 sets of travel [flights or otherwise] and 42 sets of accommodation. The FSS is experienced in offering direct and tangible support for families in recognition of the disadvantages and advantages of travelling for treatment. These can include social and emotional issues as well as financial challenges which can impact a family unit at specific times such as when preparing for travel, during access to treatment, in between treatment and post return. The FSS offers supportive care to families throughout this process to help manage their cancer journey.

Conclusions: Families travelling from one treatment centre to another can experience economic, social and emotional burden at an already challenging time. Families benefit from bespoke guidance and support during four distinct key points when travelling for treatment. Support services and further collaboration can help reduce the negative impact on a family unit.

CCI18 SIOP19-1380 | Accreditar's Family Houses: A Home Far Away from Home for Dislodged Families During Pediatric Cancer Treatment

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Background/Objectives: Portugal has three main paediatric cancer treatment centres: one in Lisbon (south), one in Coimbra (centre) and one in Oporto (north). However, children with

cancer come from all over Portugal, including Madeira and Azores islands and also former Portuguese colonies in Africa. Most of the children not living near the treatment centres do not have a place to stay with their families when in outpatient treatment. That is why Acreditar built three houses, all located within walking distance from the treatment centres.

Design/Methods: This presentation will focus on the main characteristics of our Family Houses: design, capacity, target population, number of families already benefitted, investment, costs, social impact.

Results: In total, Acreditar's Houses have 48 rooms (one room = one family) and will increase its capacity to 68. Since the opening of our first House (Lisbon, 2003) we have already lodged more than a thousand families from all over Portugal and from the Portuguese speaking countries in Africa. In 2012 Acreditar decided to start measuring the social impact of the houses once every two years. This tool clearly showed some qualitative gains of which we highlight those related to children, namely the increase of a safety feeling, the improvement of the relationship with the hospital, a better adherence to treatment, less dependency of parents, personal growth and better conditions on returning to normal life.

Conclusions: By using this tool, involving all stakeholders, i.e., families, donors, hospitals, volunteers and staff, we came to the conclusion that the return on investment amounts to six euros for every euro invested. The qualitative and quantitative gains are a strong evidence of the importance of Acreditar's Houses.

CCI19 SIOP19-1578 | Aroh - A Journey of 6 Years, from Serving 5 Hospitals to 40

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Background/Objectives: Aroh is an NGO for childhood cancer, started in 2013. Its beginnings were in Coimbatore, a small town in South India. This is about how Aroh spread to all of South India in 6 years.

Design/Methods: This is a step by step analysis of Aroh and its growth from 5 hospitals to 40. A critical and in depth look at the positives and negatives of the steps taken.

Results: Aroh is able to serve more than a 1000 kids now. This was possible only because of the associations and tie ups with other organisations. Collaboration is the key to growing.

Conclusions: This can be a motivating story for other small-town NGOs and they may be able to follow some of the methods here.

CCI20 SIOP19-0647 | The Parents Advisory Group: An International Model for Paediatric Oncology Support Groups

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Background/Objectives: The Parents Advisory Group ("PAG") operates within the Children's Cancer Centre ("CCC") of the Royal Children's Hospital, Melbourne, Australia. The PAG is comprised of volunteer parents and carers ("parent members") of patients who have received treatment in the CCC, and also senior treating medical professionals.

Following a change in the leadership of the PAG, at the commencement of 2018 the operation of the PAG underwent a 'root and branch review'. This culminated in the drafting by the parent members, and the subsequent implementation by the PAG, of a Mission Statement (constitution).

Design/Methods: First, consideration of the operation of the PAG having regard to the Mission Statement.

Second, consideration of the challenges confronted by the PAG arising out of:

- (a) Difficulties in the recruitment of parent members, especially from diverse cultural backgrounds;
- (b) The voluntary status of the parent members and their availability to undertake activities on behalf of the PAG;
- (c) The drafting and implementation of a written constitution.

Results: The PAG is optimally regulated by the implementation of a written constitution which reflects its purpose, defines its role and provides focus to its activities, and which may assist in the recruitment and management of new members.

The operation of the PAG may be used internationally as a template by other paediatric oncology parent and carer support groups.

Conclusions: The scope of the objectives established for a group such as the PAG is the product of the willingness of parents, carers and staff, including from diverse cultural backgrounds, to be recruited as members.

The PAG's Mission Statement and activities in meeting with the parents and carers of paediatric oncology patients may be used as a model for international parent and carer support groups.

CCI21 SIOP19-0636 | All Protocol Illustrated as Simplified Maps. For Doctors Children and Families, To Explain and Understand the Treatment. Designed by a Mother to a Cured Child

Z. Shalev¹

¹Information Design, Design, Pardes Hanna Karkur, Israel

Background/Objectives:

6 years ago, my 4-year old daughter was diagnosed with Leukemia ALL and recovered.

I am a designer and teacher for Way-finding design.

My job role, as I see it, is to give a secure feeling while on an unknown journey by simplified professional information.

Our family's recovery journey and experience gave me an opportunity to contribute with my design skills. Knowing the sense of helplessness as one enters the unfamiliar world of Leukemia. Feeling distressed, afraid and mentally blocked.

Design/Methods: I designed the Leukemia ALL Protocol & medical treatment information as maps. Written & illustrated in a simple and accessible way. For the use of the medical team, the patients and their families.

The Protocol as a recovery path (inspired from board-games) with icons - for intravenous treatment (inpatient & outpatient) Intrathecal (IT), Full anaesthesia etc.

Constituting a positive visual language which can be used in various cancer protocols.

Easy to visually follow the Protocol and understand. Thus gives a more secure and soothing feeling.

A sense of partnership and responsibility.

Can even reduce human error.

I was privileged to have furthered develop the project with the cooperation of the Pediatric Hemato-Oncology Department at Schneider Hospital in Israel- as the medical authority in the project: Prof. Yaniv's & Prof. Izraeli's support and Dr. Gilad who accompanied the process with dedication, contributed from his experience and knowledge.

Results: They have been handed out for the past two years to ALL patients. Proving itself as a practical tool for patients, parents and their medical team.

Please visit the link for further information: protocols4patient.wixsite.com/zshalev

Conclusions: I feel it would be beneficial to expose and present it in the conference, and appreciate to have this opportunity - to present, discuss, answer questions and further develop the concept.

POSTER DISCUSSION

Poster Discussion 01 - ALL Treatment in Limited Resource Settings

D01 SIOP19-0556 | Induction Toxicities in Childhood Acute Lymphoblastic Leukemia

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Background/Objectives: Background: In Childhood Acute Lymphoblastic Leukemia (ALL), chemotherapy-associated toxicities occur maximally during Induction. We analyzed the distribution of severe toxicities ($\geq$ Grade 3) in children with ALL treated uniformly on a risk-adapted protocol at a tertiary cancer institute in India.

Design/Methods: Methods: Children aged 1-15 years with ALL prospectively treated on ICiCLE-2014 from March to December 2018 were included. All parameters were prospectively recorded. Toxicities were graded as per CTCAE-4.0. Descriptive and univariate analysis was performed using SPSSv.24@.

Results: Results – There were 332 patients eligible, median age-5.9 years, M: F-2.5:1, with B-ALL-277 (83.4%) and T-ALL-55 (16.6%). According to initial- risk stratification, 107 (32.2%) were Standard-Risk (SR), 82 (24.7%) Intermediate-Risk (IR) and 143 (43.1%) High-Risk (HR). Total toxic events (Grade-3/4) were 366 in 239 patients, of which Grade-3, 344 (94.0%) and Grade-4, 22 (6.0%). Events in SR were Grade-3, 99 (27%), Grade-4, 2 (0.5%), in IR, Grade-3, 81 (22.1%), Grade-4, 10 (2.7%), and in HR, Grade-3, 164 (44.8%) and Grade-4, 9 (2.4%). In SR and IR, 103 (54.6%) events occurred in continuous-steroid arm compared to 86 (45.4%) in interrupted-steroid arm. Commonest toxicities were febrile neutropenia 211 (54.6%), hypertension 37 (9.6%), constipation 28 (7.2%), Varicella 19 (4.9%), bleeding 15 (3.9%) and hyperglycemia 13 (3.3%). On univariate analysis, gender, steroid-arm, number of daunorubicin doses, risk-stratification and immunophenotype of ALL were not significantly associated with toxicities. There were 16 deaths (Grade-5), of which 13 were B-ALL (SR 1, IR 6 and HR 9) and 3 T-ALL. Commonest cause of death was sepsis in 13 (82%) followed by bleeding in 3 (18%). Mortality was higher with increased daunorubicin doses and higher risk-stratification, but the association was not significant ($p=0.07$ for both), while B/T-phenotype, continuous/interrupted steroids and gender were not associated with mortality risk ($p=0.81$, 0.21 and 0.18 respectively).

Conclusions: Risk-stratified Induction for Pediatric ALL patients has an acceptable toxicity profile, while sepsis remains a major challenge regardless of treatment intensity.

D02 SIOP19-0893 | Pediatric Acute Lymphoblastic Leukemia (ALL). 17-Year Experience at Children Welfare Teaching Hospital (CWTH), Baghdad, Iraq

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Background/Objectives: Since 2000, three adapted UKALL protocols were implemented at Children Welfare Teaching Hospital in Baghdad for the treatment of pediatric acute lymphoblastic leukemia (ALL). We report the outcome of 1415 consecutive patients treated from January 2000 to December 2016.

Design/Methods: 1635 children (age 1-15 years) with ALL were registered. Mature-B-ALL, infants, Down syndrome, children pre-treated, treated elsewhere, who died prior to treatment (220) were excluded. 1415 B- or T-lineage ALL were included in the analysis. Therapy consisted of adapted UKALL-97, 2003 and 2011 protocols. Since October 2008, steroid pre-phase was included. Since March 2008, T-ALL entered BFM-derived protocol.

Results: Of 1415 patients, 781 (55%) were males and 634 (45%) females; median age was 5 years (range 1-15); 586 (41%) were from Baghdad, 829 (59%) from outside; 1285 (91%) were B-lineage ALL and 130 (9%) T-ALL; 223 were treated according to UKALL-97, 841 to UKALL-2003, 274 to UKALL-2011 and 77 to T-ALL BFM-95; 716 received steroid pre-phase, 515 (72%) were prednisone good responders. 1219 (86.1%) achieved complete remission (CR); 124 (8.8%) died during induction; 19 (1.3%) were resistant; for 53 (3.7%), the evaluation was not possible. 252 children relapsed (median time 22.2 months; range 0.8-160). OS for the entire series of patients is 81.4% at 12 months (CI 95% 79.63-83.57) and 74.6% at 24 months (CI 95% 72.3-76.9); DFS is 77.2% at 12 months (CI 95% 75.1-79.1) and 69.3% at 24 months (CI 95% 66.8-71.8); considering abandonment as an event, EFS is 69.1% at 12 months and 60.4% at 24 months. Univariate and multivariate analysis show better OS and EFS for males ($p=0.005$), age <10 years ($p=0.005$) and for patients treated during 2012-2016 period ($p=0.003$).

Conclusions: Long-term results in Iraqi ALL children are encouraging with a progressive decrease of abandonment rate and a significant improvement in OS and EFS in the last 5 years.

D03 SIOP19-1375 | Early Intensification Improves Outcome in Pediatric T-Cell Acute Lymphoblastic Leukemia

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Background/Objectives: T-cell acute lymphoblastic leukemia (T-ALL) accounts for approximately 15% of all newly diagnosed ALL in children and adolescents and associated with worse outcome compared to pre-B ALL. Patients with relapsed T-ALL have limited therapeutic options and poor prognosis. We aim to decrease T-ALL relapses by using upfront intensification. Intensification drugs included fludarabine, etoposide and cytarabine in two blocks added to our standard protocol as of Sep2014.

Design/Methods: Patient with T-ALL were treated using two different regimens; before Sep2014, patients with T-ALL were treated per St. Jude Total XV protocol; subsequently, a major change was adopted by adding two intensive blocks: 1-FLAG consolidation and 2-re-Intensification (dexamethasone, cytarabine, etoposide and asparaginase). Prophylactic cranial radiotherapy was given to patients with WBC $>100\text{k}/\mu\text{l}$ at diagnosis and/or patients with CNS2/CNS3 status.

Results: Between Jun2005 and Oct2017, a total of 76 patients (56 males) were treated and followed for a median of 48 months (range, 0.8-159 months). Median age at diagnosis was 8.5 years (range, 0.5-17.8 years). Median WBC at diagnosis was $59\text{k}/\mu\text{l}$. CNS status at diagnosis were: CNS1 (N=65), CNS2 (N=5) and CNS3 (N=6). End of induction bone marrow status were: M1 (N=70, 92%), M2 (N=3, 4%) and M3 (N=3, 4%). Twenty five patients (out of 76, 33%) received the intensified regimen as they were diagnosed after Sep2014, their median follow up was 52.4 months (range, 17-60.7 months). The 5-yr-EFS estimates for patients who received the intensified regimen vs. Standard regimen were $96\pm 4.4\%$ vs. $67\pm 6.8\%$ ($p=0.018$); and the 5-yr-OS estimates were $96\pm 4.4\%$ vs. $71\pm 6.8\%$ ($p=0.018$). Two toxic deaths were reported in the standard regimen but none for patients who received the intensified regimen.

Conclusions: We implemented a novel approach with early intensification added to a backbone of modified Total-XV regimen for patients with T-ALL that resulted in remarkable outcome with no toxic deaths.

D04 SIOP19-1084 | Treatment Delay More Than 4 Weeks Promoted Relapse of Children with B-Cell Acute Lymphoblastic Leukemia

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Background/Objectives: In this study we analyzed the clinical information of children with B-ALL treated with CCLG-ALL-2008 in our single center, and explored the influence of treatment delay on relapse and its related causes of delay to help the optimization of proposal in future clinical trials.

Design/Methods: From January 2011 to December 2014, 287 children were chosen who met criteria as following: finishing at least chemotherapy for induced remission therapy, early intensive treatment, consolidation therapy, and delayed intensive therapy. Meanwhile, the children were excluded when primary drug resistance (minimal residual disease, $MRD \geq 10^{-2}$), persistent non-remission, and relapse of disease or gave up treatment due to any other reasons during above treatment courses. Children with treatment delay were 222 cases. The relationship between treatment delay time and relapse and the causes of delay and relapse were compared. The data were analyzed by Chi-square test, COX proportional risk regression model, Kaplan-Meier Curve Survival Analysis, Bilateral Log-Rank test, Life table method. The last follow-up time was December 2018. $p < 0.05$ was considered to be statistically significant

Results: Seven years RFS in treatment delay group was $89\% \pm 3\%$ and $98\% \pm 2\%$ in non-delay group ($p < 0.05$). The relapse rate was higher in the delayed group ($p < 0.05$). According to the 25% (15 days), 50% (32 days), and 75% (76 days) delays of the treatment, relapse was higher in the group of the treatment delay more than 76 days than that less than 15 days ($p < 0.05$). The effect of treatment delay more than 4 weeks and MRD positive on 12 weeks' treatment were independent prognostic factors on relapse. The initial white blood cell count showed a tendency of affecting relapse rate ($p = 0.08$). Myelosuppression alone was an independent prognostic factor influencing relapse ($p < 0.05$)

Conclusions: Treatment delaying more than four weeks and MRD positive on treatment for 12 weeks and bone marrow suppression were independent prognostic factors on relapse

D05 SIOP19-1120 | Cytogenetics in B-Lineage Acute Lymphoblastic Leukemia (ALL); Translocation T (1;19) (Q23;P13.3) E2A-PBX1 is a Poor Prognostic Criterion in Children of African Descent

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Background/Objectives: Cytogenetics is used to stratify B-lineage ALL into prognostic risk groups. Hyperdiploidy and translocation t (12;21) indicate a favorable prognosis, whereas translocation t (9;22) and MLL gene rearrangements indicate an unfavorable prognosis. Translocation t (1;19) E2A-PBX1

has not been used in the major clinical trials in High Income Countries (HIC) as an unfavorable prognostic factor, and the literature is not conclusive.

Design/Methods: A retrospective chart review was performed on all ALL patients treated at the Charlotte Maxeke Johannesburg Academic Hospital, and Wits Donald Gordon Medical Centre, Johannesburg, South Africa from 2002 to 2018. Initial bone marrow examination included immunophenotyping by flow cytometry, cytogenetics, ploidy by flow cytometry, and Fluorescent In-Situ Hybridization (FISH).

Results: A total of 322 patients were diagnosed with ALL. Of these 241 (74.7%) were diagnosed with B-lineage ALL. There were 224 with early Pre-B/CALL, 11 with pro-B/Null ALL, and 5 patients who also had mature B antigen expression with surface membrane immunoglobulin and CD20. Thirty-six patients (16%) tested positive for t (1;19). All 5 patients with mature B elements were t (1;19) positive. The patients with t (1;19) had a mean age of 7.18 years, a male to female ratio of 0.6 to 1, and a mean white cell count of 97.8. Thirty patients (83%) were of black African descent. Cytogenetics of this group showed a complex karyotype in 17 of the 36 patients (47%) in addition to the translocation t (1;19). The EFS of the t (1;19) group was 55%, as opposed to 90% in the t (12;21) group, and 78% in the patients with no particular FISH abnormality.

Conclusions: Patients with translocation t (1;19) present in the older child, have a higher white cell count at diagnosis and occur in patients of African descent. The inferior survival rate suggests a poorer prognosis, and that t (1;19) should be used in the risk stratification of B-lineage ALL.

D06 SIOP19-0223 | Impact of Clinical Hypersensitivity and Asparaginase Antibodies on Asparaginase Drug Activity in Egyptian Pediatric Acute Lymphoblastic Leukemia Patients

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Background/Objectives: A success key in improving outcomes for children with acute lymphoblastic leukemia (ALL) is attributed to the usage of asparaginase in their treatment regimen. It is derived from human nonnative bacterial source E-coli which is a target for the immune system to illicit an allergic reaction producing anti-asparaginase antibodies that may reduce its activity.

To find possible associations between clinical hypersensitivity reactions, anti-asparaginase antibodies and asparaginase activity in Egyptian pediatric patients with ALL. Age, gender and treatment regimen were also analyzed for any associations.

Design/Methods: A prospective cohort study was carried out at Children Cancer Hospital Egypt on 83 children with ALL who were treated on St Jude Total XV protocol with different asparaginase regimen for low risk (LR) and standard/high risk (SR/HR) ALL. Twenty-eight LR patients received a total of 18 doses of 10,000 IU/m² IM asparaginase during reinduction I and II; 9 doses given every other day in each phase; while 55 SR/HR patients received 25,000 IU/m² weekly for 19 doses in continuation phase.

Results: Clinical hypersensitivity was reported in 24 patients (29%); 13 local and 11 systemic; anti-asparaginase antibodies was positive in 45 patients (54.2%) and the drug was found to be inactive in 43 patients (51.8%). Age, gender and treatment regimen were neither associated with clinical hypersensitivity nor anti-asparaginase antibodies, while systemic hypersensitivity and SR/HR regimen were significantly associated with drug inactivity; $p=0.03$ and $p=0.0005$, respectively. Anti-asparaginase antibodies were not significantly associated with hypersensitivity and activity; $p=0.6229$ and $p=0.9347$, respectively.

Conclusions: Patients having systemic hypersensitivity to E-coli asparaginase may benefit from shifting to Erwinase to avoid drug inactivation. Therapeutic drug monitoring is required to maximize the effectiveness of asparaginase therapy especially for SR/HR regimen. Further studies are needed to have a clearer understanding of the association between anti-asparaginase antibodies with hypersensitivity and inactivity.

Poster Discussion 02 - Gliomas

D07 SIOP19-0845 | Cilengitide (EMD121974) in Combination with Irradiation in Children and Young Adults with Newly Diagnosed Diffuse Intrinsic Pontine Glioma: A Phase I Study

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Background/Objectives: Despite many clinical trials, prognosis of children with diffuse intrinsic pontine glioma (DIPG) remains very poor. Cilengitide (EMD121974), is a selective antagonist of $\alpha v\beta 3$ and $\alpha v\beta 5$ integrins. A Phase I study was designed to evaluate Cilengitide in combination with irradiation, followed as maintenance therapy until progression, in patients with newly diagnosed DIPG. Objectives of this multicenter open-label dose-escalation trial were to determine the Maximum Tolerated Dose (MTD) of Cilengitide, Dose-limiting Toxicities (DLT), best objective response rate (ORR) according RANO criteria, 6-months Progression Free (PFS) and Overall Survival (OS).

Design/Methods: Patients aged 6 months-21 years with newly diagnosed DIPG were enrolled according to a 3 + 3 dose-escalation design, followed by an expansion cohort. Cilengitide was infused intravenously, twice weekly, and 5 dose levels (240-1800 mg/m²) were evaluated. Concomitant radiotherapy was given (54 Gy). DLT were determined on the 1st cycle (42 days) of treatment using the NCI-CTC v4.0 scale.

Results: Thirty-two patients were enrolled with a median age of 6 years (range, 3-15). Median treatment duration was 4.9 months (0.5-10.5). Fifteen of the 17 patients included in the escalation part of the trial were evaluable for MTD determination (3 patients / dose level). No DLT was observed, thus the MTD was not reached. Fifteen more patients were included in the expansion part at dose level 1800 mg/m². Grade > 3 adverse events were observed in 28 patients (87.5%). Best ORR was 19.4% (95%CI: 7.5-37.5%); 6-months PFS and OS were 31.3% (CI95% 16.4-47.3) and 78.1% (95%CI: 59.5-88.9) respectively. Tumor sequencing showed 18/25 (72%) H3F3A mutation, and 5/25 (20%) HIST1H3B mutation. Four additional patients harbored H3K27M immunohistochemistry positive staining. Integrins immuno-staining was positive in 6/13 and 2/13 patients for $\alpha v\beta 3$ and $\alpha v\beta 5$ respectively.

Conclusions: Cilengitide was well tolerated in combination with irradiation but failed to improve the outcome of children with DIPG.

D08 SIOP19-0769 | TP53 Pathway Alterations are Driving Radioresistance in Diffuse Intrinsic Pontine Gliomas (DIPG)

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Background/Objectives: Diffuse Intrinsic Pontine Gliomas (DIPGs) are the most severe pediatric brain tumours. While accepted as the standard therapeutic, radiotherapy is only efficient transiently and not even in every patient. The goal of the study was to identify the underlying molecular determinants of response to radiotherapy in DIPG.

Design/Methods: We assessed *in vitro* response to ionizing radiations in a collection of 13 DIPG cellular models derived from treatment-naïve biopsies reflecting the variability encountered in patients at diagnosis and correlated it to their principal molecular alterations. Response to radiotherapy of an extended cohort of 73 DIPG was analysed according to their genotype. Using a kinome-wide synthetic lethality RNAi screen, we further identified target genes that can sensitize DIPG cells to ionizing radiations.

Results: We uncover *TP53* mutation as the main driver of increased radioresistance and validated this finding in 4 isogenic pairs of *TP53-wildtype* DIPG cells with or without *TP53* knockdown. In an integrated clinical, radiological and molecular study, we show that *TP53-mutated* DIPG patients respond less to radiotherapy, relapse earlier after radiotherapy and have a worse prognosis than their *TP53-wildtype* counterparts. Finally, a kinome-wide synthetic lethality RNAi screen identifies *CHK1* as a potential target, which inhibition increases response to radiation specifically in *TP53-mutated* cells.

Conclusions: Here we demonstrate that *TP53* mutations are driving DIPG radioresistance both in patients and corresponding cellular models. We suggest alternative treatment strategies to mitigate radioresistance with *CHK1* inhibitors. These findings will allow to consequently refine radiotherapy schedules in DIPG.

D09 SIOP19-1147 | Treatments and Outcome of High Grade Gliomas Diagnosed in Children Younger Than 5 Years – SFCE Study Between 2002 and 2015

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Background/Objectives: The outcome of children younger than 5 years old diagnosed with a high grade glioma (HGG) might be better than the older kids. Nevertheless, the treatment is combining surgery, chemotherapy and radiotherapy. To prevent long-term sequelae of irradiation, therapeutic strategies avoiding radiotherapy were prioritized by the French working group of Brain Tumors.

Design/Methods: A French national multicentric retrospective study was conducted to report all cases of patients under 5 years old diagnosed with a HGG between 2002 and 2015. Clinical, histological, radiological and therapeutic data were obtained.

Results: 37 patients were identified with a mean age of 2.4 years (range: 0.1-4.9). Thirty tumors were supratentorial. Histologies were 8 glioblastomas, 6 anaplastic oligoastrocytomas, 6 anaplastic oligodendrogliomas, 6 malignant glial and neuroglial tumors, 3 grade 3 astrocytomas, 3 anaplastic pleomorphic xanthoastrocytomas, and 5 unclassified malignant astrocytomas. Nineteen out of 37 (54%) were treated after surgery with chemotherapy (mainly BBSFOP protocol) without adjuvant radiotherapy. With a median follow up of 84.5 months (range: 1-178), 5-year OS and EFS were 57%+/-8% and 32%+/-7% respectively. Outcome was significantly better in patients under 3 years (5-year OS: 63% +/- 10%, 5-year EFS: 45% +/- 10%) (p=0.04). Twenty three (66%) relapsed with a median delay of 3.7 months. Second line treatment included after new surgery chemotherapy with temozolomide for 14 (78%) and focal radiotherapy for 12 patients. The 5-year OS after relapse was 36% +/-10%. Finally, 10 patients did not receive any radiotherapy and did not relapse (7 with BBSFOP protocol). Long-term sequelae with radiotherapy were mostly neurological, endocrinological and hearing consequences.

Conclusions: Therapeutic strategies comprising first-line chemotherapy are feasible and can avoid radiotherapy and its consequences in 27% of young children (10/37). A molecular

analysis is planned to better understand treatment responses and patient outcome.

D10 SIOP19-1553 | Clinical Characteristics and Outcome of Children with Primarily Multicentric High-Grade Gliomas. A Retrospective Analysis

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Background/Objectives: Since primarily multicentric high-grade gliomas (HGG) in children are extremely rare, data concerning optimal management of these patients is lacking.

Design/Methods: We conducted a retrospective data analysis to determine incidence and describe clinical characteristics and outcome of patients with primary multicentric HGG enrolled in five consecutive HGG protocols of the Pediatric Oncology and Hematology Society of the German Language Group (GPOH).

Results: Forty-eight children with primarily multicentric HGG were retrieved from the HIT-HGG data base. Median age at diagnosis was 9.4 years (range: 0.2–21.4). The most frequent primary tumor sites were the cerebral hemispheres (n=15), followed by the thalamus and basal ganglia (n=10), pons and brainstem (n=9), hypothalamus, pineal region (n=4 each), cerebellum, spinal cord (n=3 each). Multicentric lesions were located supratentorial (25.0%), infratentorial (3.6%), supratentorial and infratentorial (5.3%), spinal (12.5%), leptomeningeal and ventricular (25.0% each). In 2 children (3.6%) only cerebrospinal fluid was positive for atypic cells. Forty-six patients underwent surgery (biopsy n=16, subtotal resection n=26, gross total resection n=4) at diagnosis. In 2 patients with diffuse intrinsic pontine glioma (DIPG) diagnosis was based on magnetic resonance tomography only. 43 children received chemo-/radiotherapy (mainly temozolomide-based), 4 chemotherapy only. In 1 case no adjuvant treatment was administered. At a median follow-up of 11.9 months (range: 0.7–191.9) 5 children are alive, 39 died and 4 were lost to follow-up. Median progression-free and overall survival was 4.4 months (n=40; interquartile range: 3.2–7.8) and 11.1 months (n=43; interquartile range: 7.2–17.6).

Conclusions: The prognosis of primary multicentric HGG in children seems to be comparable to that of unicentric disease. Since little is known about the molecular background of multicentric growth pattern of HGG, molecular characterization is urgently needed.

D11 SIOP19-0418 | High-Throughput Microna Profile in Adult and Pediatric Primary Glioblastomas: The Role of MIR-10B and MIR-630 in the Tumor Aggressiveness

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Background/Objectives: MicroRNA expression has been associated with biological behavior in glioblastomas (GBM). The aim of the study was to identify miRNAs signatures associated with glioblastoma, comparing with non-neoplastic white matter samples (WM) by the miRNA microarray technique and analyzes by *in vitro* studies the 2 more differentially expressed microRNAs between GBM and non-neoplastic control.

Design/Methods: Primary GBM samples from 29 consecutive patients (20 adults and 9 children) and 11 non neoplastic WM controls were analyzed using the Agilent “Human microRNA Microarray Kit (v3)” to determine the expression profile of microRNAs. Among the most differentially expressed microRNA detected by microarray data six were chosen to be validated by qRT-PCR in 43 GBM samples and the most underexpressed and the most overexpressed were chosen to *in vitro* functional studies (proliferation, invasion, migration and clonogenic assays) after overexpression and knockdown, using lentiviral vectors in the GBM cell lines U87 and U251 respectively. Overexpression and knockdown of the miRs analyzed were confirmed by qRT-PCR.

Results: The unsupervised hierarchical clustering analysis distinguished three main groups of samples being two with predominance of GBM samples and a group formed only by cerebral white matter. GBM samples showed significant differential expression of miR-10b-5p, miR-34a-5p, miR-136-5p and miR-630 when compared with non-neoplastic white matter when analyzed by Mann-Whitney test ($P < 0.05$), being the miR-10b-5p the most overexpressed and the miR-630 the

most underexpressed. In functional studies the overexpression of miR-630 decreased proliferation and invasion in U87 GBM cell line while the inhibition of miR-10b decreased proliferation and colony formation in U251 GBM cell line, suggesting that they could act as suppressive tumor and oncogenic miR, respectively.

Conclusions: The present study highlighting molecular aspects of adult and pediatric GBM and shows the biological importance of miR-10b and miR-630 in these tumors.

D12 SIOP19-1442 | Telomere Length Maintenance in Pediatric High-Grade Gliomas

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Background/Objectives: Recent data have led to a major reclassification of pediatric high-grade gliomas (pHGGs) based on molecular subgrouping. In adult gliomas, *IDH1/2* and Telomerase Reverse Transcriptase promoter (*TERTp*) mutations represent key molecular alterations, whereas in pediatric tumours are restricted to a small proportion of cases. The most prominent difference between pediatric and adult HGG is the frequency of histone H3.3 (*H3F3A*) mutations, with K27M and G34R/V variants representing different clinico-pathological and biological subgroups. This finding led to a novel diagnostic entity entitled “diffuse midline glioma H3K27M-mutant”; whereas, the G34R/V variant have not been completely elucidated.

Elongation of telomeres, necessary for tumor cell immortalization is performed via reactivation of telomerase or Alternative Lengthening of Telomere (ALT). *TERTp* mutations and hyper-methylation result in up-regulation of telomerase activity; neoplastic cells which do not reactivate telomerase, trigger ALT. Previous studies have identified the connections of *ATRX* and *H3F3A* mutations with ALT phenotype; comparison between K27M and G34R/V mutations in terms of telomere length, is not fully elucidated.

In this study we analyzed the activation of telomere elongation in pHGGs, highlighting the difference between G34-mut and K27-mut H3.3.

Design/Methods: We screened a cohort of 50 pHGGs for telomere elongation using telomere-specific FISH (Telo-FISH), loss of *ATRX* nuclear expression by IHC, *H3F3A* and *TERTp* mutations by DNA sequencing, *TERTp* methylation by methylation-specific-PCR (MS-PCR).

Results: *TERTp* mutations were rare in our cohort (4%) and not associated with telomere length increase. We frequently observed ALT activation (42%) associated with *H3F3A* and

ATRX alterations. pHGGs with no alterations on *TERTp*, *ATRX* and *H3F3A* evidenced basal levels of telomere length. Interestingly, all G34-mut cases activated ALT differently from K27-mut pHGGs.

Conclusions: Our results show the differences between the two histone-defined subgroups regarding telomeric profile and activation of ALT, supporting the finding that G34- and K27-mutated H3.3 pHGG are independent biological and clinico-pathological subgroups.

Poster Discussion 03 - Neuroblastoma Treatment in Limited Resource Settings

D13 SIOP19-1619 | Treatment of Neuroblastoma in Infants Younger Than 18 Months with the TPOG Neuroblastoma Treatment Protocol; On Behalf of the Turkish Pediatric Oncology Group

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Background/Objectives: To evaluate clinical characteristics, treatment outcome and survival rates of infants with neuroblastoma.

Design/Methods: Eligible 412 infants (<18months) with neuroblastoma who were treated with TPOG-NB-2009 protocol were analyzed.

Results: Stages of 412 patients: Stage-1 26.5%, stage-2 9%, stage-3 24.3%, stage-4 27.7%, stage-4S 12.6%.

Low-RG (n:170): Infants with Stage-1 (n:109) neuroblastoma were followed-up after surgery, primary relapse occurred in two. Infants with Stage-2 (n:30) neuroblastoma were followed-up after surgery: two received chemotherapy, one died with progression. There were 31 Stage-4S neuroblastoma. The median follow-up time was 28months, 10-years EFS 92%, OS 98%.

Intermediate-RG (n:178) There were 59 infants in IRG-FH, 119 infants in IRG-UFH. Stage distribution stage2 (n:6), stage3 (n:80), stage4 (n:74), stage4S (n:18). MYCN (-)

in 118 infants. 1p-del 40/101, 11q-del 19/100, 17q+gain 56/100. Primary surgery was performed in 44 patients. Response to induction chemotherapy (A8+A9) 83%. Delayed surgery was performed in 97. 12 patients received radiotherapy to primary site. Three treatment refractories, 10 primary relapses occurred. Ten deaths occurred: infections (n:4), surgery-related (n:3), progression (n:3). The median follow-up time 29months, 10-years EFS 84%, OS 93%.

High-RG (n:64) 53 patients in CCT arm; stage-4S (n:3), stage-3 (n:18), stage-4 (n:32). Surgery was performed in 6 cases, response to induction chemotherapy (A9+A11) 81%. Delayed surgery was performed in 31. Four CNS relapses, 4 primary relapses, two bone+bone-marrow relapses and 8 treatment refractories occurred, 15 of 21 deaths related to progression, 6 deaths due to infection. Eleven patients in HDCT+HSCT arm, three bone relapses occurred. Five patients died with progression, two died because of HSCT-related complication. The median follow-up time 13months, 7-years EFS 35%, OS 44%. Twenty patients received radiotherapy to primary tumor.

Conclusions: Survival rates of infant neuroblastoma patients were comparable to the literature. OS and EFS rates were significantly different between risk groups and between MYCN+/- patients. CNS relapses were noticeable in HRG infants.

D14 SIOP19-1081 | Neuroblastoma Management in South Africa Between 2000 and 2014

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Background/Objectives: Children with neuroblastoma have particularly poor survival outcomes in low and middle-income countries.

Design/Methods: As preparation for a harmonised neuroblastoma treatment protocol, a multi-institutional review was designed to document historical treatment approaches, determine overall survival (OS) and prognostic factors. Demographic data, disease stage, treatment protocol and outcome were collated and risk stratification was redetermined using these three systems. Two-year OS and prognostic factors were calculated.

Results: Between January 2000 and December 2014, 390 patients with neuroblastoma were reported from nine paediatric oncology units. Median age was 39.9 months and the majority (70%) presented with stage 4 disease. Chemotherapy regimens included OPEC/OJEC (44.8%), St Jude NB84 protocol (28.96%) and Rapid COJEC (22.17%). In high-risk (HR) disease 30.8% obtained post-induction metastatic complete remission. Only 44.4% received surgical interventions across all risk groups, while 16.5% of HR patients received radiotherapy. The 2-year OS was 94.1% for very low risk, 81.6% low risk, 66.7% intermediate risk versus 27.6% for HR groups ($p < 0.001$, 95% CI). The 2-year OS of the NB84 was 41.0% in comparison to OPEC/OJEC with 32.5% and Rapid COJEC with 24.8% ($p = 0.039$). There were fewer treatment related deaths in patients receiving OPEC/OJEC 2.0%), compared with NB84 (6.2%) and Rapid COJEC (6.3%) ($p = 0.037$). Median survival time for the whole group was 13.0 months. On multivariate analysis stage ($p < 0.0001$), LDH > 750 U/L ($p < 0.0001$), ferritin > 210 g/dl ($p < 0.02$), MYCN amplification ($p = 0.01$), INSS risk classification ($p < 0.0001$), chemotherapy regimens ($p < 0.04$, 95%CI) and surgical resection ($p < 0.01$, 95% CI) were identified as significant prognostic factors.

Conclusions: The majority of patients presented with Stage 4 disease, which impacted negatively on OS, while patients with low risk disease achieved survival rates comparable to those in well-resourced settings. A harmonised treatment protocol will pay particular attention to patients with advanced disease and may lead to improved outcomes for neuroblastoma patients.

D15 SIOP19-0049 | Clinical Features and Prognosis of 116 Infants with Neuroblastoma in Single-Center in China

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Background/Objectives: To analyze clinical characteristics and prognosis of 116 infants with neuroblastoma.

Design/Methods: The clinical data of children less than 18 months old with neuroblastoma that were diagnosed and treated at the hematology-oncology center of BCH from January 2007 to June 2017 was retrospectively analyzed. Their clinical features were summarized and the prognosis was evaluated. The SPSS19.0 statistical package was used.

Results: 116 patients with < 18 months old were treated, including 64 males and 52 females. The median age was 10 months old (1 -18 m). The median time of follow-up was 19.5 months (1-88 m). The univariate analysis showed that stage 4, high risk, bone or bone marrow metastasis, MYCN gene amplification, and the serum LDH >500 IU/L were poor prognostic factors ($P < 0.05$). There were 10 cases with MYCN (+). The infants with MYCN (+) showed INSS stage 3 or 4, higher LDH and higher NSE than those without MYCN amplification ($P=0.028$, $P=0.002$, $P=0.001$). There were 13 deaths, of which 9 cases died of tumor relapse or progression. The 3-year EFS of 116 patients was 83.6% and the OS was 86.7%. The 5-year EFS was 76.7% and OS was 86.7%. The 3-year OS of infants with < 12 months old was 90% and those with 12-18 months old was 80.7%. There was no significant difference ($P=0.101$) between them. The 3-year OS in patients with stage 4, high risk, and MYCN (+) were 74.4%, 57.1% and 26.7% respectively. They were significantly lower than the earlier stage, low and intermediate risk groups and without MYCN gene amplification ($P=0.013$, $P=0.000$, $P=0.000$).

Conclusions: The prognosis of infants with < 18 months old with neuroblastoma is good. The prognosis is poor in patients with MYCN gene amplification or advance stage. The main cause of death in infants with neuroblastoma is disease relapse or progression.

D16 SIOP19-0065 | Toxic Side and Recent Curative Effect of ^{131}I -MIBG Consolidation Therapy in Children with High Risk Neuroblastoma

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Background/Objectives: To observe the toxic side and recent effect curative of ^{131}I - metaiodobenzylguanidine (^{131}I -MIBG) in children with high risk neuroblastoma (HR-NB), and to evaluate its effectiveness and safety.

Design/Methods: This was a retrospective cohort analysis of patients with HR-NB diagnosed from January 2014 to February 2018. The toxicity of organic function after ^{131}I -MIBG

were observed to evaluate the safety. The viration of lactic dehydrogenase(LDH), neuron specific enolase(NSE), Vanillylmandelic acid(VMA), primary tumor size, bone marrow cells and minimal residual disease(MRD) were analyzed at the time of initial diagnosis, before and after ^{131}I -MIBG. Meanwhile, the survival rate was compared with HR-NB patients who were not treated with ^{131}I -MIBG in our center, so as to evaluate the effectiveness of ^{131}I -MIBG.

Results: 1. General clinical features at diagnosis:Thirty-nine cases of primary tumor were located in the retroperitoneal adrenal gland, and 3 cases in the posterior mediastinum. All the patients had distant metastasis. 2. Status of patients before ^{131}I -MIBG: Twenty-five cases of VGPR, 3 cases of PR, 1 case of MR, 5 cases of PD and 15 cases of suspected PD were found before consolidation. 3. Evaluation of ^{131}I -MIBG: 4/6 cases of patient with slightly higher LDH before ^{131}I -MIBG returned to normal after treatment. Four/seven patients with elevated NSE decreased and 5/10 patients with abnormal urinary VMA returned to normal after treatment. Nine/ten cases of bone marrow MRD positive patients turned negative after treatment. The 3-year overall survival rate was estimated to be 69.87%, which is significantly higher than that of patients without ^{131}I -MIBG in the same period($P<0.05$). The 3-year event-free survival rate was 50.41%. And there was no significant difference compared with the regular treatment group($P>0.05$). 4. Toxic effects:All 34 patients had myelosuppression, including 9 cases of grade I,10 cases of grade II,10 cases of grade III and 5 cases of grade IV.

Conclusions: Preliminary clinical findings show that ^{131}I -MIBG is an effective consolidation therapy for children with HR-NB, and could significantly delay the progression of the disease. The toxic reaction after treatment was mainly myelosuppression and severe thrombocytopenia.

D17 SIOP19-0143 | Factors Affecting Outcome in Children with High-Risk Neuroblastoma Treated with Autologous Hematopoietic Stem Cell Transplantation in Low Income Countries

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Background/Objectives: Improvement of the outcome in patients with high risk neuroblastoma is attributed to consolidation of induction chemotherapy by autologous transplant. Recently there is a great improvement of outcome by tandem autologous transplant followed by immune therapy in form of antiganglioside (Anti GD2).

Design/Methods: A retrospective study which included 73 High risk neuroblastoma patients recruited from 2012 till 2015 who underwent autologous hematopoietic stem cell

transplant. Age, stage, pathology, Myc-N status, extent of metastases, response to induction chemotherapy and extent of surgical respectability were correlated to outcome post transplant.

Results: No significant impact of metastatic sites, stage or extent of resection on the outcome post-transplant. Patients with amplified MYC-N had inferior 3 y EFS, OS compared to those without (P value: 0.96 for EFS, 0.48 for OS), patients with objective response post induction (CR, VGPR, PR) had 3y EFS, OS of 53.3%, 64.2% compared to those with (SD, mixed response) 49.3%, 63.5% respectively (P value: 0.45 for EFS, 0.75 for O.S). Buslphan/ Melephalan conditioning was given for 70 patients while 3 patients received CEM (2 patients died from progressive disease and 1 from diffuse alveolar hemorrhage), for BU/MEL group 3y OS was 66.1% (p value 0.001%). 3 y OS, EFS of the whole group was 63.3%, 51.3% respectively where 27 patients relapsed, 25 patients died (18 from progressive disease, 6 patients from transplant related toxicity and 1 patient from therapy related AML). Our hospital data published 2013 revealed that 4 years OS, EFS were 42.7% and 35.6%, the improvement in survival in our study mostly due to the use of the more intensified induction COG A3973

Conclusions: The impact of prognostic factors on outcome was nullified by transplant, the more intensified induction the better the outcome. More financial support is needed to use immune therapy and tandem transplant to further improve the outcome.

D18 SIOP19-0498 | Treatment Outcome of Neuroblastoma in Thailand: A Lesson from Center with Limited Resources

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Background/Objectives: Treatment of neuroblastoma depends on various factors including tumor staging and MYCN amplification. However, the test for MYCN amplification is not available in most centers in Thailand. The treatment stratification in our institute depends mainly on staging and Shimada histology. To avoid under-treatment in such patients, most of them were shifted to a higher risk group. The objective of this study is to assess the treatment outcome and survival of children with neuroblastoma treated in our institute.

Design/Methods: The retrospective chart reviews of neuroblastoma patients were conducted and results were analyzed.

Results: Eighty-four patients were enrolled to the study. Median age at diagnosis was 2.8 years. According to the

INSS classification and COG risk stratification without using MYCN amplification, majority of the patients were in INSS stage IV (66.7%) and high risk (HR) group (72.6%). Most patients received combination treatment of surgery and chemotherapy. Sixty-one patients (75.3%) had grade III & IV hematologic toxicity; HR group patients had more grade IV hematologic toxicity than the low-risk (LR) and intermediate-risk (IR) groups (53% vs 13.5%). Five-years overall survival (OS) for the whole group, LR, IR and HR group were 44.8%, 87.5%, 86.2% and 27.8% respectively. Twenty-eight patients (42.4%) relapsed at the median time of 1.8 years. The median follow-up time was 2.6 years (5 month-15 years).

Conclusions: Although some LR and IR patients were falsely classified into HR group, the survival rate of the HR group remained unsatisfied whereas LR and IR groups had excellent outcome. Moreover, HR patients experienced more treatment toxicities due to a more intensive treatment. The accurate tumor stratification method including the use of MYCN amplification can identify the patients' true risk group. Treatment reduction in those who were falsely classified into HR group will prevent unnecessary intensive chemotherapy resulting in less treatment toxicities without compromising the treatment result.

Poster Discussion 04 - Physical Activity Interventions

D20 SIOP19-0009 | Implementation of a Program Based on Adapted Physical Activity and Recommendations for Second Cancers Prevention for Adolescents and Young Adults with Cancer: PREVAPAJA Study

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Background/Objectives: About 700 adolescents and young adults (AYAs; 15 to 25 years) are diagnosed annually with cancer in the French Auvergne-Rhône-Alpes region. While their long term survival is about 80%, they are six times more likely to develop a second primary cancer (SPC) compared to their peers. This risk is multifactorial and depends on the type of first cancer, treatment received and prevalence of risk factors (smoking, overweight, sedentary lifestyle, environmental exposures.).

PREVAPAJA aims to implement a clinical program based on physical activity (PA) and cancer prevention recommendations for AYAs with cancer.

Design/Methods: AYAs attended PA sessions during the active treatment period (4–6 months) and participated to individual information meetings on SPC risk prevention. Physical activity (IPAQ, 6MWT), sedentary, anthropometrics (BMI), quality of life (QLQ-C30) and fatigue (VAS) were assessed at baseline (T1) and at the end of treatment (T2). They participated to a final meeting by phone 1 year after T1 (T3) to assess their level of physical activity (IPAQ) and changes in health behaviors.

Results: 63 AYAs (39 boys, 24 girls; median age=18 years) participated in the study. PA level increased between 360 MET-min/week [0–2373] at T1, 1059 MET-min/week [0–9690] at T2 and 1116 MET-min/week [0–11133] at T3. Sedentary time decreased from 56 h/week at T1, 40 h/week at T2 to 30h/week at T3. Fatigue assessed decreased between T1 and T2 ($p < 0.01$) and overall quality of life improved statistically significantly between T1 and T2 ($p < 0.001$).

Information meetings showed important differences in consideration for cancer risk factors.

Conclusions: This study showed the feasibility of a clinical program based on PA intervention and cancer prevention recommendations for AYAs with cancer. It responded to AYAs' needs for support and information regarding physical activity and SPC prevention. Beneficial outcomes regarding PA level and quality of life should encourage to systematically propose PA intervention in AYA with cancer.

D21 SIOP19-1438 | Benefits on Muscular and Walking Performance from Combined Resistance and Endurance Training During Intensive Cancer Treatment in Pediatric Oncology: Results from the Randomized Controlled Mucki-Trial

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Background/Objectives: Disease- and treatment-related reductions of muscular and aerobic performance have been observed in childhood cancer patients. In adult cancer patients, specific exercise training revealed positive effects on muscular and aerobic capacity which were associated with

benefits on fatigue and quality of life. Within the “Effects of Combined Resistance and Endurance Training in Pediatric Cancer Patients During Intensive Treatment Phase (Mucki-trial)” training effects on muscular and walking performance were evaluated.

Design/Methods: In this stratified, randomized and controlled trial, childhood cancer patients aged between 4 and 18 years were enrolled during intensive cancer treatment phase (ICT). Individuals within the exercise group (EG) obtained usual care and participated in supervised exercise training. Training was focused on child adapted playful, moderate intense resistance and endurance exercises and took place 3 to 5 times weekly over a period of 6 to 8 weeks. Individuals of the control group (CG) received usual care. Pre- and post-intervention handheld dynamometry testing for knee flexor strength and six minute-walk test were performed.

Results: In total 18 patients were included in the EC and 17 in the CG. Group-time-interactions on muscular and walking performance were evaluated by analysis of covariance adjusting for baseline values and stratification factors. Subsequent results revealed favoring effects for EG in knee flexor strength ($F(1,20) = 5,733$; $p = 0,027$; $\eta^2p = 0,223$) and walking performance ($F(1,25) = 4,270$; $p = 0,049$; $\eta^2p = 0,146$). Compliance to the training was rated very good to good. No severe adverse events occurred during training and testing sessions.

Conclusions: The present results provide further evidence for beneficial effects from adapted exercise programs in childhood cancer patients suffering from different tumor entities. Adapted exercise programs have been getting attention only since recently in pediatric cancer. In this context, the present findings support further elaboration and implementation of adapted exercise offers in pediatric oncology.

D22 SIOP19-1048 | A Randomized Trial of Early Physical Activity During Childhood Cancer Treatment

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Background/Objectives: Physical fitness is significantly altered in children with cancers. Data are limited regarding the safety and efficacy of early physical activity programs (PAP) during childhood cancers treatments.

Design/Methods: We conducted a randomized controlled open-label trial involving children/adolescents aged 5-19 years under treatment for cancer (ClinicalTrials.gov identifier NCT02284061). It aimed to evaluate the safety, feasibility and

efficacy of an early 12-month PAP. For each patient, baseline (M0) was set as the earliest time point when the patient was medically considered capable to start the PAP. Patients were randomly assigned in a 1:1 ratio to an immediate start (M0) of the PAP (interventional arm) or started the PAP 6 months later (M6) (control arm). The primary outcome was the intention-to-treat measure of aerobic endurance using the six-minute walk test (6MWT) at M6. Secondary outcomes included the PAP feasibility, safety, and changes in other physical functions, psychological health, social participation and quality of life parameters.

Results: The trial involved 80 children/adolescents (age range 5.0-18.4 years), of whom 41 were assigned to the interventional arm and 39 to the control arm. Underlying malignancies were leukemia (39%), lymphoma (20%), brain tumors (15%), bone tumors (15%), neuroblastoma (4%), and other solid tumors (6%). Baseline characteristics did not differ significantly between the arms. All patients completed the study with no serious adverse event. At M6, the mean 6MWT distance ($\pm$ SD) was higher in the interventional arm vs the control arm (623 ± 75 vs 557 ± 83 m; $p<0.001$). Upper and lower limb strength and muscular tone were also significantly increased in the interventional arm (3.3 ± 1.0 vs 2.9 ± 0.6 m, $p=0.039$; 70 ± 43 vs 41 ± 20 s, $p=0.001$ and 69 ± 35 vs 50 ± 20 s, $p=0.007$, respectively). Other physical parameters, quality of life and self-esteem scores did not differ significantly.

Conclusions: In children/adolescents under treatment for cancer, an early PAP is feasible, safe, and improves aerobic endurance.

D23 SIOP19-0998 | International Pediatric Oncology Exercise Guidelines (iPOEG): A Delphi Consensus Project

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Background/Objectives: In pediatric oncology, exercise may mitigate negative cancer-related effects and promote positive physical and psychosocial outcomes. Despite accumulating evidence for exercise, few patients and survivors are active enough to confer benefits. A lack of pediatric oncology-specific exercise guidelines has been identified as one barrier to exercise participation. As such, the objectives of this project were to: (1) assess the current state of evidence for exercise in pediatric oncology; (2) identify operational standards for exercise; and (3) come to consensus with a team of experts on exercise guidelines in pediatric oncology.

Design/Methods: A Delphi consensus project is being undertaken with 122 international experts (eg, clinicians,

researchers) in pediatric oncology and exercise. A series of online surveys were distributed and experts answered questions covering current literature, terminology, exercise prescription, and operational standards. Responses were collected and analyzed using content analysis and descriptive statistics. Consensus is being defined at 80% agreement.

Results: Online survey response rates were $>80\%$. There has been consensus amongst experts with regards to exercise evidence in pediatric oncology. Moreover, experts have identified and agreed upon operational standards for exercise among patients, out-patients, and survivors. To date, the experts have nearly reached consensus on the final international Pediatric Oncology Exercise Guidelines (iPOEG). The process will conclude at an international meeting September 2019, wherein the final iPOEG document will be outlined by experts and key stakeholders (eg, community-based organizations, patients/families). The process of coming to consensus and the iPOEG will be presented at the SIOP conference.

Conclusions: The exercise guidelines developed in this project will provide practical direction and support for individuals at multiple levels (eg, clinicians, community-based organizations, patients/families). The iPOEG will be disseminated locally, nationally, and internationally in an effort to extend and promote the inclusion of exercise in pediatric oncology. Acknowledgements: The iPOEG expert consensus committee.

Poster Discussion 05 - Psychosocial

D25 SIOP19-0397 | The Emotion Thermometer in Survivors of Childhood Cancer Attending Follow-Up Care

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Background/Objectives: Childhood cancer survivors (CCS) have an increased risk for psychological distress even long after end of treatment. To support high quality in CCS' follow-up care, timely and prompt assessment of psychological late-effects is increasingly advocated. The Emotion Thermometer (ET) measures psychological distress in four emotion domains (*distress, anxiety, depression, anger*) and need-for-help. We aimed to (1) assess distress in CCS applying the ET before follow-up appointments and (2) describe the user experience with the ET.

Design/Methods: In this longitudinal study, CCS (age at study ≥ 15 , ≥ 1 year after end of treatment) attending a follow-up appointment in one of the three outpatient clinics in Switzerland completed two online questionnaires (before and after follow-up appointment). We used the ET cut-off ≥ 4 for each thermometer, and for categorization ETsum scores: >9 mild, >14 moderate, >20 severe. We used eight questions to assess the experience with ET.

Results: Forty-three CCS completed the ET (mean age: 21.6 years, range: 15-35; 24 females). Distress was present in 28 (65%) CCS, further categorized into mild ($n=25$), moderate ($n=8$) and severe ($n=10$) distress on the ETsum score. Need for help was expressed by all individuals with severe distress. The single thermometer scores showed *distress* in 51%, *anxiety* in 21%, *depression* in 21% and *anger* in 23%. CCS found the ET easy to use, understand and helpful to express their feelings.

Conclusions: The results show that a large number of survivors attending follow-up care experience psychological distress and express need for help when levels of distress are severe. Regular screening with the well-accepted ET may help to detect distress such that it can be adequately addressed during follow-up care.

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D26 SIOP19-0710 | Infusion Pump Alarms at Night: Do They Affect Sleep and Fatigue in Parents of Pediatric Cancer Patients?

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Background/Objectives: Spending the night in the noisy and bright hospital negatively affects sleep, and impacts quality of life and daily functions like decision making. In healthy participants alerting electronic sounds were more disruptive compared to other hospital sounds. If applicable for parents of cancer patients, alarms would be easier to adjust than influences on sleep like stress and caring for a child during the night. This study aimed to determine sleep and fatigue in relation to infusionpump alarms in parents of cancer patients.

Design/Methods: In this prospective observational study, inrooming parents of patients aged 2-18 years, admitted for a scheduled course of chemotherapy were eligible. Data on nightly infusionpump alarms of their child –and when present, roommate– were collected. At the end of admission, parents filled out sleep- and fatigue-questionnaires (PROMIS Sleep Disturbance (PROMIS-SD); PROMIS Sleep Related Impairment; Insomnia severity index (ISI); PROMIS Short Form

Fatigue). The relation between alarms and sleep was assessed using linear regression analyses.

Results: Thirty-one parents of 23 children (60% mothers; mean age 41.1 (6.3); median time since diagnosis 4.0 months (IQR 3.3-7.0)) with 48 nights of alarmdata participated. Alarms sounded median 3.5 times per night (IQR 1-7), and lasted median 7.3 minutes per night (IQR 2.1-15.3). Parents scored significantly worse than the norm on sleep disturbances (PROMIS-SD, $P 0.01$), 57.7% reached criteria for sub-threshold insomnia and 15.3% for moderate-severe insomnia. We found no significant relation between the number, or duration of alarms and sleep or fatigue.

Conclusions: Alarms sound frequently at night and parents sleep poorly during admissions; however, there was no relation between both. This implies that subjective sleep disturbances are related to other factors and the alarms do not significantly contribute in our population. Future research should focus on the influence of alarms on objective sleep outcomes, and on identifying the most demanding influences on subjective sleep.

D27 SIOP19-0746 | Fatigue in Children Post-Cancer Treatment and Other Long-Term Diseases

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Background/Objectives: Recently, fatigue in chronically ill adults was conceptualized as a transdiagnostic symptom, meaning that fatigue exists largely independent from the somatic diagnosis. Children post-cancer treatment and with long-term diseases such as an autoimmune disease describe fatigue as prevalent and distressing. Therefore, we aim to investigate 1) the prevalence and extent of fatigue among children post-cancer treatment and chronic diseases, and 2) the effect of fatigue on health-related quality of life (HRQoL).

Design/Methods: Cross-sectional study in the outpatient clinics of two children's hospitals. Children 2-18 years old in the first year after end of cancer treatment, with cystic fibrosis, or an autoimmune disease, were eligible. Fatigue and HRQoL were assessed using the PedsQL multidimensional fatigue scale (lower scores indicate more fatigue; range 0-100) and

PedsQL generic core scales. Linear regression and ANCOVA analyses were used to compare fatigue scores across disease groups, and against two control groups. The effect of fatigue on HRQoL was calculated. Data were adjusted for age, sex, and reporting method.

Results: 481 children were assessed (60% participation rate, mean age 10.7 ± 4.9 , 42% male), of whom 93 children post-cancer treatment (mean age 7.7 ± 5.0 , 54% male). Children in all disease groups reported more fatigue than the general population (mean difference -6.6, 95%CI -8.9, -4.3), with a prevalence of severe fatigue of 21.2%. Post-cancer treatment, the prevalence of severe fatigue was 24.7%. Still, compared to the other disease groups, fatigue scores post-cancer treatment did not differ significantly from the other groups on any fatigue domain. Fatigue was associated with lower HRQoL on all domains.

Conclusions: Fatigue is a prevalent symptom independent of disease, age, and sex and affects HRQoL. No differences in fatigue scores were found between children post-cancer treatment and other long-term diseases. Our findings underscore the need to systematically assess fatigue. Future studies should determine generic biological and psychosocial treatment targets.

D28 SIOP19-0095 | Resilience and its Association with Depression and Quality of Life in Chinese Parents of Children with Cancer: A Multicenter Cross-Sectional Study

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Background/Objectives: Promoting the psychological well-being and quality of life for parents of children with cancer is critical. Resilience usually refer to the ability to move forward or stay normal under adversity. Along with the paradigm shift from problem-oriented approach to nurturing strengths in the postmodern period, enhancing resilience is amenable to better improve parental mental health. This study aims to explore parental resilience level and its association with psychological outcomes as well as children's disease-related characteristics.

Design/Methods: A cross-sectional study was conducted in two tertiary hospitals in Mainland China. Questionnaires were distributed to parents of pediatric cancer patients in both inpatient and outpatient between August 2018 and November 2018. The measurement instruments for resilience, depression and quality of life were Connor-Davidson resilience scale, Self-rating depression scale and Short form of the medical outcomes study questionnaire, respectively.

Results: A total of 181 parents of children with cancer were identified. Compared with normal adult population in China, the parents of children with cancer showed statistically significant lower resilience level, poorer quality of life and much higher depression. Only relapse of children's disease was related to parental resilience ($\beta=0.17$, $R^2=0.08$, $p=0.033$), after adjusting other demographic characteristics. The resilience was negatively associated with depression ($r=-0.656$) and positively correlated with quality of life ($r=0.369$). Participants with the lowest resilience resources had higher odds of depression (OR=23.72, 95%CI 3.15,178.64), and increased risk of serious depression (OR=6.68, 95%CI 2.52,17.73).

Conclusions: Healthcare professionals should pay more attention to parents of children with cancer recurrence. Given that parents with low resilience are at greater risk for poor psychological outcomes, future study may consider developing and evaluating interventions that can help enhance the resilience of parents of children with cancer, so as to promote their psychological wellbeing and quality of life.

D29 SIOP19-1415 | Social-Emotional Functioning in Survivors of Pediatric Brain Tumors With and Without a Best Friend

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Background/Objectives: Survivors of pediatric brain tumors (PBTS) are at risk for social problems. Research suggests PBTS are socially isolated in classroom settings, but less is known about their experience of friendships. Our objective was to assess the social-emotional functioning of PBTS with and without a best friend.

Design/Methods: PBTS (n=48, 54.2% female, 87.5% white, 33.3% medulloblastoma) were enrolled on a study assessing social functioning. Youth were 10.61 (SD=1.38) years of age and 5.60 (SD=2.45) years off-therapy. Participants completed self-report measures of social-emotional functioning (PROMIS Peer Relations; Self-Perception Profile for Children (SPPC)) and were asked to identify their best friend. Parents completed measures of child social functioning (Social Competence Inventory (SCI), NIH Toolbox measures) and an indicator of facilitative parenting (Facilitative Parenting Scale (FPS)). Independent samples t-tests were used to compare functioning based on presence of a best friend (p-value set at <0.10).

Results: Nine (18.8%) PBTS were unable to name a best friend. There were no differences between groups on medical/demographic variables. PBTS without a best friend reported poorer functioning on indicators of social

competence (PROMIS $t(44)=2.54$, $p<0.02$; SPPC Social Competence $t(44)=2.28$, $p<0.02$) and self-worth (SPPC Global Self-Worth $t(44)=1.98$, $p=0.05$). Parents indicated that PBTS without a best friend experienced more peer rejection (NIH Peer Rejection $t(46)=-1.72$, $p=0.09$) and were less prosocial (SCI Prosocial Orientation $t(42)=1.90$, $p=0.06$). Parents of PBTS without a best friend reported engaging in fewer facilitative parenting behaviors (FPS Total $t(43)=1.86$, $p=0.07$), including parental warmth ($t(45)=2.25$, $p<0.04$) and behaviors associated with supporting friendships ($t(45)=1.76$, $p=0.08$). Effect sizes (Hedge's g) ranged from medium (0.65; Supports Friendships) to large (0.99; PROMIS).

Conclusions: A notable proportion of PBTS cannot identify a best friend. These youth demonstrate deficits in self- and parent-reported social-emotional functioning as compared to PBTS who can identify a best friend. Interventions to help parents facilitate friendship opportunities may be beneficial.

Poster Discussion 06 - Survivorship

D30 SIOP19-0352 | Health Promotion for Adult Overweight or Obese Childhood Cancer Survivors: Is There a Place for Trained Health Promotion Professionals Within Aftercare?

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Background/Objectives: The recently published UK Long-Term Plan (NHS 2019) highlights need for holistic interventions to prevent and manage chronic disease. Childhood cancer survivors (CCS) have a higher risk of Second Malignant Neoplasms (SMN's) and chronic illness as a result of their treatment. Such risks are known to be associated with excess weight gain (Zhang et al. 2016) justifying the need for successful health promotion and maximising 'teachable moments' (Frazelle & Friend 2016) by aftercare (late effects) teams. A study was carried out in an Aftercare clinic assessing whether support via a health promotion professional benefited CCS.

Design/Methods: Overweight or obese (OWO) CCS attending clinic were offered help with healthy lifestyle changes (N=35). Those that accepted (N=21, 60%) received support via a qualified health promotion professional within the Aftercare team. Support was based on a weight inclusive strategy (Tykla, 2014), recommendations from the National Institute for Health and Care Excellence (NICE) and evidence-based behaviour change theory. Patients were given a choice of Level 1 (Health education, signposting and/or liaison with other relevant healthcare professionals) or Level 2 support

(Level 1 plus review of food/activity diary and regular follow up). To assess outcomes BMI and weight were compared at point of referral and at 12 months.

Results: Intervention: Level 1 $n = 7$ (33%) Level 2 $n=14$ (67%). 81% of patients ($n=17$, Level 1 $n=6$, Level 2 $n=11$) achieved reduction in BMI. Unsuccessful = 19% (Level 1 $n=1$, Level 2 $n=3$). Average annual weight loss 9.7Kg (range 1.5 - 25.5Kg). Level 1 6.1Kg (range 4.0 - 11.2Kg), Level 2 10.6Kg (1.5 - 25.5Kg).

Conclusions: Most lost weight with absolute loss greater within the Level 2 cohort. This suggests a place for trained health promotion professionals within aftercare but further study is needed to determine whether additional support offered in level 2 justifies resource and whether weight loss is sustained.

D31 SIOP19-0423 | Cumulative Burden of Subsequent Neoplasms, Cardiovascular and Respiratory Morbidity in Long-Term Survivors of Childhood and Young Adult Cancer

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Background/Objectives: Many studies of the late effects of treatments in long-term childhood cancer survivors focus upon one single disease. However, long-term survivors are at increased risk of multiple chronic conditions. In this study we estimate the cumulative burden of subsequent tumours, cardiovascular and respiratory morbidity in long-term survivors of young people with cancer.

Design/Methods: Information on five-year survivors of cancers diagnosed aged 0-29 years from 1992-2010 were extracted from the Yorkshire Specialist Register of Cancer in Children and Young People. Hospital admissions for cardiovascular and respiratory conditions were obtained via linkage to all hospital inpatient admissions from 1997-2015. All subsequent malignant neoplasms (SMN) diagnosed were ascertained from national cancer registrations. The cumulative incidence for each outcome was estimated, with death as a competing risk. The mean cumulative count was used to estimate the cumulative burden of all events where an event was either a hospitalisation for respiratory or cardiovascular disease or SMN diagnosis. Multiple failure-time survival models were used to assess the association between treatment exposures and cumulative burden.

Results: A total of 3686 long-term survivors were included. By age 40 the cumulative incidence of an admission for respiratory disease was 51% (95% CI 46-55), cardiovascular disease was 25% (95%CI 22-28), developing a SMN was 6% (95%CI 5-8) and admissions for both respiratory and cardiovascular disease was 12% (95%CI 10-14). By age 40, an aver-

age of 212 events per 100 survivors were observed (95%CI 176-260). The risk of experiencing multiple events was higher for those treated with chemotherapy drugs with known lung toxicity (HR=1.22, 95%CI 1.04-1.42).

Conclusions: Survivors of childhood and young adult cancer experience a high burden of morbidity due to respiratory, cardiovascular diseases and SMNs. This research identifies the importance of considering multiple morbidities and recurrent events when quantifying the burden of late effects.

D32 SIOP19-1335 | Metabolic Syndrome and Vascular Disease Occur At Young Adult Age in Long-Term Survivors of Childhood Nephroblastoma and Neuroblastoma

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Background/Objectives: Because of increasing survival rates of childhood nephroblastoma and neuroblastoma, long-term side effects as metabolic syndrome (MetS) and subsequent diabetes mellitus and cardiovascular disease, have become more prominent. We compared metabolic blood biomarkers and vascular parameters between survivors of these malignancies and controls, and studied treatment-related risk factors for abnormalities.

Design/Methods: Seventeen serum biomarkers and nine vascular parameters were tested in survivors of childhood nephroblastoma (n=67), neuroblastoma (n=36) and controls (n=61) in a single center cohort. Differences between survivors and controls and within survivors were assessed by bootstrapping the difference in median values. Principal component analysis (PCA) was used to study the relative contribution of all biomarkers to explain variance among participants. Multivariable linear regression models were used to define treatment-related risk factors. MetS was scored using NCEP-ATPIII-criteria.

Results: Median attained age was 30.0 years for survivors and 31.8 years for controls. At a median follow-up of 27.5 years, triglycerides ($\Delta=0.17\text{mmol/L}$), cystatin C ($\Delta=0.06\text{mg/L}$) and creatinine ($\Delta=5\mu\text{mol/L}$) were significantly higher in survivors compared to controls. PCA of serum biomarkers showed that dyslipidemia (PC1, explained variance 22.7%) was the most discriminative component in the study population, followed by impaired glucose metabolism and kidney function (PC2, explained variance 12.1%). In univariable analysis, abdominal radiotherapy was associated with features of dyslipidemia, hypertension and central arterial stiffness, and nephrectomy with kidney disease and insulin resistance.

In multivariable analysis, abdominal radiotherapy was significantly associated with higher triglycerides ($\beta=0.508$) and central diastolic blood pressure ($\beta=5.63$), and nephrectomy with elevated cystatin C ($\beta=0.123$). MetS was present in 14 survivors and 2 controls (OR=4.6, $p=0.032$).

Conclusions: At relatively young age, survivors of childhood nephro- and neuroblastoma, especially after abdominal radiotherapy, show disturbed metabolic biomarkers and vascular parameters. This illustrates the need to screen for these abnormalities and to timely start interventions to prevent MetS and vascular disease.

D33 SIOP19-1024 | Predicting Subsequent Malignant Neoplasms in Childhood Cancer Survivors Using the MIPOGG Decisional Algorithm

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Background/Objectives: The McGill Interactive Pediatric OncoGenetic Guidelines (MIPOGG) contains 140 evidence-based tumour-specific decisional algorithms to assist physicians in identifying children with cancer at elevated risk of having an underlying cancer predisposition syndrome (CPS). MIPOGG application in validation cohorts of paediatric patients with cancer, independent of tumor type, has generated genetic referral rates for CPS evaluation of approximately 30%. Since subsequent malignant neoplasms (SMN) are a common feature of patients with a CPS, particularly when exposed to treatment-related risk factors (chemotherapy, irradiation), we sought to evaluate MIPOGG's performance in predicting SMN in a childhood cancer survivor (CCS) cohort.

Design/Methods: Utilizing the Ontario paediatric cancer registry (POGONIS), we identified CCS diagnosed and/or treated at the Hospital for Sick Children, Toronto, at age <18 years, (1986-2015) who developed a SMN. MIPOGG was retrospectively applied in all patients using clinical, family history and tumor-specific features recorded at the time of the primary malignancy, generating a recommendation for or against genetic evaluation for a CPS. Cumulative doses of chemotherapeutic agents and radiotherapy details were recorded.

Results: 198/205 CCS who developed a SMN (median time to SMN: 11.1 years, IQR 5.6-16.4) had sufficient information available for MIPOGG application. MIPOGG recommended genetic referral for CPS evaluation in 39.9% of patients (n=79) and no referral in 60.1% (n=119). A signif-

icantly greater proportion of patients were irradiated in the "MIPOGG - No Referral" group compared to the "MIPOGG - Referral" group (74% vs 38%, $p < 0.01$).

Conclusions: MIPOGG may have additional value for SMN prediction over and above its use in CPS detection, potentially identifying children who may be particularly susceptible to late effects of radiation and chemotherapy. Expansion of this study to five provincial paediatric cancer centres, with matched case-control analysis encompassing MIPOGG application and interrogation of treatment-related exposures will inform the feasibility of SMN risk prediction tool development.

D34 SIOP19-1695 | Coronary Artery Disease Surveillance for Childhood, Adolescent and Young Adult Cancer Survivors – Recommendations from the International Guideline Harmonization Group

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Background/Objectives: Childhood, adolescent and young adult (CAYA) cancer survivors are at risk of developing coronary artery disease (CAD). The International Guideline Harmonization Group (IGHG) and PanCareSurFup Consortium commissioned a taskforce to propose surveillance recommendations.

Design/Methods: A panel of 25 international experts (pediatric/medical/radiation oncologists, pediatric/adult cardiologists, pediatricians, internists, epidemiologists) from 10 countries evaluated concordance/discordance between international guidelines, conducted a systematic literature

search, graded the evidence per the Grading of Recommendations Assessment Development and Evaluation criteria, and formulated recommendations. Selection criteria included English language studies published between January 1, 1990 and November 1, 2018, of ≥ 20 cancer survivors, diagnosed before age 35 years, off active treatment, and assessed post completion of therapy. Case reports, case series, and narrative reviews were excluded.

Results: Thirty studies (8 multivariable analyses) reporting the occurrence of CAD in cancer survivors were identified. The risk was increased among survivors exposed to radiotherapy involving the heart (low quality of evidence); no significant effect of chemotherapy was identified (very low to low quality of evidence). Male gender, older age at diagnosis, and ≥ 1 modifiable cardiovascular risk factor (overweight/obesity, hypertension, dyslipidemia, smoking, diabetes) increased the risk (very low to moderate quality of evidence). No studies assessed the diagnostic value of surveillance modalities for asymptomatic CAD, treatment with lipid-lowering or anti-hypertensive agents, or lifestyle modifications.

Conclusions: IGHG recommends that healthcare providers should be aware of the risk of premature CAD in CAYA cancer survivors. Evidence is insufficient to recommend a particular surveillance modality for asymptomatic CAD. Risk assessment according to national/local guidelines is recommended, with initiation and frequency based on treatment history and cardiovascular risk factors. Surveillance and management of established modifiable risk factors is recommended. These recommendations aim to promote optimal care and preservation of cardiovascular health for CAYA cancer survivors.

D35 SIOP19-0048 | Bone Mineral Density Evolution and its Determinants in Long-Term Survivors of Childhood Acute Leukemia: A Lea Study

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Background/Objectives: Conflicting results have been reported regarding osteopenia in childhood acute leukemia survivors. The aim of this prospective study is to analyze determinants that can influence bone mineral density (BMD) evolution.

Design/Methods: Long term follow-up LEA cohort includes patients after treatment of childhood acute leukemia. Those who had dual energy X-ray absorptiometry scan between 10-18 years and after the age of 18 were selected. All scans were centrally reviewed. BMD was measured at lumbar spine (LS), femoral neck (FN), total hip (TH) and whole body (WB), and expressed in Z-score.

Results: Eighty nine patients (female 41, lymphoblastic leukemia 67, relapse 26, hematopoietic stem cell transplantation (HSCT) 45, mean age 15.4 ± 2.2 and 20.1 ± 1.8 years at first and second scans respectively) were studied. LS mean Z-score was -1.2 ± 1.1 at first scan and -1.1 ± 1 at second assessment. A significant improvement was observed at second scan for FN and TH: mean Z-score -0.6 ± 1 and -0.6 ± 1.2 versus -0.9 ± 1 and -0.8 ± 1.1 , $p=0.033$ and 0.036 respectively. WB mean Z-score remained stable. At second evaluation, 14.6% of patients had Z-score < -2 at the LS, 4.3% at the FN, and 7.2% at TH. Neither gender, type of leukemia, history of HSCT or relapse, nor cumulative corticosteroid doses or growth hormone deficiency had a significant impact on Z-score variation. Weight gain influenced Z-score variation at TH. Patients treated for hypogonadism tend to improve their Z-score at LS. Patients without metabolic syndrome had stable Z-score at LS (-1 ± 1 versus -1.1 ± 1), and improved their Z-score at FN (-0.5 ± 1 versus -0.8 ± 1 , $p=0.024$), those with metabolic syndrome had worse results at the 2 sites (-1.2 ± 1 versus -0.7 ± 1 , and -0.8 ± 0.8 versus -0.4 ± 0.9 , $p=0.042$ and 0.024 respectively).

Conclusions: Low BMD is relatively uncommon in adults. Patients with metabolic syndrome seem to be at higher risk of BMD decline and should benefit from specific intervention.

IPSO

IPSO: Oral Poster Session

DIPSO01 SIOP19-0354 | Intraoperative Neuromonitoring in Pediatric Pelvic Surgery

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Background/Objectives: Intraoperative neurophysiological monitoring (IONM) is an established tool to assess neurological functions during brain and spine surgeries. In pelvis surgery IONM can allow to identify particular sacral nervous structures and monitor this function. There are few evidences about IONM in pelvic surgery in adults and even less those concerning its use in children. Aim of this study is to review our cases of children operated for tumors involving pelvic structures, to correlate the IONM data with those of neuroimaging and with the clinical outcomes, to assess the impact of the IONM on surgical strategies and clinical follow-up.

Design/Methods: We retrospectively analysed neurological, urological and radiological pre-operative data of patients underwent surgery for removal pelvic tumors. An at last 3-months postoperative clinical follow-up was considered. IONM was performed by using a multimodal approach which included the registration of trans-cranial motor evoked potentials (tcMEP), somatosensory evoked potentials (SSEPs), continuous electromyography (EMG) and BCR (bulbo-cavernosus reflex). Triggered EMG for direct mapping of the structures involved in the surgery was available and performed by using electrical stimulation as required by the surgeon

Results: Eight patients (M:F 3:5), median age 3,8 years) were enrolled. Histology of tumors was: germ cell tumors (two endodermal sinus tumor, two mature teratoma), bladder rhabdomyosarcoma ($n=2$) and neuroblastic tumors (one neuroblastoma, one ganglioneuroma). In all cases radical resection was performed. IONM techniques application showed feasible and stable signals in all cases. No patients suffered from clinical or radiological deterioration in the follow-up.

Conclusions: Our experience shows the relevance of IONM in pelvic surgery, related to a radical resection and a good neurological/urological outcome in the clinical follow up. IONM is useful for the collection of functional data related to the lesion topography and can directly influence the surgical strategy.

DIPSO02 SIOP19-1386 | Surgical Complications in Abdominal Tumour Surgery in Children: Experiences at a Single Paediatric Surgery Unit

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Background/Objectives: Surgical complications frequently develop in children after tumour operations, with rates of up to 30% cited in the literature. Various approaches have

been followed in recent years to reduce these complications rates, with preoperative chemotherapy and intensified preoperative preparation holding pride of place. The purpose of this analysis is to evaluate complications associated with tumour surgery and how to minimize them.

Design/Methods: We collected the data of 91 patients underwent tumour surgery, between 1996 and 2018. Of all patients, clinical data, surgical data and the postoperative history were reviewed including: 1. Patient features (nutritional risk index, serum albumin, Body Mass Index BMI); 2. Tumour Pattern (seat, scope and type); 3. Diagnostic and Therapeutic Findings (Intensified Surgical Planning, Neoadjuvant Chemotherapy, Volume-Outcome Effects). For this evaluation, we considered relevant vascular or organ injuries that were not part of the therapeutic concept and relevant problems that presented directly after surgery and that could be attributed to the surgical procedure.

Results: Between 1996 and 2018 a total of 91 children underwent abdominal tumour operations. The three most common tumours requiring surgery were neuroblastoma (44/91, 49%), nephroblastoma “group” (26/91, 29%), and ovarian tumours (12/91, 13%). A total of 12 (11.3%) surgical complications developed: there were five (42%) vascular injuries, three (25%) instances of insufficient organ perfusion, in two (16.5%) the tumour was opened and in two (16.5%) the biliary tract was injured.

Conclusions: Tumour surgery is associated with considerable risks in children and is very important to search for new “approaches” that could potentially minimize these risks. Although the development of complications is a multifactorial “problem”, it is important to establish statistical significance for single parameters. It is safe, indeed, three-dimensional-printed models, through improved surgical planning, could optimize outcomes also for patient with abdominal tumours.

DIPSO03 SIOP19-0992 | Short 2 Day Paediatric Surgical Oncology Review Course – Zambia Experience

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Background/Objectives: A two day Paediatric Surgical Oncology course was held in Zambia supported by St. Jude Children's Research Hospital. The paediatric surgical training program in Zambia began in 2015 and is still in its infancy. The objective was to scale up workforce capacity and standardize cancer surgical care.

Design/Methods: The course was held on 12/2/19 and 13/2/19, with seven paediatric surgeons, five paediatric surgical trainees, and a paediatric oncologist in attendance. Day one included open discussions of common paediatric solid tumors and talks on drivers of poor outcome among others. Day two was a practical workshop that included preoperative images, operative videos, and 3D printed patients' tumors. A post-course survey was conducted by handing out questionnaires to all participants.

Results: All 13 participants felt the course provided useful operative strategy and management of complications; 12 participants stated the course highlighted the role of multidisciplinary approach; 11 participants felt it identified causes of poor cancer outcome in LMICs and set goals and deliverables. Nine participants ranked summary of indication and timing of resection, biopsy and therapy as the most helpful preoperative planning course strategy; while preoperative oncology checklist received low ranking. A total of 10 participants ranked breakdown of procedures to critical steps and discussion of operative video as the most helpful strategy, while 3D printed tumor models received low ranking. Establishing a multidisciplinary approach, Wilms tumor lymph node sampling, and standard tumor biopsy strategies were changes noted in practice since the course was held.

Conclusions: There is a role for paediatric surgical oncology short courses in capacity building and standardization of surgical care. Summary of indication and timing of resection, biopsy and therapy; discussion of operative videos and breakdown of procedures to critical steps were perceived as more effective tools, while 3D printed models were a less effective learning tool.

DIPSO04 SIOP19-0430 | Outcomes of Surgery in Ganglioneuroma and Ganglioneuroblastoma in a UK Single Centre

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Background/Objectives: Ganglioneuroma and ganglioneuroblastoma form part of the spectrum of paediatric and adult neuroblastic tumours. This study aims to examine the surgical outcomes of ganglioneuroma and ganglioneuroblastoma treated in our institution.

Design/Methods: A retrospective study of all patients (paediatric and adult) who underwent surgery for ganglioneuroma or ganglioneuroblastoma from January 1995 to December 2018. Data collected: degree of surgical resection, intraoperative findings, imaging, histopathology, overall survival,

post-operative complications. Statistical analysis: X^2 test, odds ratio, Kaplan Meier, Log-rank tests; a p value of <0.05 was taken as significant.

Results: Thirty two patients were identified (male female ratio 18:14, 1.2: 1). Fifteen (47%) had ganglioneuroma, seventeen (53%) had ganglioneuroblastoma (n=4 nodular, n=13 intermixed). Two age groups were defined: <16 years old (n=18, median age = 4.5 years, range 1-15) and >16 years old (n=14, median age = 41 years, range 19-71). Median follow up was 29 months (range 1-142). Complete resection was achieved in 50% of patients (n=9 in <16 age group, n= 7 in >16 years age group, p=1). Post-operative complications occurred in 22% (n=3 in <16 group and n=4 in >16 group, p= 0.68). Overall survival was 87.5% (n=4 deaths, 1 in the <16 age group, 3 in the >16 group, p=0.09). Death was unrelated to surgery in 1 patient in the >16 age group.

Conclusions: Surgical management of ganglioneuroma and ganglioneuroblastoma is challenging. It is associated with significant morbidity in both children and adults. There is however no observed difference in mortality and complications between the two groups. There is a need to do a further national study to assess outcomes in the UK.

DIPSO05 SIOP19-0057 | Dong's Liver Segmentation Based on the Portal Vein Branch: A Digital Image Analysis

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Background/Objectives: A good understanding of liver anatomy is required for performing precise liver resection. However, the currently described methods of liver segmentation based on portal and hepatic veins are inconclusive. We proposed a system of liver segmentation based on previous reports and our data.

Design/Methods: Three-dimensional computed tomography software was used to analyze the portal vein branching pattern in 1260 patients. We analyzed four different types of liver segmentation.

Results: The digital liver model obtained from the 3D reconstruction of CAS (Hisense) displayed clear intrahepatic portal vein vessels of level four. Perform a digital liver segments study based on the analysis of level four vascular distribution areas. As the less anatomical variation of left hepatic portal vein, we classified the livers into four types of liver segmentation mainly based on right hepatic portal vein. Type A is similar to Couinaud or Cho's segmentation, containing 8 segments (537 cases, 42.62%). Type B contains 9 segments as there are three ramifications of right-anterior portal vein (464 cases, 36.82%). The main difference for Type C is the

variation of right-posterior portal vein which is sector shape (102 cases, 8.10%). Type D contains the cases with special portal vein variations, which needs three-dimensional simulation to design individualized liver resection plan (157 cases, 12.46%).

Conclusions: The new system of liver segmentation enables a better classification of individual patients into one of the different types, thus assisting preoperative surgical planning.

DIPSO06 SIOP19-1453 | An Unusual Complication of Tumor Surgery: Chylous Leak

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Background/Objectives: Postoperative chylous leak is an uncommon complication of tumor surgery associated with significant morbidity in children. Extended resections and lymph node dissections may lead iatrogenic trauma to main chyle ducts, cisterna chyli or lymph nodes causing chyle leak appearing as milky fluid and elevated triglyceride levels in the surgical drains. Chylous leak can be managed by conservatively or surgical/interventional methods but there is not any guideline or general recommendation list. This clinical study is designed to evaluate effectiveness of conservative treatment.

Design/Methods: The data of patients who had postoperative chylous leak after tumor surgery in our institution between 2010 and 2019 were evaluated retrospectively. Patient demographics, disease characteristics, postoperative management and outcome were reviewed.

Results: Twelve patients were identified as having a postoperative chylous leak after a surgery for tumor excision. Mean age of patients was 73 months (6-136 months). Nine patients with neuroblastoma had tumor excisions with laparotomy (n= 6), thoracotomy (n=2) and neck dissection (n=1), one patient had nephroureterectomy for malignant rhabdoid tumor of kidney, one patient had adrenocortical carcinoma resection and one had liver and lymph node resection for transitional cell carcinoma. All patients received total parenteral nutrition and total bowel rest for a mean of 13 days (6-27 days). Five patients had chylous leak more than a week despite lack of enteral feeding. These patients had intravenous somatostatin for a mean of 12 days (5-16 days) to decrease chyle production further. Eventually chylous leak ceased in all patients and surgical drains were removed after no leak is observed with enteral feeding.

Conclusions: Postoperative chylous leak is a relevant complication of tumor surgery associated with increased length of hospitalization. Conservative treatment with total parenteral nutrition and stopping enteral feeding seems to be effective. Somatostatin helps in resistant cases.

DIPSO07 SIOP19-0307 | Surgical Management and Outcome of Malignant Ovarian Germ Cell Tumors in Children – A Multicenter International Study

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Background/Objectives: To evaluate outcome of paediatric malignant ovarian germ cell tumors treated by four institutions.

Design/Methods: Retrospective analysis of all patients presenting between January 2014 and January 2019. Management protocols were Children's Oncology Group (COG) in three centers and Children's Cancer & Leukemia Group (CCLG) in one center. We applied COG staging to all patients. Overall survival (OS), event free survival (EFS) and univariate prognostic factors estimated by Kaplan-Meier and log rank test.

Results: The study included 37 patients with a median age of 10.5 years (1 – 18y). Thirty five patients had fertility preserving surgery. Surgical staging procedures were adopted in all cases. Nine (24.3%) patients underwent delayed resection. Mixed germ cell and yolk sac tumors represented 75.7% of patients. There were 7 (19%), 14 (37.8%), 12 (32.4%) and 4 (10.8%) stage I, II, III and IV respectively. Seven patients were low risk (LR), 26 intermediate risk (IR) and 4 high risk (HR). Platinum-based chemotherapy was administered as per risk stratification and protocol. Follow up to March 2019 revealed that 5 patients had relapsed (2 local, 2 distant and one both). There were no significant differences between pathological types regarding OS and EFS with p value 0.392 and 0.420 respectively. Three years OS was 83.7%: 100% for stage I and II, 62% for stage III and IV (p=0.003); 100% for LR, 89% for IR, 24% for HR (p=0.000). Three years EFS was 86.5%: 96% for stage I and II, 71% for stage III and IV (p=0.025); 100% for LR, 92% for IR, 26% for HR (p=0.000).

Conclusions: Surgical resection combined with chemotherapy achieves excellent outcome for malignant ovarian germ cell tumors. COG staging and risk stratification were significantly correlated with prognosis, whereas tumor pathology had no significant impact. These tumors are rare entities that require multicenter collaboration to obtain meaningful statistical results.

DIPSO08 SIOP19-0854 | Management of Paediatric Benign Ovarian Tumors: A Comparative Study Between England and Egypt

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Background/Objectives: To compare clinicopathological features and management of paediatric benign ovarian tumors between a tertiary referral English center and three tertiary Egyptian institutions.

Design/Methods: Retrospective review of all children presenting with benign ovarian tumors (excluding simple cysts) between January 2014 and January 2019. A standardised dataset used by both sides to compare patients' characteristics, surgical approaches and type of surgery performed. Statistical analysis was done using t and chi-square tests.

Results: Eighty nine patients were included (54 English and 35 Egyptian). Median age at diagnosis in England was 13 years (2-16y), while in Egypt was 7 years (9m-16y) with p value =0.001. Mature teratomas or dermoid cysts were the commonest finding in both England and Egypt, 75.9% and 82.8% of cases respectively. Presentation with acute abdomen represented 27.8% and 28.6% of cases in England and Egypt, respectively. Incidental diagnosed lesions accounted for 15% of English patients, whereas none of the Egyptian cases discovered incidentally. There were variations in diagnostic imaging; England: US (54), MRI (37) and CT (only one) – Egypt: US (35), CT (17) and MRI (only one). Minimally invasive surgery (MIS) was performed in only 15% English patients and 23% Egyptian (p=0.334). Ovarian sparing surgery (OSS) was performed in: England 35%, Egypt 37%; p=0.851. OSS was performed using MIS in 87.5% (7/8) of English patients and 100% (8/8) of Egyptian. Patients presented as emergencies generally had open oophorectomies: England; 86.7% open and 80% oophorectomy – Egypt; 100% open and 90% oophorectomy. Recurrence or metachronous disease occurred in 5.6% and 5.7% of English and Egyptian patients, respectively.

Conclusions: There were no significant differences regarding surgical management, tumor pathology and recurrence between both countries. Age, incidental diagnosis and imaging modalities had notable differences. In England and Egypt,

MIS had significant correlation with ovarian preservation, whereas emergency surgery generally resulted in an open oophorectomy.

DIPSO09 SIOP19-0237 | Ewing Sarcoma of the Thorax: Treatment and Outcome

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Background/Objectives: The aim of this study is to evaluate the clinical, therapeutic characteristics and outcome in children and adolescents with Ewing sarcoma family tumors (ES) of the thorax.

Design/Methods: The data of 38 patients (21 female, 17 male) with ES of the thorax among 180 children and adolescents with ES (21%) treated in the Istanbul University Oncology Institute from January 1991 to December 2018 were evaluated retrospectively.

Results: The median age was 12 years (1-18), the primary sites were ribs in 22 (58%), scapula in 5, clavicle in 4, soft tissue of the chest wall in 4, vertebra/paravertebral soft tissue in 3. Fifteen (39%) were metastatic at diagnosis, 35 had high tumor volumes. All patients received chemotherapy consisting of alternating courses of vincristine, adriamycin/actinomycinD, cyclophosphamide and ifosfamide-etoposide for a year and local treatment (surgery/radiotherapy). At progression/relapse, vincristine, topotecan, cyclophosphamide or vincristine, irinotecan, temozolamide were some regimens used (Kebudi et al, *Pediatr Hematol Oncol.* 2013; *J Oncol Pharm Pract.* 2018). Local treatment was primary surgery in five, 21 were operated after neoadjuvant chemotherapy; 21 received radiotherapy. All nonmetastatic patients with a scapula (5 patients) or chest wall soft tissue primary (3) and total resection, survive with no evidence of disease. The 3 year survival in all, in nonmetastatic and metastatic patients were 41%, 62% and 14% respectively ($p = 0.002$). The 3-year OS was 66% in 180 ES patients (29% were metastatic) of all sites.

Conclusions: Thirty-nine percent of the patients with ES of the thorax were metastatic and 92% had large volume tumors, which may account for an inferior outcome compared to all ES patients in the same center (3 year S 41% vs. 66%). Patients with scapula primaries and small chest wall tumors had the best survival. Metastasis was a poor prognostic factor.

DIPSO10 SIOP19-0522 | Translation of Operative Reports into an Anatomic Cadaveric Study for Improving Perivascular Exposition Area During Resection of Abdominal Neuroblastoma

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Background/Objectives: Recent studies suggest that the extent of tumor resection correlates with survival of patients with high-risk neuroblastoma. Our aim was to translate clinical data into a study on human cadavers in order to establish a structured exposure approach for resection of neuroblastoma that involves the whole upper abdomen.

Design/Methods: First, all patients of the German multicenter NB97 study were included in a retrospective analysis if operative reports, pre-/postoperative imaging were available, and if no first remission after abdominal resection of INSS 4 neuroblastoma occurred. We identified initial tumor distribution within three upper abdominal regions (UAR) and the spectrum of exposure techniques. Then, these exposure techniques were translated into a study in 8 human cadavers. The exposure techniques of left (LMVR) and right (RMVR) medial visceral rotations including thoracoabdominal exposure, and access to bursa omentalis (AC) were analyzed. A score for the perivascular exposition area (PEA) at truncus coeliacus, distal arteria hepatica communis (AHC), left and right arteria renalis was evaluated for each technique. PEA was scored as suitable for 1: only nearly intact anatomy, 2: small, 3: large tumor.

Results: 73.1% of eligible NB97 patients had an initial tumor extent in >1 and 38.8% in all 3 UAR. Exposure technique analysis yielded single unilateral exposure technique in 72.4%, unilateral combinations in 22.3% and bilateral combinations in 4.6% of patients. The highest mean of PEA was achieved by LMVR at truncus coeliacus (2.75) and left arteria renalis (2.62), by AC at AHC (3.0), and by RMVR at the right arteria renalis (3.0). We found the sequence of LMVR, then RMVR, and finally AC to give the best PEA of all vessels in the UAR.

Conclusions: Increasing perivascular exposition area for large tumors involving all UAR can be achieved by the sequential use of LMVR, RMVR then AC in combination with thoracoabdominal exposure.

NURSES

Nurses: Poster Discussion Session 1

DN01 SIOP19-0767 | More Complex and Intensive Treatment Regimes in Children with Cancer Increases Nursing Care Needs

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Background/Objectives: We experienced children's increasing and multi-faceted needs for nursing care due to more intensive and complex cancer treatment regimens. There is limited evidence of this increase and the objectives were to determine the development and assess the correlation between nursing care needs and nurse resources.

Design/Methods: In this observational study we used PIMI, a classification tool to measure nursing care needs of children with cancer and nurse resources. The children are categorized daily in six care categories ranging from A (minimal) to E (highly-intensive). PIMI provides an algorithm for the optimal number of nurses needed in the specific category, and a comparison of the optimal number of nurses for the entire group of children with the actual number of nurses available. Data were collected between January 2016 - February 2019 and analyzed with descriptive statistics.

Results: Out of 560 days, 83% were below the optimal number of nurses needed, 2% on, and 15% above. All results are daily averages with range in parentheses: Number of children has increased from 17 (9-23) to 19 (14-24), the optimal number of nurses needed has increased from 10 (5-16) to 12 (9-16), and the actual number of nurses has stayed unchanged from 8 (5-11) to 8 (5-12), whereas the number of nurses with <1 year of experience has increased from 2 (0-6) to 3 (0-9). There was a decrease in children in category B from 10 (3-17) to 9 (0-15), and an increase in category C from 7 (0-15) to 8 (4-12) and in category D from 0 (0-3) to 1 (0-10). Children in categories A and E were unchanged.

Conclusions: There has been an increase in the total number of children and a shift towards more intensive nursing care needs. The actual staffing level does not correspond to the children's needs for nursing care.

DN02 SIOP19-1723 | Brazilian Portuguese Translation and Cross-Cultural Adaptation of the Nutrition Screening Tool for Childhood Cancer (SCAN)

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Background/Objectives: Malnutrition, especially in the pediatric oncology population, has a significant impact on the child's prognosis. To its prevention multiple strategies are needed, the first of which is through early nutritional screening. Murphy et al (2016) developed and validated the SCAN (Nutrition Screening Tool for Childhood Cancer) tool specifically for pediatric oncology and not yet translated into any language. This study aims to translate and culturally adapt the SCAN tool into Brazilian Portuguese.

Design/Methods: This study documents the translation and cross-cultural adaptation of the tool from the original version (English) into Portuguese according to an internationally accepted methodology. At the first stage, translation was performed by two independent translators, followed by their synthesis and reconciliation. The reconciled version was back translated to english by an english-native independent translator and, then a pre-final version of the tool that retained all linguistic equivalence was developed. In the fifth step, a pre-test of the pre-final version was performed in order to verify the understanding of the items and a final version of the tool was developed at the last step.

Results: The pre-final version of the SCAN tool was applied to 37 health professionals directly involved with pediatric oncological care (physicians, nursing and nutrition staff) in order to verify its understanding. Brazilian-portuguese is complex due to many different meanings for the same word, according to the professional and cultural background. The main alterations were the adaptation of technical terms in order to unify and facilitate evaluation by different observers, and the adjustment of particular oncological terms specifically, some of them exemplifying on a clinical context.

Conclusions: The Brazilian Portuguese Nutrition Screening Tool for Childhood Cancer was easily understood by health professionals, and it should be useful in clinical practice and in scientific research in Brazil. Our next step is to evaluate the reproducibility of the translated version.

DN03 SIOP19-0615 | Upgrading Nursing Curriculum to Prepare Nurses to Care for Children and Adolescents with Cancer, Tanzania: Distance E-Learning Evaluation

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Background/Objectives: Tanzanian nurses, like other low-income countries, account for 80% of the healthcare work force and are front-line workers available at all primary health facilities. Preparing nurses with specialized training has a significant potential to limited delayed care of children with cancer. An e-Learning nursing course offered by Ministry of Health under support of African Medical and Research Foundation (AMREF) and included a Medical and Surgical Nursing module with oncology nursing session. This survey assessed whether the e-Learning nursing in-service prepared students to care for children/adolescents with cancer in Tanzania.

Design/Methods: A cross-sectional consented online survey was performed within-service distance e-learning nursing students who were upgrading from a nursing certificate to a nursing diploma. The survey included demographics, experience caring for children with cancer and knowledge gained about childhood cancer during their e-learning program. Data were collected in real time and analyzed using Redcap.

Results: Thirty-three students participated in the survey. Most (40%) worked in a health center, other sites included dispensary (27%), district hospital (17%), or regional hospital (13%). Seventeen percent had cared for children with cancer in their setting. However, the majority of the nurses (97%) stated they were not prepared to care for these patients before training. A total of 77% had not had a module on caring children with cancer in their certificate curriculum. Nevertheless, 55% believed they could care these patients after the e-Learning training. Forty-eight percent stated they could identify early signs of childhood cancer and provide palliative care and 97% recommended integrating childhood/adolescent cancer in nursing curricula.

Conclusions: The findings of this survey support the need to integrate childhood/adolescent cancer care competencies in pre-service and in-service curricula of nursing training programs in Tanzania to improve patients 'early diagnosis and outcomes.

DN04 SIOP19-1488 | Haematology Oncology Newly Qualified Nurse Education Programme in Edinburgh

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Background/Objectives: Newly qualified nurse education within the haematology and oncology department in Edin-

burgh unstructured previous to the role of Clinical Skills Facilitator. A new nurse would be assigned a preceptor, complete a supernumery period of 2 weeks and start to take patients. Learning and education was unstructured and inequitable depending on the experience of preceptor and the time constraints of nursing workload. Objective of developing a structured education programme was to ensure equitable, fundamental education within paediatric haematology and oncology. Provide protected education from specialists and protected supernumery status for two months from start of post to ensure the newly qualified nurse has the recourses, education and opportunity to provide current evidence based care to our patients confidently.

Design/Methods: Discussion with nursing management would allow for the 8 week supernumery status. Development of five individual study days during the programme would include topics, what is cancer and common malignancies, Haematology/Oncology emergencies, Introduction to SACT and safe handling, related specialities and a clinical skills day.

Results: The programme has run four times since 2017. Feedback from delegates and multi-disciplinary team has been positive regarding the progress of the nurses who have engaged in the programme. Comments did include, 'interactive sessions,' 'understanding malignancies will help support parents and the children I will be looking after,' 'I will be able to recognise the signs before they lead to an emergency,' 'I really enjoyed effects of SACT on fertility,'

Conclusions: This programme will continue to run in Edinburgh Royal Hospital for Children and Young People (RHCYP) and will be advancing as nursing responsibilities and expectations advance.

DN06 SIOP19-1291 | Achieving Sustainable Practice Changes: Evaluation of a Pediatric Oncology Nursing Certificate Program in Tanzania

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Background/Objectives: Specialized pediatric oncology nursing is often lacking in resource-limited settings. A 10-week clinical nursing course was implemented in Tanzania to address this. The course was coordinated by an experienced pediatric oncology nurse and taught to 7 nurses by international faculty. Designed to accommodate the nurse's daily work schedule, mentors precepted 1:1 at the bedside. Changes implemented during the course included: adopting

patient-centered care (PCC), improving existing pediatric early warning signs (PEWS) system, and implementing a two-person approach to chemotherapy administration.

Design/Methods: Pre/post-course evaluations were done to assess the initial impact of the course. A six-month evaluation was conducted using a structured questionnaire combining both true/false statements and open-ended questions to assess the continued impact and the sustainability of these system changes. Participants completed the pre/post-course evaluation and a range of colleagues were interviewed at 6 months.

Results: Participant feedback revealed the nurses had increased confidence delivering care and were supportive of clinical changes. 8 nurses and 3 physicians completed the 6-month evaluation. Eighty-two percent reported that PCC was still being implemented, acknowledging the benefits of improved patient care and overall communication. Ninety percent reported the PEWS system is practiced consistently each day. All unanimously agreed on the necessity for its routine use. Highlighting its power, an example was given of hypertensive children previously missed until symptomatic, now are identified and treated on presentation. All respondents agreed that the implementation of a 2-person chemotherapy check was safer and all felt more confident giving chemotherapy with the 2-person verification in place.

Conclusions: The nurses were able to successfully implement several system changes during the course with sustainability of these new practices over time. Course evaluations will guide the next training program planned for Fall 2019. Monitoring clinical indicators, including time from fever to antibiotic administration, will further document the positive impact of this course.

DN07 SIOP19-0241 | Comparative Analysis of Fall Risk Assessment Tools in Pediatric Oncology: A Quality Improvement Project

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Background/Objectives: Unintentional fall among hospitalized children is a major patient's safety issue and is leading cause of negative health consequence. Accurate assessment and use of validated fall risk assessment instrument are the key measures to prevent such incidents and improve patient's safety. Currently there is significant lack of studies regarding validated pediatric fall risk assessment tools. Thus, the purpose of this quality project was to have comparative analysis of two different fall risk assessment tools; i-e Humpty Dumpty and Little Schmidy for their sensitivity, specificity, and inter-rater reliability.

Design/Methods: The important measures which were taken to implement this quality project were literature review, pilot testing of Little Schmidy against the currently used Humpty Dumpty tool, nursing documentation review, health care professionals training and physician/nursing leadership meetings.

Results: A pilot testing was done for 1 month on all admitted patients. After the comparative analysis, it was identified that there were too many pitfalls in Humpty Dumpty fall risk instrument in regards to its applicability and reliability in pediatric oncology population. The major drawbacks in this instrument were gender as predictor for fall, minimum one score for each factor even if it doesn't exist and some confusing statements in the elements of cognitive/environmental factors. In contrast to this, Little Schmidy tool was found to be more concise and easily applicable to identify high risk patients in order to enforce specific targeted interventions. This tool was then implemented after the approval from Hospital based Quality Council.

Conclusions: Fall is the most common public health concern globally but can be prevented with proper assessment and targeted interventions. Training of health care professionals, use of validated fall risk instrument and evidence based fall prevention strategies are some critical approaches which can reduce the substantial physical and psycho-social impact of fall related injuries and incidents.

Keywords: Falls, Pediatric patients, Quality improvement.

Nurses: Poster Discussion Session 2

DN08 SIOP19-0255 | Post Transplant Lymphoproliferative Disorder in Pediatric Solid Organ Transplant Recipients: What's That All About?

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Background/Objectives: Post transplant lymphoproliferative disease (PTLD) is a major complication of solid organ transplantation. The incidence of transplantation in pediatrics is steadily rising making PTLD the most common form of lymphoproliferation in childhood (Llaurador, 2017). Features of PTLD are similar to an immune system malignancy with abnormal proliferation of lymphoid lineage cells, typically B cells, in the setting of immunosuppression and often associated with EBV infection (Dharnidharka, 2017). Care of these patients is becoming more prevalent in the pediatric oncology population, requiring a multidisciplinary approach with the transplant teams. We identified a knowledge deficit among oncology nurses, and a need to enhance collaboration between multiple care teams.

Design/Methods: Having experienced a rising incidence of patients with PTLT within our heme-malignancy program, we created an education program for oncology nurses to increase their awareness and understanding of this diagnosis and treatment options. We performed an extensive review of the literature and developed a 1 hour education program that reviewed PTLT following solid organ transplantation including risk factors, pathophysiology, clinical presentation, diagnostic workup and treatment options. Case studies of PTLT were presented to allow for learner participation.

Results: The program was well received and nurses reported feeling more confident caring for these patients in a multidisciplinary setting after PTLT education was provided.

Conclusions: With the rising incidence of pediatric transplantation it is critical that the oncology nurse be aware of this diagnosis and treatment options to provide optimal care and education to the patient and family. Disease specific education about PTLT should be part of the oncology nursing education program.

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DN09 SIOP19-0742 | Educational Strategy to Empower Junior Nurses to Undertake Parental Teaching within a Tertiary Paediatric Oncology Centre

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Background/Objectives: The treatment of children and young people (CYP) with a cancer diagnosis can be complex. However, there will be times when CYP are at home, therefore needing to be confident in managing side effects, identifying healthcare professionals to liaise with and adhering to treatment specific advice. Prior to discharge after initial diagnosis every family receives a parent held oncology record book (PHOR), containing the aforementioned information. For the family's understanding of the PHOR to be assessed, a knowledgeable nursing workforce is required. The objective was to create and implement an education strategy to empower junior nurses to provide teaching contained in the PHOR, to parents/carers of CYP with an oncological diagnosis.

Design/Methods: A timeline was established for PHOR teaching for all new and current junior nurses within the unit.

An initial foundation day was mandatory followed by an introductory study day covering all aspects of the teaching. A competency document was implemented, identifying dates of study days, witnessing a senior nurse delivering teaching, being supervised and deemed as competent. Parental teaching was also added to the list of requirements in the initial probationary period.

Results: Evaluation forms after each study day and formal feedback was obtained from all nurses. Results indicated they felt more equipped for the task and were supported by their senior colleagues. At the end of the initial six-month probationary period all nurses had completed their PHOR competencies and were confident in delivering teaching unsupervised.

Conclusions: Implementation of an education strategy for junior nurses to deliver PHOR teaching in the form of teaching and a competency document has increased the confidence and competence of nurses to carry out this task as well as their understanding of treatments and side effects. With an increase in competent nurses, patients received their information earlier on in treatment.

DN10 SIOP19-1113 | Early Detection of Childhood and Adolescents Cancer and Awareness In Ghanzi, Botswana: Nurses Role

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Background/Objectives: Nurses are the first line of contact with clients and are ones who make early detection of diseases. In low income countries like Botswana children are being misdiagnosed with cancer making it difficult to treat and manage childhood cancer in timely manner. This is why this study aims to find out whether nurses at Ghanzi district in Botswana know their role in early detection of cancer in children and adolescents.

Design/Methods: This cross-sectional study used a self-administered questionnaire-based survey with a convenient sample of nurses working at Ghazi District. The locally developed survey included closed and open-ended questions on demographics, experience in caring children with cancer and training on Pediatric oncology. Data were analysed by using SPSS.

Results: A total of 16 nurses participated in this study (37.5% Male, 62.5% Female). Majority (62.5%) were from primary hospital and 37.5% were from clinics. Hundred percent stated that they acquired basic training in Paediatric and adolescent cancer care during their training in colleges and universities and none had any further advanced training. Fifty-percent of participants had cared children/adolescent with cancer in their hospital setting. Majority (75%) responded that did not know

the early signs of cancer in children/adolescents. A total of 75% of nurses showed that it is essential that they know more about paediatric/adolescent oncology.

Conclusions: The study results shows that the role of nursing in caring children with cancer in Ghazi, Botswana is compromised due to the lack of knowledge in early detection of childhood/adolescents cancer especially at primary level of hospital

DN11 SIOP19-0445 | Strategies Used by Pediatric Oncology Nurses to Cope with Job Stress: A Case of the Uganda Cancer Institute—Author Request

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Background/Objectives: **Background.** Nursing staff encounter a high incidence of physical, and psycho-social stressors at work. Pediatric-oncology Nurses are exposed to extremely stress-provoking situations in the complex care of children and their families. The Uganda Cancer Institute (UCI) serves approximately 500 new pediatric cases annually. There are 10 nurses on the inpatient ward and 4 nurses in OPD. The World Health Organization (WHO) recommends a nurse patient ratio of 1:5 and at UCI the ratio ranges from 1:20. With these ratios the degree of stress is increased for nurses and the quality of care for patients is decreased. It is important to identify how nurses cope with job stress to design strategies to address stressors for UCI pediatric nurses and prevent unfavorable patient care outcomes.

Objective. A pilot study was designed with the specific aim to explore the experiences of pediatric oncology nurses working at the UCI with a goal to formulate a tool, to use in a broader subsequent study aimed at identifying strategies to help nurses decrease job related stress.

Design/Methods: A qualitative study was implemented utilizing purposive sampling. The sample population included eight nurses working in the UCI Pediatric department both inpatient ward and OPD. Data collection was conducted through face to face unstructured interviews. Interview data was analyzed using a conventional content analysis approach.

Results: Four main themes emerged from the content analysis of the interview transcripts. The strategies used by nurses to cope with job stress were: a. situational control of conditions; b. sharing and seeking help; c. self-controlling; and d. spiritual-coping.

Conclusions: The experiences of the pediatric oncology nurses explored revealed current strategies employed to cope with job stress were inadequate. This information can be foundational for designing strategies that the UCI administration

can use to support oncology nurses and increase quality of care delivered.

DN12 SIOP19-0281 | Nurse's Practice on Pain Management in Children with Cancer at Muhimbili National Hospital, Tanzania: Parents' Perspectives

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Background/Objectives: **Background:** Pain is a common problem for children/adolescents with cancer. Pain usually originates from disease, treatment and associated procedures, and results in lower quality of life. Proper assessment, effective management and family education are essential for pain control. Nurses have a front-line responsibility for pain control due to their disproportionately larger amount of time spent with patients compared to team members.

Objective: Determine parents' perspectives on nurses' practice towards pain management in children with cancer admitted to Muhimbili National Hospital (MNH).

Design/Methods: This cross-sectional study used a questionnaire-based survey with a convenient sample of consented parents/guardians of children with cancer admitted at MNH. The locally developed survey included closed and open-ended questions on demographics, pain assessment, pain management and health education. REDCap was used for data collection, data entry (in real time with REDCap mobile application), and analysis.

Results: Sixty parents/guardians participated (61.7% male and 38.3% female). A majority (66.7%) reported not being given information about pain management during admission. Over half (52.5%) were given information by nurses a few days after admission. Forty-three percent reported that nurses assess their child's pain by asking the child where the pain is and touching the site. One quarter of the parents (24%) reported pain is not managed on time and 78.6% of this group reported the reason was the nurses are always busy with something else. All participants agreed they would like to be educated on pain management through group health education sessions (45.0%), leaflets on pain and its management (45.0%), or one-to-one talk, especially during the time of admission (16.7%).

Conclusions: The survey findings suggest that there is a need to improve nurses' practices on pain management in MNH for children with cancer through proper pain assessment and management as well as early (upon admission) and continuous pain management education of parents/guardians.

DN13 SIOP19-1353 | “The Essential Role of Nursing Education in the Care of Central Lines in Resource-Constrained Settings”

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Background/Objectives: Long-term intravenous (IV) access is needed when caring for children with cancer. Central venous access devices (CVADs) provide a consistent line to obtain blood specimens, administer supportive medications, fluids and chemotherapy. Due to prolonged periods of immunosuppression, children with cancer are at a high risk of developing central line-associated bloodstream infections (CLABSI), which can lead to catastrophic complications, including sepsis and death. With increasing use of CVADs in low-and-middle income countries due to difficulty finding and maintaining IV access over time, specialized education and appropriate resources are needed for nurses to successfully care for CVADs and decrease the associated complications.

Design/Methods: A baseline assessment of current challenges associated with CVAD use was conducted in a pediatric ward in Kenya via observation and discussion held during a Continuing Medical Education (CME) session about CVADs, specifically Infusaport safety. Ten health care professionals participated in a one hour-long CME approved by nursing administration. An informal period for discussion was utilized to establish a baseline of current resources and bedside procedures in caring for Infusaports.

Results: Prior to this CME, these professionals had little to no formal training or education regarding care of CVADs. Barriers identified for nurses to provide adequate care included: insufficient training on CVAD use and associated risks to the patient, lack of sufficient supplies (ie: needles and dressings), and a lack of current application of a daily maintenance care bundle, including procedural guidelines and timelines for hygiene, dressing changes, and access to prevent CLABSI.

Conclusions: Well-trained nurses are crucial to prevent CLABSI, utilize scarce resources effectively and improve patient outcomes. Without formal education and supplies to routinely care for CVADs, the life-threatening risks to patients increase significantly. Implementation of a daily maintenance care.

DN14 SIOP19-1273 | Chemotherapy Safety Training in Botswana

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Background/Objectives: Botswana has one pediatric oncology unit, at Princess Marina Hospital (PMH), through a partnership between government and the Baylor College of Medicine/Texas Children's Hospital Global HOPE (Hematology Oncology Pediatric Excellence) initiative. In order to improve current practices in chemotherapy handling and administration, we performed an educational intervention on safe handling of chemotherapy.

Design/Methods: A chemotherapy safety course was given over two days, for two hours each day. Topics included chemotherapy classification, handling, safety and administration. Pre- and post-tests were completed by the participants as well as a course assessment and self-assessment regarding providing chemotherapy to children using a 5-point Likert scale.

Results: Thirty-two health care professionals completed the course (1 patient navigator (3%), 5 physicians (16%) and 26 nurses (81%)). Fourteen of the nurses routinely worked on the pediatric oncology ward, representing 78% of the nurses on staff at the time of the course. The pre-test knowledge assessment median score of 41% correct (Interquartile Range (IQR) 27%, 59%) improved to 82% (IQR 45%, 91%) following the course. Prior to the course, the participants rated their comfort with giving chemotherapy to children as a median of 3 which increased to 5 by the end of the course.

Conclusions: A focused chemotherapy safety course that limits the impact to the clinical service is feasible with an improvement in knowledge and comfort in providing chemotherapy to children. Through this course, a chemotherapy safety checklist was reviewed and revised based on the nurses' input. Recently, a distance-based online model of nurse training has been initiated to build upon the knowledge gained with this training.

DN15 SIOP19-0125 | Development of a Web-Based Assessment Tool That Evaluates the Meal Situation When a Child With Cancer Has a Percutaneous Endoscopic Gastrostomy

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Background/Objectives: Background: Children with cancer often suffer side effects from their treatment. If a child cannot eat orally, a percutaneous endoscopic gastrostomy (PEG) can improve his or her well-being, psychosocial development and growth by enabling the supply of nourishment and facilitating the administration of necessary medicines. Few data exist on children with cancer's comfort when using a PEG. The aim of this study was firstly to develop three versions of a web-based assessment tool in which children, families, and healthcare professionals would be able to register their observations and assessments for evaluating the meal situation when a child has a PEG and secondly to validate the content of the tool.

Design/Methods: Methods: A qualitative design was chosen with purposive sampling of participants. Five children with cancer, five parents, five registered nurses and five paediatricians participated first in an interview and then in a member check of the web-based tool. The data were analysed with content analysis.

Results: The results highlighted four categories of issues which needed to be revised in the web-based tool: words which were difficult for the participants to understand, items which contained several questions, items which needed to be split into more items to be answerable and the layout of the questionnaire. The web-based tool was revised according to the categories, and then a member check evaluated and finally confirmed the revisions.

Conclusions: A web-based tool may be able to evaluate the meal situation when a child with cancer has a PEG. The tool may be able to detect early failures of the PEG, facilitating early action from the healthcare professionals in supporting the child and his or her parents in their care of the PEG. In the long run, this web-based tool may also be able to increase the quality of care of children living with a PEG.

POSTER VIEWING

Brain Tumours

V001 SIOP19-0945 | Childhood Medulloblastoma: Experience of Salah Azaiz Institute (Tunisia) Between 1994 and 2014

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Background/Objectives: Medulloblastoma (MB) is the most common of the malignant brain of childhood. With advances in the management of this tumor in these two last decades, survival rates are improving, and less side effects are observed, especially in high income countries. However treating

children with MB in countries with limited resources remain challenging. The aim of our study was to describe epidemiological, clinical and therapeutic features of MB treated in Salah Azaiz Institute (ISA) in Tunisia and to report oncological outcomes.

Design/Methods: We retrospectively review a cohort of 90 children with pathologically confirmed MB treated in our center between 1994 and 2014.

Results: MB rate was 24.8% of all childhood central nervous system tumors treated at ISA. Mean age was 9 years. The sex ratio was 1.72. The median pre-consulting interval was one month. The first presenting symptom was mostly related to raise intracranial pressure. Cerebral MRI was practiced initially in 59% of patients. Tumor resection was performed in all patients with total or subtotal resection in 72.2% of cases. The histological variant was classic in 76.7%. Metastases were found in 16.7% of cases. We assigned 55 patients to the standard risk group and 35 patients to the high risk group. Eighty four patients received adjuvant radiotherapy. Dose to the neuraxis was reduced in 43 patients with standard risk. The mean dose in the posterior fossa was 54 Gy. The median interval from surgery to the initiation of radiotherapy was 17.6 weeks. Fifty four patients received adjuvant chemotherapy that consisted mainly on Platinum-based regimen. The 5-years OS and DFS rates were respectively 70% and 53%. Relapses were observed in 40.2% of cases after a mean period of 15 months.

Conclusions: Our results are encouraging despite gaps and challenges but still unsatisfactory. A standardized management strategy would improve our therapeutic results and our outcomes.

V002 SIOP19-0965 | Relapsed Medulloblastoma: Which is the Best Treatment?

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Background/Objectives: Despite progress in the management of medulloblastoma (MB), approximately one third of children with MB will progress or relapse despite being treated. The best approach for these patients remains unclear. The aim of our study is to describe discovery's circumstances of relapsed children with medulloblastoma treated in the radiotherapy department in Salah Azaiz Institute and to describe their pattern of treatment and outcomes.

Design/Methods: In a retrospective case serie of 90 pediatric MB treated in our department from 1994 to 2014, 33 patients relapsed. For this group, data about circumstances of discovery, the time of relapse, the site and the pattern of treatment were recorded. Overall survival (OS) after relapse were

estimated using the Kaplan–Meier method and differences in outcome were tested using the Log Rank method.

Results: After a mean period of 15 months, thirty three relapses (40.2%). Intracranial hyper pressure was the most frequent sign (27.3%). Six cases (18.2%) were found on surveillance imaging when the patients had not yet developed symptoms. Signs of spinal injuries were found in 4 patients (12.1%). Ten patients (30.3 %) had isolated local relapses in the posterior fossa and fifteen patients (45.4%) had metastatic relapses with a supratentorial localization in 8 cases. Multiple relapses occurred in 7 patients (21.2 %). Treatment consisted of combinations of surgery in 14 patients (42.4 %), radiotherapy in 5 cases (15.1%), and chemotherapy in 21 cases (63.6 %). In four patients, no relapse treatment was given. The mean follow up was 8.17 months (1–36 months). OS at 3 years after relapse was 20 %. Only surgery was correlated with better survival ($p = 0.016$).

Conclusions: The approach to treatment of patients with relapsing MB depends on a range of factors mainly the age, the site of relapse, the symptomatology and the prior received therapy. Surgery should always be performed when possible.

V003 SIOP19-1647 | Response to the First-Line Chemotherapy in Pediatric Low-Grade Gliomas According to Histopathology and Braf Alterations

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Background/Objectives: Low-grade gliomas (LGGs) are the most frequent brain tumors in children and comprise a heterogeneous group of tumors with different locations, histologic type and clinical behavior. The main molecular alterations shown by LGGs relate to the activation of the MAP Kinase pathway and can be caused by either duplication or mutation of the *BRAF* gene. The objective of this study is to assess the radiological response to first-line chemotherapy in pediatric LGGs according to histologic type and *BRAF* alterations.

Design/Methods: We performed a population-based study of all patients diagnosed with a pediatric LGGs between 2006 and 2015 at Gustave Roussy and treated with vincristine-carboplatin, as first-line chemotherapy. Pathology samples were reviewed according to 2016 WHO classification. *BRAF* alterations were detected using immunohistochemistry, fluorescence in situ hybridization and/or sequencing. Tumor response was assessed by an independent central review.

Results: Fifty-nine patients were included in this study: 44 pilocytic astrocytomas (75%) and 15 gangliogliomas (25%). Twelve LGGs harbored the *BRAF* V600E mutation and 40 *BRAF* duplication. In 6 cases, no *BRAF* alterations was found (1 patient had no mutation but fluorescence in situ hybridization could not be performed). At the end of the first-line of chemotherapy, the objective response rate (complete or partial response) of pilocytic astrocytomas and gangliogliomas was 61% and 33%, respectively. The objective response rate of tumors with *BRAF* duplication, *BRAF* V600E and wild-type LGGs were 67.5%, 25% and 33.5%, respectively. The 3-year event-free survival of patients with *BRAF* duplication LGGs was 62% versus 47% for those with *BRAF* V600E LGG.

Conclusions: *BRAF* V600E LGG constitutes a distinct entity with poor prognosis when treated with standard treatments.

V004 SIOP19-0634 | Childhood Medulloblastoma and Pineblastoma Treated with Saphos Study Protocol at King Fahad Medical City (KFMC): 10 Years Experience at Single Tertiary Center in Saudi Arabia

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Background/Objectives: Background/Objectives: KFMC is the major tertiary care center for children with brain tumors in Saudi Arabia. The aim of this study is to analyze demographic data, treatment strategy and clinical outcome in Saudi children with Medulloblastoma (MB) and Pineblastoma treated with Saudi Arabian Pediatric Hematology Oncology Society (SAPHOS) treatment study protocol.

Design/Methods: A retrospective study of 65 patients newly diagnosed MB and Pineblastoma (>3 year and < 16 year) All treated at KFMC between 2009–2016. All received multimodal therapy consisting of maximal surgical resection followed by Risk adapted craniospinal radiation concurrent with oral VP16 then adjuvant chemotherapy consisting of 3 cycles of Cisplatin Plus Oral VP16 alternating with 3 cycles of cyclophosphamide and vincristine. Post-chemotherapy, maintenance with oral Isotretinoin was given for 6 months' Molecular analysis was done using next generation targeted

sequencing (NGS) from FFPE tissue for 560 cancer-relevant genes. Molecular subgroup analysis was done for 36 MB patients: WNT group (11.1%), SHH (19, 4%), group 3 (14%), and group 4 (55.5%).

Results: The majority of patients (70.8%) were male, median age at diagnosis 85 months, 46.2% treated as average-risk (AR) & 53.8% treated as high-risk (HR). Pineablastoma patients (7.7%) were treated as high-risk. 5years overall survival OS: for AR patients 89.7% and for HR patients 78.6%. Median time to start radiation was 31.00 days. A median follow-up of 46 months: 5-years PFS for the entire study patients was 80.7% and 5-year OS was 84.6%. 5-year OS for the WNT subgroup and SHH subgroup was 100%, 20% for Group 3, 77.8% for Group 4.

Conclusions: Our study protocol results was acceptable compared with international studies although most of our patients had high risk features. Oral VP16 was tolerable and convenient during craniospinal radiation. this study will form baseline to unify treatment protocols for children with brain tumor in Saudi Arabia

V005 SIOP19-1156 | Survival of Children with Medulloblastoma in Saudi Arabia Results of Prospective Saudi Arabian Pediatric Hematology Oncology Society SAPHOS National Multi-Centers Study Protocol

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Background/Objectives: Medulloblastoma (MB) is the most common malignant brain tumor in children.

The aim of this study determine the survival of pediatric Medulloblastoma and other Embryonal tumors treated with Saudi Arabian Pediatric Hematology Oncology Society (SAPHOS) national multi-centers study Protocol

Design/Methods: A prospective study of newly diagnosed MB in 130 children (>3 year and < 16 year) treated at All

study centres between 2009-2016. All received multimodal therapy consisting of maximal surgical resection followed by Risk adapted craniospinal radiation concurrent with oral VP16 then adjuvant chemotherapy consisting of 3 cycles of Cisplatin Plus Oral VP16 alternating with 3 cycles of cyclophosphamide and vincristine. Post-chemotherapy, maintenance with oral Isotretinoin was given for 6 months.

Results: The majority of patients were male 86 (66.2%), median age at diagnosis 84 months. 55 (42.3%) treated as Average risk AR and 75 (57.7%) treated as high-risk HR, 61 (47%) patients had metastatic disease M2/3. Median time to start radiation was 35.5 days. Only 4 patients (3.1%) developed second malignant neoplasm. Molecular subgroup analysis was done for 36 MB patients: WNT group (11.1%), SHH (19, 4%), group 3 (14%), and group 4 (55.5%). At median follow-up of 65 months, 5-years Event Free Survival PFS for the entire study patients was 72.3% and 5-year Overall Survival OS was 76.9%. 5years OS for AR patients 83.3% and for HR patients 72.0%. There were no statistically significant survival differences between patients who received maintenance oral Isotretinoin and patients who did not.

Conclusions: Our study protocol results and toxicity was acceptable compared with international studies although most of our patients had high risk features. this study will form baseline to unify treatment protocols for children with brain tumor in Saudi Arabia

V006 SIOP19-0257 | Treatment Refusal, Abandonment and Interrupted Therapy Among Children with CNS Tumors in Jordan

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Background/Objectives: Treatment refusal/abandonment is reported to contribute significantly to poor survival in LMIC. Several medical, social and financial contributing factors were reported. We aimed to assess this among Jordanian children diagnosed with CNS tumors.

Design/Methods: We retrospectively reviewed the database of pediatric neuro-oncology service at KHCC/Amman (2010-2018). Patients who refused therapy were reviewed for their clinical characteristics, social status and reasons. We excluded patients referred for 2nd opinion, radiotherapy-only or who traveled abroad for treatment

Results: Four hundred and seventeen patients were included; 13 (3%) refused all therapy and 8 (2%) refused it partially (6 refused/stopped chemotherapy, 1 refused diagnostic-biopsy (brainstem), 1 had surgery (DIPG) against recommendations). Median age was 5years (0.3-17years); sixteen females (76%). Third lived in another city (2-4 hours away). Most parents

were university-graduates (20/25) and 5 high-school. Most fathers (16/17) had a job and 13/17 mothers were housewives. Median number of siblings was three (2-9). Sixteen tumors were high-grade and 19/21 children had lansky score >50. Reported causes for refusing therapy were: poor prognosis and expected intensive therapy (5, DIPG/GBM/ETMR/ATRT/PNET), conflicting abroad consultations (4 DIPG, 1 Thalamic), using alternative-therapies (3), "chemotherapy myths" (2), surgical-morbidities (2, brain-stem), quality of life (1, spinal LGG), social/financial burden (1, LGG; nine siblings/poverty), and undocumented (2). Patients completely refused therapy were referred to palliative-care; seven died (tumor progression), five lost follow-up and one alive (spinal LGG). Those who refused therapy partially; three died, three alive (CR) and two (brain-stem, thalamic) had tumor progression.

Conclusions: To our knowledge, this is the first report on treatment refusal/ abandonment in children with CNS tumors in Jordan. Our universal cancer insurance, high population-density around Amman and twinning-program likely contributed to the low incidence. Poor tumor prognosis, conflicting abroad consultations and use of alternative-therapies were the most reported causes. Family support/ education and better community rehabilitation-services may help decrease abandonment.

V007 SIOP19-0897 | Primary Leptomeningeal and/or Neurocutaneous Melanosis – French Cohort Study of the Last 20 Years: Clinical, Radiological, Pathological, Molecular Features and Follow-Up

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Background/Objectives: Leptomeningeal and/or neurocutaneous melanosis are rare tumors derived from melanocytes, with variable grade of malignancy. Prognosis remains currently very poor. They often occur in children with predisposing syndrome such as neuro-cutaneous diseases. In view of the scarcity of cases, little information is known and its management is not clearly defined. The current availability of innovative therapeutic approaches such as targeted and

immuno-therapies makes it necessary to improve our knowledge concerning the clinico-radiological presentation of this disease as well as the results obtained with the treatments historically proposed.

Design/Methods: We performed a French national descriptive retrospective multicenter study including patients under 18 with lepto-meningeal and/or neurocutaneous melanosis treated between January 1998 and June 2018.

Results: Nineteen patients were included. The most common initial symptoms were intracranial hypertension (58%), seizures (31%) and neurological impairments (26%). The main tumor location was supratentorial (52%) and 70% of the patients presented with neurocutaneous syndrome. Median time between first symptoms and diagnosis was 31 days (range: 0-365). Tumor cells were detected in cerebrospinal fluid in 8/11 patients. BRAF V600E mutation was detected in only 1/7 tumor, and NRAS Q61R mutation in another one. Surgery was performed in 5 patients, with 2 complete resections, 11 (58%) received chemotherapy and 5 (26%) were irradiated. Only 3 patients survived and the 1-year overall survival was 35%. Combination of surgery, chemotherapy and radiotherapy was associated with the best survival rate.

Conclusions: Multidisciplinary management involving neurosurgeons, radiation therapists, dermatologists and oncologists remains crucial. A better biological tumor characterization is necessary in order to provide rationale for the development of targeted- and immuno-therapies in this disease, as it has been successfully developed in cutaneous melanoma. This study lays foundations for a more in-depth understanding of these pathologies.

V008 SIOP19-0771 | Multiplex Digital PCR is a Powerful Method to Detect Alterations of the Map Kinase Pathway in Pediatric Low Grade Glial and Glioneuronal Tumors

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Background/Objectives: Low grade glial and glioneuronal tumors are the most common pediatric central nervous system (CNS) neoplasms. They constitute an heterogeneous group of tumors with overlapping pathological criteria and frequent genetic alterations in the MAP kinase pathway. Digital PCR (dPCR) is a highly sensitive molecular tool and allows the detection of mutations or copy number variations using a very small amount of DNA. This is an important advantage over other techniques that often require large amounts of DNA and/or RNA. We decided to develop a dPCR multiplex panel

for the molecular characterization of pediatric CNS tumors. This allows simultaneous detection of BRAFV600E mutation and KIAA1549-BRAF fusion, as well as, FGFR1N546K & K656E mutations and FGFR1 exon 8 duplication.

Design/Methods: We used the high sensitivity of dPCR to analyze these molecular alterations on small amounts of FFPE tissue from a cohort of 10 pilocytic astrocytoma, 11 ganglioglioma, 17 dysembryoplastic neuroepithelial tumour and 2 'pediatric type' diffuse gliomas in which the BRAF and FGFR1 status were known by other approaches.

Results: The dPCR multiplex assay efficiently detected BRAF and FGFR1 mutations as well as KIAA1549-BRAF fusion and FGFR1 duplication with 100% sensitivity and specificity.

Conclusions: The use of multiplexed dPCR panel allow fast results, with high sensitivity and specificity and low cost. The assay can be performed by using DNA with no need of RNA for fusion transcript detection.

V009 SIOP19-1286 | Anaplastic Ependymoma: Experience of Three Centers in Western Part of Turkey

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Background/Objectives: The aim of this study is to evaluate clinical features and prognosis of anaplastic ependymoma patients.

Design/Methods: We evaluated the records of the anaplastic ependymoma patients retrospectively, treated in three centers in western part of Turkey between 1999 and 2018.

Results: Twenty-eight patients (16 female, 12 male) with anaplastic ependymoma were documented retrospectively, from a total of 32 patients. The median age at diagnosis was 4.3 years (4 months-17 years) and 19 patients (67,9%) were ≥ 3 years of age. The most common complaint was nausea and vomiting (n=16), followed by headache (n=8). The locations of tumor were infratentorial (n= 18), supratentorial (n= 6) and spinal cord (n= 4). At diagnosis, ten patients had spinal and leptomeningeal metastasis. All of the patients underwent surgery as a part of initial treatment. Gross total resection (GTR) was achieved in 18 patients (64, 3%) and subtotal resection in 10 patients (35,7%). Twenty-three patients

(82, 1%) received RT (craniospinal RT (n=11), cranial RT (n=10), spinal RT (n=2)). Twenty-five patients received chemotherapy, most of them treated according to POG 9031 protocol (n=15). Median follow-up time was 4 years (0-15 years). In the follow-up period, 2 patients had refractory disease and 10 (35, 7%) patients relapsed (local (n=7), distant (n=3)). Median time to relapse was 23 months (9 - 96 months). For these patients remission achieved in 3 of them, other 7 patients died with progressive disease. Five-year event-free survival (EFS) and overall survival (OS) rates were 55, 6% and 59, 7%, respectively. GTR was the most important prognostic factor. Patients who achieved GTR had 5-year EFS 77% and OS 82% whereas patients with subtotal resection had 5-year EFS and OS 12, 5% and 22, 5% (p= 0.004, p=0.003). Age at diagnosis, gender, location of tumor, frontline radiation therapy had no effect on EFS and OS rates.

Conclusions: In our study population, EFS and OS were similar to other studies in our country. In our study, surgery was the most important prognostic factor. GTR was associated with better EFS and OS in anaplastic ependymoma.

V010 SIOP19-1127 | High Expression of a Novel Isoform of TET1 (TET1^{ALT}) is Associated with Presence of Metastasis at Medulloblastoma Diagnosis

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Background/Objectives: Medulloblastoma (MB) represents the most common malignant brain tumor in childhood and comprises four main molecular subgroups: WNT, SHH, Group 3 and Group 4. Epigenetic changes play an important role in MB development, and our group described the importance of deregulation expression of *TET* genes in this tumor. TETs enzymes are responsible for DNA demethylation, and their reduced levels were associated with a hypermethylated phenotype. Full TET1 (TET1^{FL}) has a CXXC domain that binds to unmethylated CpG island. However, it was described a novel isoform of TET1, TET1^{ALT}, that lacks the CXXC domain. TET1^{ALT} is aberrantly activated in multiple cancer types and associated with a poor prognosis. The aim of this study was to evaluate the correlation between the RNAm expression level of TET1^{FL} and TET1^{ALT} and clinical features in samples from patients with MB.

Design/Methods: Total RNA was extracted from primary medulloblastoma samples and cerebellum control using Trizol. cDNA was synthesized using High-Capacity cDNA

reverse transcription kit. qPCR was performed on Quant Studio 12 K Flex (Thermo) using SYBR Green Mix and specific primers for TET1^{FL} and TET1^{ALT}. Results were normalized to the housekeeping genes *HPRT* and *GUS*. Gene expression data was associated with clinical features of patient: sex, age at diagnosis, tumor resection, metastasis and overall survival. Statistical analysis was performed with SPSS program, using Mann-Whitney and Kruskal-Wallis tests.

Results: No differences were observed in the *TET1FL* and *TET1ALT* expression levels when comparing MB samples and cerebellum control. However, considering subgroups, TET1^{ALT} showed a higher expression in MB group 3 and 4. We observed a higher expression of TET1^{ALT} in patients that present metastasis at the diagnosis.

Conclusions: Together, these observations suggest that the high expression of TET1^{ALT} is associated with molecular subgroups that exhibited worse prognosis and with presence of metastasis in medulloblastoma.

V011 SIOP19-1129 | Differential Methylation of DAB2IP Gene in SHH Medulloblastoma Subgroup

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Background/Objectives: Medulloblastoma (MB) represents the most common malignant brain tumor in childhood. Gene expression studies of MB allowed the classification of the tumor in four subgroups: WNT, SHH, Group 3 (G3) and Group 4 (G4). MB originates in cerebellum from genetic and epigenetics alterations in pathways that control the neurogenesis of neuronal progenitor cells and granule neuronal precursors. DAB2IP (DOC-2/DAB2 interacting protein) is a Ras-GAP protein that showed a site-specific methylation during cerebellar development. *DAB2IP* expression was described as a tumor suppressor and positive marker for survival in MB, however there is description about methylation control of *DAB2IP* in MB. In the present work, we aimed to analyze *DAB2IP* expression and methylation across MB subgroups.

Design/Methods: DAB2IP expression and methylation profile were analyzed in independent cohorts of MB patients by using public data accessed through the R2 Genomics Analysis and Visualization Platform.

Results: Three datasets were used for transcriptional profile: Pfister dataset (including 16 WNT, 46 SHH, 41 G3 and 64 G4); Gilbertson dataset (including 8 WNT, 10 SHH, 16 G3 and 39 G4); and Root dataset (including 8 cerebellum con-

trol). Meanwhile, Hovestadt dataset was used for methylation profile (including 33 WNT, 60 SHH, 72 G3, 111 G4 and 8 cerebellum control). SHH subgroup showed decreased in *DAB2IP* expression, and higher levels of methylation, specifically in CG14122599 and CG14383549 position, when compared to cerebellum control and to other MB subgroups. In the literature, CG14122599 and CG14383549 were associated with the control of *DAB2IP* expression; and methylation of these specific CGs points was associated with poor prognosis in cancer.

Conclusions: These data suggested that differential expression of DAB2IP in SHH MB could be associated with specific CG methylation.

V012 SIOP19-1407 | High SKP2 Gene Expression is Associated to Molecular Subgroups with Poor Prognosis and Notch Pathway and SKP2 Pharmacological Inhibition Leads to Antitumor Effects in Medulloblastoma

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Background/Objectives: Medulloblastoma (MB) is a neuroepithelial tumor from cerebellum and it is currently subdivided in 4 molecular subgroups, WNT, SHH, Group 3 and Group 4. Notch/SKP2 axis have been associated to some cancers, but, there is no studies investigating in MB. The aim of this study was evaluating the role of SKP2 and Notch/SKP2 axis, and the effect of Notch pathway and SKP2 inhibition in medulloblastoma cell lines.

Design/Methods: Gene expression levels of SKP2 and ligands (*DLL1*, 3 and 4; *JAG1* and 2) and receptors (*NOTCH1-4*) from Notch pathway were evaluated in MB samples (datasets: Cavalli, 2017 and Pfister, 2000), subdivided in molecular subgroups, and compared to cerebellum samples (dataset: Cho, 2011) by using the R2 Genomics Analysis and Visualization Platform. MB cell lines were submitted to Notch pathway (Dapt) and SKP2 (Szl-p1-41) pharmacological inhibition and the cell viability, apoptosis and colony formation assay, as well as the protein expression were evaluated.

Results: SKP2 and all Notch ligands and receptors showed higher gene expression in MB when compared to cerebellum. A higher SKP2 expression was detected in the WNT and SHH subgroups, however, when compared the twelve molecular subgroups MB, a higher SKP2 expression was observed in poor prognosis subgroups, TP53-mutant SHH and

MYC-amplification G3. After Dapt and SzI-P1-41 treatment was observed decrease in cell viability and colony formation of MB cell lines, and increase in apoptosis. Decrease in cleaved Notch1 (NICD1) and SKP2 protein expression and increase in p27kip1 after Dapt treatment, and increase in p27kip1, p21Cip1 and NICD1 protein expression in MB cells submitted to SzI-P1-41 were observed.

Conclusions: These results suggest that the high SKP2 expression is associated to molecular subgroups of poor prognosis in MB and also suggest an interaction between Notch pathway and SKP2 with Notch pathway and SKP2 pharmacological inhibition leading to antitumor effects in medulloblastoma cells.

V013 SIOP19-1214 | Fertility Preservation in Young Female Patients in a Pediatric Brain Tumor Clinic

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Background/Objectives: Fertility preservation (Fp) is an important quality of life issue for many female survivors of childhood brain tumors. Therapy may cause future primary ovarian dysfunction by damage to the hypothalamus / pituitary by surgery or cranial irradiation, damage to the ovaries from craniospinal radiation and direct gonadotoxic effect of chemotherapy.

Design/Methods: We retrospectively reviewed the charts of all 120 female patients with a brain tumor treated in our center between the years 2010-2018 for data on Fp.

We documented the reasons for offering/ not offering Fp, what methods were used, the rate of uptake of the procedure and any complications encountered in this population.

Results: A total of 120 girls aged 3 months to 18 years were treated for a brain /spinal cord tumor at our center during the study period. Only 18 (aged 10m-13yrs) out of the 120 girls were offered Fp. The procedure was only offered to girls with a medulloblastoma, primitive neuroectodermal or rhabdoid tumor. Of the 18 offered Fp, 6 parents refused for religious reasons or reluctance for further invasive procedures. All 12 who underwent Fp were prepubertal and had oophorectomy with ovarian tissue cryopreservation and 7 are currently alive and disease free. There were no complications or treatment delays. Fp was not offered to any girls with high grade gliomas (HGG) or low grade gliomas (LGG) or ependymomas since the prognosis was considered too good

or too bad to warrant Fp. 26 of these (21 LGG, 3 HGG and 2 ependymoma) received prolonged chemotherapy and are alive.

Conclusions: Fp is a safe procedure that should be offered more widely to girls with brain tumors. Aggressive tumors that were once considered deadly have now become treatable and the disease course is often unpredictable. Every child should have the chance of a normal future, in particular becoming a parent.

V014 SIOP19-0603 | Oligodendrogliomas in Children, Adolescents and Young Adults: A South Thames Neuro-Oncology Unit Study

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Background/Objectives: Oligodendrogliomas account for 1-3% of paediatric brain tumours. Due to its rarity, paediatric oligodendrogliomas are still a poorly defined entity. Our objective was to determine the outcomes of an off-trial population of children, adolescents and young adults (AYA) with oligodendroglioma at our institution.

Design/Methods: Patients aged up to 21 years diagnosed with oligodendroglial tumours (WHO grades II and III) between 1990 and 2016 were eligible for analysis. Descriptive statistics and survival outcomes were analysed.

Results: Sixteen patients were identified. Median age 15.8 years (range 1-21 years). Surgical resection was complete in two cases who did not receive further adjuvant therapy. Fourteen patients had a subtotal resection. WHO grade II (n=8) and grade III (n=8); information on 1p19q co-deletion was available in 3 patients, no deletions were identified. All patients with subtotal resection received radiotherapy; five of them also received adjuvant chemotherapy: PCV (n=3) or temozolomide (n=2). The progression-free survival at 2 and 5 years was 62.5% and 25%, respectively. The overall survival at 2 and 5 years was 75% and 68.8%, respectively.

Conclusions: Oligodendrogliomas constitute a rare brain tumour within the paediatric and AYA populations. This research contributes to the body of knowledge in this entity and highlights the need for adjuvant therapy in cases with postoperative residual disease.

V015 SIOP19-1105 | Pediatric Patients with High Risk Medulloblastoma: Experience in an Oncology Unit

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Background/Objectives: Report epidemiology, feasibility, toxicity and outcome of patients with high risk medulloblastoma (MB) treated between January 2013 and December 2018 in Hospital de Niños Ricardo Gutierrez. Compare outcome to our previous publications where these patients presented 100% mortality before 12 months out of treatment.

Design/Methods: We reviewed medical records of patients older than 3 years of age with high risk MB (M+, anaplastic histology and/or residual disease post surgery) treated according to ACNS0332 COG protocol recommendations. After surgery, patients received 36 Gy CSRT with boost to sites of disease. During radiation: 30 doses of carboplatin (35 mg/m²/dose), with vincristine (1.5 mg/m²) per week for 6 weeks. Maintenance: 6 cycles with cisplatin (75mg/m²/dose, day1), cyclophosphamide (1gr/m²/dose, days 2-3) and vincristine (1.5mg/m²/dose, days 1-8)

Results: 204 patients with central nervous system tumor were admitted since 2013: 37 MB, 8 high risk patients treated with this scheme. Median of age: 90 m (r: 62 - 172). Male /female ratio: 1. Three metastatic patients (2p M1, 1p M3). All patients achieved macroscopic complete resection. Six anaplastic tumors. Median time to radiotherapy: 31.5 days (r: 20 -51). Toxicity: 8 p grade 4 haematologic toxicity (2 require dose reduction), 4/8 grade 3 renal toxicity (tubulopathy), 2/8 grade 1-2 ototoxicity. Seven patients alive, six in complete remission with median follow up of 18 months (r: 10-46). Two patients relapsed (1p LCR+spinal cord metastasis, 1p local +spinal cord metastasis): 1p live with disease and 1p died due to progressive disease. EFS: 75% OS: 87.5%

Conclusions: High risk medulloblastoma treatment with carboplatin as radiosensitizer was feasible with manageable toxicity. Although more time of follow up is needed, outcomes in terms of OS and EFS are similar to international reports and significantly better than previous reported in our center in which this group of patients presented early relapses and could not be rescued.

V016 SIOP19-0931 | The Role of Irinotecan-Bevacizumab as Rescue Regimen in Children with Low-Grade Gliomas: A Restrospective French Study in 72 Patients

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Background/Objectives: Second-line therapies are needed for children with progressive low grade glioma. The combination of irinotecan and bevacizumab was shown effective in this setting. The definition of its place in the management has to be refined in larger studies.

Design/Methods: We reviewed the files from children < 19 years of age with progressive, refractory or functionally threatening low-grade glioma treated between June 2009 and September 2016 in 7 centers of the Societe Française des Cancers de l'Enfant (SFCE) with the association of bevacizumab (10 mg/kg) and irinotecan (125 mg/m²) biweekly.

Results: Seventy two evaluable patients (median age 7.8 years [range, 1-19]) received a median of 16 courses (range, 3-30). The median duration of treatment was 9 months (range, 1.4-16.2). The 6-month and 2-year progression-free survivals were 90.3% [IC 95% 83.7-97.4] and 38.3% [IC 95% 28.2-51.9] respectively with a median progression-free survival of 17.5 months (range, 2.3-90). Most of the patients (96%) experienced at least radiological stabilization. Only four patients suffered progressive disease on treatment. Twenty five patients (35%) experienced a PFS>24 months. Younger patients had a worse PFS (p=0.005). No progression occurred after treatment in 19 patients with a median follow-up of 35.6 months (range, 7.6-90 months). Prior chemoresistance, NF1 status, duration of treatment or the radiologic response did not predict PFS. The most frequent toxicities related to bevacizumab included grades 1-2 proteinuria in 21, grades 1-2 epistaxis in 10, grades 1-2 fatigue in 12 and grades 1-2 hypertension in 8 while gastro-intestinal toxicity was the most frequent side effect related to irinotecan.

Conclusions: Bevacizumab-irinotecan is a useful therapeutic modality for children with recurrent LGG who have failed standard chemotherapy regimens. Age at treatment initiation appeared to be potential prognosis factor for a shorter

PFS. Patients with absence of response to prior chemotherapy responded as well as the others to the combination.

V017 SIOP19-1215 | Neurocognitive Deficits and Brain Morphologic Changes in Children Treated for Posterior Fossa Tumors

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Background/Objectives: Long-term neuropsychological deficits associated with pediatric posterior fossa tumors (PFT) have been reported. Brain Magnetic Resonance Imaging (MRI) and post-processing methods could reveal morphologic correlates of neurocognitive dysfunction in PFT survivors. The aims of the study are to describe neurocognitive disorders with the Developmental Neuropsychological scale (NEPSY) in children with PFT and to determine whether the extent of morphological cerebellar injury correlates with neurocognitive sequelae.

Design/Methods: Patients with PFT aged < 16 years old were enrolled. Children underwent NEPSY assessment and a 1.5 T MRI at least 1 year after treatment conclusion. NEPSY tasks scores were standardized for age and defined as impaired if < 7 points. Volume of interests of PFT were drawn on T1 volumetric MRI scans using MRICron and were normalized using a pediatric template. The percentage of overlapping lesions in task-impaired patients has been obtained.

Results: Seven patients with PFT were included in the final analysis (5 males, 71%). Median age at diagnosis was 63 months (IQR: 39-80). Five children had a pilocytic astrocytoma and were surgically treated, 2 had medulloblastoma and underwent radiotherapy and chemotherapy too. Median follow-up for MRI was 28 months (25.5-42), median time between MRI and psychological evaluation was 5 months (0-10.5). Patients showed worst performance in attention: response sets (2.9), inhibition A (2.4) corresponding with a maximum color map overlaps in vermis uvula; memory: word list interference (4.3), memory for designs immediate (4.6) showing respectively a strong overlap in cranial region of cerebellar vermis, uvula, left dentate nucleus and in caudal portion of vermis; visuo-spatial processing: block construction (6.9), picture puzzle (5.6) represented by higher overlaps in cranial vermis and perinodulus areas.

Conclusions: Loss of integrity in PF structures confirms the role of cerebellum in cognitive and motor functions. An early neurocognitive intervention may improve the outcome of pediatric patients treated for PFT.

V018 SIOP19-1341 | RNA-SEQ And In-Silico Analyses Reveal That Musashi Gene is Aberrantly Expressed in Medulloblastomas of the Groups 3 and 4 Strata

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Background/Objectives: Introduction: Medulloblastoma (MB) is classified into 4 molecular subgroups: WNT, SHH, Group-3 and 4. Groups 3 and 4 are less characterized genetically and compose a challenging MB stratum regarding diagnosis and treatment approaches. Musashi-1 (*MSII*) is a highly conserved RBP protein; its hyperexpression is strongly associated with poorer prognosis in several human cancers. **Aim:** To evaluate and compare *MSII* gene expression in MB (by *in-silico* public databases) and in a Brazilian cohort of MB patients (by RNA-seq and qRT-PCR). To correlate *MSII* expression to MB subgroups and clinical parameters: overall survival (OS), extent of resection, age, metastatic disease, histology.

Design/Methods: Methodology: *In-silico* analyzes were performed using GSE85217 database (n=763), and through RNA-seq (n=16) by R-platform DESeq2 package. Additionally, 64 primary MB samples (WNT;n=19, SHH;n=17, Group-3;n=9 and Group-4;n=19), were assessed for qRT-PCR validation of *MSII* expression. Statistical analyzes: Mann-Whitney.

Results: *In-silico* analysis (GSE85217) of *MSII* gene showed an overexpression for Group-3 and Group-4 ($p<0.001$) MB when compared to WNT and SHH subgroups. Additionally, the mRNA expression levels of *MSII* gene on primary MB tumors of Groups-3 and 4 ($p<0.001$) were also higher. RNA-seq results from 16 MB samples showed the same pattern of expression as observed for *in-silico* analysis, although not reaching statistical differences. Yet, validation by qRT-PCR with 64 samples was able to recapitulate the higher *MSII* expression on Groups 3 and 4 MB ($p<0.001$). There was no clear association between higher *MSII* expression and clinical parameters for our cohort. Still, *in-silico* OS analysis including a robust number of cases (n=763) showed inferior outcomes for children with MB overexpressing *MSII* ($p<0.01$).

Conclusions: These results demonstrate and validate the overexpression of *MSII* for Groups 3 and 4. Clusterization of *MSII* overexpression may suggest a role of *MSII* on tumor aggressiveness and poor prognosis for these MB strata.

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V019 SIOP19-1623 | Molecular Based Diagnosis and Precision Medicine for Children and Adolescents with CNS Tumors in Greece: The Contribution of an International Collaboration

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Background/Objectives: Tumors of Central Nervous System (CNS) remain a major cause of cancer-related morbidity and mortality during childhood. Recent advances in genome and epigenome research allow for molecular classification of CNS tumors, treatment stratification and therapeutic target identification. In many countries, including Greece, this molecular based diagnosis is not possible yet, mainly due to financial reasons.

Design/Methods: To evaluate the importance of molecular findings to patients with CNS tumors, a retrospective analysis of clinical, histopathological and molecular data was performed.

Results: During a 5-years period, more than 120 patients (<18 years old) with CNS tumors were diagnosed and treated in our institute. However, only 18 patients (10 males/8 females, 7 first diagnosis/11 relapses) were further analyzed in the laboratories of DKFZ in Heidelberg. Thirteen patients were analyzed with targeted next-generation sequencing and genome-wide methylation arrays, based on the PTT2.0 study and five patients have been enrolled in the INFORM-registry. Based on these results, 6 patients were reclassified in molecular subgroups (5 Medulloblastomas/1 Posterior-Fossa-A-Ependymoma). In three cases the methylation analysis confirmed a not definite histological diagnosis (1 Pineoblastoma/2 High-Grade-Gliomas), allowing the clinicians to start treatment. Two cases with uncommon diagnosis/clinical history, non-classifiable according to the DNA methylation profile, were proposed for further analysis as possible rare entities. Targeted therapy was initiated in 5 patients, two of them with good response so far. Significantly, one patient with multiple relapses of a spinal tumor and different histological reports received high score for Dermatofibrosarcoma protuberans and was treated with Tyrosine Kinase Inhibitor, being stable for more than two years.

Conclusions: Our results indicate the clinical benefits of molecular data integration into the diagnostic and therapeutic process, highlighting the importance of international collaboration in pediatric neuro-oncology. Since 2018 a collaboration was established between ACCC/DKFZ (Athens Comprehensive Cancer Center/German Cancer Research Center), supporting further analysis of tumor samples, participation in clinical trials/registries and training of new scientists.

V020 SIOP19-0495 | 10 Years of Weekly Web Conference for Brain Tumor of Adolescent/Young Adult (AYA) on Behalf of ANOCEF, GO-AJA and SFCE Societies

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Background/Objectives: The skills of adult versus pediatric neuro-oncologists are not completely similar though additive. Because the tumors and their protocols are different and the tolerance and expected sequelae are specific. Multidisciplinary meetings including adult and pediatric neuro oncologists are warranted to share expertise.

Design/Methods: Since 2008, on behalf of ANOCEF, GO-AJA and SFCE societies, a weekly national web based conference was held in France. Any patient with the following criteria could be discussed: Adolescent and Young Adults aged between 15 and 25 years, and any adult with a pediatric type pathology, including medulloblastoma, germ cell tumors, embryonic tumors, ependymoma, pilocytic astrocytoma.

Results: Number of cases discussed increased from 8 to 202/year, with a mean number of 3 cases (1 to 7) discussed at each meeting. In 2018, 36 meetings were held, with a mean of 8 participants (2 to 14) issued from various French centers. 168 cases were discussed in 2018. Mean age was 30 years old (7 to 67). 45% were discussed at diagnosis; The patients had mostly medulloblastomas (n=47), ependymomas (n=24), low (n=21) or high grade gliomas (n=11), pineal tumors (n=20), germ cell tumors (n=9) and embryonal tumors (n=6). The rate of inclusion in protocols was increased since the opening of this web conference, especially for the germ cell tumor GCT SIOP protocol that is opened without age restriction, and in RSMA standard risk or MEVITEM relapse adult medulloblastoma protocols.

Conclusions: Multidisciplinary Web conference for AYAs is feasible and fruitful. It shares knowledge and increases the inclusion rate in protocols. It should be developed further.

V021 SIOP19-1123 | Pediatric Low Grade Gliomas Tumors. Experience in a Pediatric Institution

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Background/Objectives: Central nervous system tumors (CNS) are the most frequent solid tumors in pediatric patients. Low grade gliomas (LGG) represent almost the 40% and are a group of tumors with heterogenous histology. To describe epidemiological and clinical features, histology, molecular biology, treatment and outcome of patients (p) with LGG.

Design/Methods: We reviewed medical records of p with LGG (according to WHO 2007 CNS classification) treated in the Hospital de Niños Ricardo Gutierrez between January 2005 and January 2019. Patients with diffuse intrinsic brainstem gliomas were excluded.

Results: CNS admitted:481p. LGG:119p (24%) Male/Female ratio:1,16. Median age:7 years (r:0.4-18). Associated syndromes 9p (0,75%):Neurofibromatosis 7p/Tuberous sclerosis 2p. Localization:Infratentorial (cerebello) 55p (46%). Supratentorial 52p (44%) (suprasellar 19p, optic pathway (OP) 14p, hemispheric 12p, thalamus 4p, intraventricular 3p), Medullar 8p, Brainstem (exophitic) 4p. Histology: pilocytic astrocytoma 64p (53%), pilomyxoid variant astrocytoma 27p, ganglioglioma 8p, diffuse glioma 5p, subependymal giant cell astrocytoma (SEGA) 1p, pleomorphic xantoastrocytoma 1p, oligodendroglioma 2p, mixed neuroglia tumors 4p and no histology 7p (6p OP glioma and 1p SEGA). BRAF V600E status: 3p positive (3 suprasellar/OP gliomas) and 24p negative (15p BRAF-KIAA fusion). Treatment: surgery 112p (95%):complete resection (CR) 63/112p (56%), partial resection/biopsy (PR) 49/112p. Patients with PR:20p (23%) watch and wait approach, 25p (54%) with symptoms recieved chemotherapy and 1p received radiotherapy after chemotherapy failure. Follow-up lost 2p. Status 117p: complete remission: 68p (58%), stable disease 37p (32%), and progression 12p (10%)(9 died and 3 under treatment). Two p BRAFV600E+ with progressed disease are in treatment with vemurafenib with good response. 5 years OS 90% and SLE 88%. Median follow-up time: 5 years (0.1-15).

Conclusions: In our population, LGG represents a quarter of admitted CNS. A small number was associated with neurofibromatosis and tuberous sclerosis. Cerebellum and pilocytic/pilomyxoid astrocytoma were the most frequent localization and histology subtype respectively. This results are similar to international reports. The main treatment was surgery achieving complete remission in most cases. Systemic treatment was indicated in irresectable/symptomatic tumors. The detection of BRAF V600E enabled target

therapy in patients with no other effective chemotherapy option.

V022 SIOP19-1419 | CDC27 Gene May Play a Role in the Decreased Survival of the Medulloblastoma SHH Subgroup

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Background/Objectives: Medulloblastoma (MB) is the neoplasm of the central nervous system most common in childhood and comprises four major subgroups [Wingless (WNT), Sonic hedgehog (SHH), group 3, and group 4]. SHH-driven medulloblastomas represent an intermediate prognosis subgroup, with overall survival rates ranging from ~60-80%. Antagonists of SHH signaling are in clinical trials for MB. However, both humans and mice models acquired resistance to the treatment and relapsed within a short period, suggesting that such inhibitors may be ineffective when administered as monotherapy. SHH-MB displays varying degrees of chromosomal instability and alterations in the expression of the mitotic spindle checkpoint genes are likely to contribute to this phenotype.

Design/Methods: Here, in a CRISPR screening experiment of mitotic spindle genes we identified *CDC27* as a determinant of sensitivity to Sonidegib, a SHH pathway inhibitor.

Results: Interestingly, MB-SHH cell lines UW228, UW473, DAOY, ONS-76 and D283 (subgroup 3) present protein overexpression of *CDC27* compared to the negative control (cerebellum). Additionally, *CDC27* is higher expressed in MB compared to normal cerebellum and its expression is associated with a worst prognosis in the MB-SHH group.

Conclusions: Together, these observations suggest that *CDC27* gene may be involved in the decreased survival of MB-SHH patients and also it may be a potential target to MB treatment in the Shh subgroup.

V023 SIOP19-0219 | Clinical, Radiological, Histopathological, Molecular Description and Identification of Prognostic Factors for Desmoplastic Infantile Gangliogliomas and Astrocytomas: A Multicentric Cohort Study

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Background/Objectives: Desmoplastic infantile gangliogliomas/astrocytomas (DIG/DIA) are rare tumors. Their prognostic factors are not well established. The aim of the study was to describe the clinical, radiological, surgical, histopathological and molecular findings as well as treatment and follow-up of children with DIG/DIA

Design/Methods: All patients with DIG/DIA diagnosed in France from January 1998 to December 2016, were included in this retrospective study and centrally reviewed. The following criteria were analyzed: mitotic count, cellular area (surface rate), poorly differentiated neuroepithelial component (surface rate), neuronal markers expression (present/absent), Ki-67 labeling index, BRAF mutation status and chromosomal alteration by array-comparative genomic hybridization (array-CGH). Survival analyses were performed to assess the prognostic significance of clinical, histopathological and molecular criteria on progression-free survival (PFS)

Results: Thirty seven patients were included. The most common presenting symptoms were seizures (54.2%) and increased head circumferences (51.2%). Typically, most of DIG/DIA appeared as a cystic mass associated with a peripheral solid component, while 11.1% were only solid. Three patients presented with metastatic disease. First line surgery was performed in 36 patients (19 complete and 17 subtotal tumor resections). Nine patients (24%) received chemotherapy. Median follow-up was 57 months (range: 2-228). Complete surgical resection was not associated with a higher PFS ($p = 0.77$). High mitotic count ($HR = 1.174$; $p < 0.001$), high Ki-67 labeling index ($HR = 1.051$; $p = 0.01$), BRAF V600E mutation ($HR = 3.852$; $p = 0.029$) and the presence of chromosomal alteration ($HR = 3.631$; $p = 0.036$) were associated with a lower PFS. The 5-year overall survival and PFS were 93% and 62% respectively. The most common long-term sequelae were epilepsy (65.5%) and hemiparesis (62%)

Conclusions: The 5-year PFS was 62% with no difference after total or subtotal resection. High mitotic count, Ki-67 index, BRAF mutation status and array-CGH are of interest as predictors of outcome

V024 SIOP19-1443 | Genotype-Phenotype Correlations in Gliomatosis Cerebri Revisited

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Background/Objectives: The entity « gliomatosis cerebri » (GC) has been removed from the 2016 WHO classification update because of the heterogeneity of the molecular profiles of these neoplasms which often corresponded to known entities of gliomas (Herrlinger, Acta Neuropathol 2016). While this was grounded mainly on adult-type of gliomas, there was no study published on pediatric cases. Our aim was to explore the diversity of pediatric GC from the molecular and radiological point of view.

Design/Methods: Nineteen centrally reviewed cases of GC corresponding to the classical radiological definition were studied by whole exome sequencing (at more than 100X for the tumor and more than 70X for the blood) and methylation array. Radiology was reviewed centrally to classify the phenotype between multicentric or not, grey matter and/or white matter involvement. Clinical data were also recorded.

Results: The spectrum of molecular alterations found in the tumor was large. Copy number variations were found in only six out of 19 cases. The most frequent targetable somatic mutations identified were *EGFR* (7/19), *PI3KCA* and *PTEN* (6/19), and *NF1*, *KRAS* or *NRAS* (6/19). *ATRX* mutation were rare (1/19) compared to other pediatric gliomas and we did not find any H3K27M mutation including in cases with midline involvement. *TP53* mutations or LOH were present in 8/19. One patient had a germline *TP53* mutation. We did not identify a link between the imaging appearance on MRI and the molecular profile.

Conclusions: GC in children represent like in adults a large variety of tumors entities. Targetable mutations can be found which may represent therapeutic possibilities worth to explore

on an international scale due to the rarity of the disease. Further molecular analyses are needed to understand the causes of this extremely invasive phenotype.

V025 SIOP19-1477 | Glioma Oncogenesis in Constitutional Mismatch Repair Deficiency Syndrome: A Molecular and Clinico-Pathological Study in 15 Patients

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Background/Objectives: Gliomas are frequently seen in the second decade of life in children with constitutional mismatch repair deficiency (CMMRD) syndrome. They are often associated with a high mutation load but their characteristics have not been extensively described.

Design/Methods: Your study describes 15 cases including 2 siblings from the radiological, histological et molecular (Whole Exome Sequencing) points of view.

Results: Tumors were frequently associated with lesions of different ages (multicentric) or vascular malformations. Different histologies were observed with a majority of glioblastomas (n=9) and giant tumor cells were almost always present. Immunohistochemistry was positive for p53 in 14/15 (concordant with mutations detected with sequencing) and was negative for ATRX in 11/15 (concordant with mutations detected with sequencing in all but one patient). PDL1 expression was only seen in 6/15. Mutation load was above 100/Mb in all but four; all hypermutated tumors had secondary mutations in *POLE* or *POLD1*. *PMS2* and *MSH2* were the two most frequently MMR genes mutated. The distribution of the variant allele frequency was most frequently bi- or tri-modal suggesting different waves of mutations gains. SomaticSignatures and DeconstructSig identified various combinations of signatures in the different exomes. Qualitatively mutations observed in the CMMRD samples were different from those observed in common pediatric high-grade gliomas (pHGG): absence of K27M and G34R/V mutations in *H3F3A*, absence of *BRAF* V600E mutation, absence of *IDH1* R132H mutation, *TP53* mutations were present in all but one.

Conclusions: CMMRD-associated gliomas represent a distinct entity of pHGG with a specific oncogenesis.

V026 SIOP19-0172 | Benefits of Neo-Adjuvant Chemotherapy in Metastatic Medulloblastoma: A Comparative Study in 92 Children

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Background/Objectives: Background: Preoperative chemotherapy is often used in oncology to treat metastatic disease and facilitate surgery of the primary tumor, but rarely for brain tumors. Feasibility of this approach has been evaluated for medulloblastomas in a pilot study, but currently no comparative study was available to evaluate its benefits and risks.

Design/Methods: Methods: We retrospectively compared 2 non-randomized therapeutic strategies in 92 patients treated for a metastatic medulloblastoma between 2002 and 2015 at Gustave Roussy: 54 children operated at the diagnosis (group A) and 38 children treated upfront with conventional chemotherapy, ie carboplatin and etoposide regimen (group B) before surgery of the tumor. The whole treatments including chemo/radiotherapy according to age and risk factors were similar in both groups. We compared tumor excision rate, surgical morbidities, response to chemotherapy, patient behavior and their neuropsychological outcome.

Results: Therapeutic strategy with neo-adjuvant chemotherapy yielded a significant better rate of complete excision of the tumor (93.3% versus 57.4%, p=0.0013). No additional risks were reported (toxic complications due to chemotherapy, rate of post-operative complications or additional local progression of disease). A radiological objective response to chemotherapy was observed in 82% of patients and the histological review of 19 matched pairs of tumor (before and after chemotherapy) showed that histological diagnosis of medulloblastoma was feasible and accurate even after chemotherapy. Five-years PFS and OS rates were similar with both strategies. A longitudinal neuropsychological evaluation highlighted a better intellectual outcome in the group B (Full Scale Intellectual Quotient and perceptual reasoning/organization index were 6.5 points higher) but it did not reach statistical significance.

Conclusions: Neo-adjuvant chemotherapy is a safe and efficient strategy for metastatic medulloblastomas. It allowed a better extent of surgery and a trend towards a better neuropsychological outcome without jeopardizing survival.

V027 SIOP19-0130 | Damage to the Cerebellum and Thalamus Causes Detrimental but Distinct Impairment on Memory, Acquisition and Recall, of Verbal and Non-Verbal Information

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Background/Objectives: Children diagnosed with brain tumors arrive at the Israel Cancer Association for neuropsychological assessments (NSA), psychological treatment for child and parents and school centered rehabilitation programs. One of the most common finding is memory problems, which in turn effects their learning ability and scholastic success.

Design/Methods: In order to define and distinct the diverse memory problems seen, we compared two groups of patients, those with damage to the cerebellum to those with damage to the thalamus. We used two assessment tools, the Rey Osterrieth Complex Figure Test (ROCF) and Memory for Stories from the WRAML. Using tests from the verbal and non-verbal domains allowed us to address the effect the neurological damage has on integrating and organizing knowledge that children are challenged with daily.

Results: It was found that children with damage to the cerebellum copy the ROCF at an average level, but have significant organizational difficulties which affect their recall. But, when recalling a story, the context aided them at acquisition, which improved their recall. In contrast, children with damage to the thalamus copy the ROCF with significant distortions which effect their recall. But, contrary to the first group, the context did not aid them and their acquisition and recall of the story remained distorted. The aid came from presenting a "thalamus detour", i.e. putting emotional cues when listening to the story.

Conclusions: The study showed that damage to the cerebellum and thalamus cause diverse memory difficulties, which are due to different neuropsychological processes. Damage to the cerebellum causes organization problems, which content improves when recalling. Damage to the thalamus causes the acquisition to be distorted, which emotional cues diminish. Understanding the different processes underlying these different memory problems allowed us to create a better scholastic intervention for each child which is the focus of our rehabilitation program.

V028 SIOP19-1276 | Tyrosinase Immunohistochemistry can be Employed for the Diagnosis of Atypical Teratoid/Rhabdoid Tumors of the Tyrosinase Subgroup (ATRT-TYR)

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Background/Objectives: Atypical teratoid/rhabdoid tumor (ATRT) is comprised of three molecular subgroups (i.e. ATRT-TYR, ATRT-SHH and ATRT-MYC) characterized by distinct DNA methylome profiles and subgroup-specific transcriptional networks. Because molecular subgroups also differ with regards to clinical features, molecular subgrouping of ATRT is expected to influence clinical management soon. This holds especially true for the identification of ATRT-TYR, a subgroup named after the enzyme tyrosinase. We have previously shown that tyrosinase is over-expressed on mRNA and protein level in ATRT-TYR, but the sensitivity and specificity of tyrosinase immunohistochemistry for the diagnosis of ATRT-TYR has not yet been determined.

Design/Methods: Archival samples of 130 ATRT were examined. DNA methylation profiling from formalin-fixed paraffin-embedded tumor samples was done using standard protocols using the HumanMethylation450 BeadChip array or its successor, the Methylation EPIC BeadChip array (Illumina). Tyrosinase immunohistochemistry was done using a mouse monoclonal antibody certified for *in vitro* diagnostic use (DAKO clone T311) and was evaluated blinded to molecular subgroup status.

Results: In line with previous observations, ATRT-TYR most often were of infratentorial location (Chi-square 36.042, df2, $P < 0.0001$). The vast majority of ATRT-TYR (44/48; 92%) displayed positive tyrosinase staining. In contrast, tyrosinase staining was only encountered in 2/53 ATRT-SHH (4%) and 0/29 ATRT-MYC (0%; Chi square 106.46; df2; $P < 0.00001$). Positive tyrosinase staining had a sensitivity of 92% and a specificity of 98% for the diagnosis of ATRT-TYR; the positive and negative predictive values were 96% and 95%, respectively. In infratentorial ATRT, positive tyrosinase staining had a sensitivity of 93% and a specificity of 100% for the diagnosis of ATRT-TYR.

Conclusions: Tyrosinase immunohistochemistry has high specificity and sensitivity for the diagnosis of ATRT-TYR and can be employed until confirmatory results from DNA methylation profiling studies become available.

V029 SIOP19-1510 | Impact of Extent of Resection in a Modern Pediatric Medulloblastoma Cohort

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Background/Objectives: Subtotal resection (STR) (residual disease >1.5cm²) has been associated with worse outcomes in pediatric medulloblastoma. For otherwise standard-risk patients, STR triggers high-risk designation and high-dose craniospinal irradiation (CSI). Yet it remains unclear if increasing CSI dose is required for residual local disease.

Design/Methods: We studied the association between extent of resection (EOR) and event-free survival (EFS) in a proton treated medulloblastoma cohort of patients age 2-23 years from May 2000 to December 2016. EOR was defined by operative report and post-operative imaging as gross-total resection (GTR) or near-total (NTR, <1.5 cm² residual tumor) compared to subtotal (STR, ≥1.5 cm²) or biopsy alone (Bx). We stratified by tumor burden in M2-3 patients, defined as leptomeningeal versus discrete metastases.

Results: Median follow-up was 7.4 years. Of 197 total patients, 148 (75%) were M0, 13 (9%) of whom had residual disease >1.5 m2. Five-year EFS (89% vs. 100%) was not significantly different (p=0.74) between the 9 and 4 who received 36 and ≤23.4 Gy CSI, respectively. Among the remaining 49 (25%) metastatic patients, GTR/NTR was statistically less common compared to M0 patients (72% vs. 91%, p<0.01) and even less common in patients with leptomeningeal (n=23) compared to discrete metastatic spread (56% vs. 84%, p=0.04). GTR/NTR vs. STR/Bx was predictive of improved 5-year EFS in our full cohort (82% vs. 69%, p=0.02), in patients with M2-3 stage (74% vs. 42%, p<0.01) and leptomeningeal spread (64% vs. 34% p=0.03), but not with M0-1 stage (84% vs. 93%, p=0.91).

Conclusions: Non-metastatic children with localized disease >1.5cm2 had similar 2-year EFS irrespective of CSI dose, but larger numbers and follow-up are needed. The predictive association between EOR and 5-year EFS in our medulloblastoma cohort was attributable to patients with leptomeningeal spread in whom STR was more common and a marker of advanced disease.

V030 SIOP19-0540 | Pediatric Ependymoma; An Institutional Experience from a Developing Country

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Background/Objectives: Ependymoma represents the third most common childhood brain cancer. Mostly located in the posterior fossa. Surgery followed by irradiation is the main line of treatment. We aim with this study to describe survival outcomes, as well as the impact of different disease and treatment variables on the outcome. In addition, to highlight the difficulties facing our team in the National Cancer Institute of Egypt.

Design/Methods: The data were collected retrospectively between January 2009 and December 2014 with follow-up until September 2016. All of the patients had their surgical intervention done outside our institute and histopathology was revised before starting treatment. Management including radiotherapy with or without chemotherapy was tailored individually according to the extent of tumor resection as well as the tumor grade.

Results: Forty-Seven patients presented to the hospital in the given period. Most of them presented with signs of increased intracranial tension (n=39, 83%) and lower limb weakness (n=21, 44.7%). Tumors were located in the infratentorial region in 63.8% of the cases. Grade II represented 68.1% of the tumors. Surgical resection was conducted in 32 (68.1%) patients and radiation was done in 34 (72.3%) patients. Twelve patients achieved a complete response while 8 showed a partial response; 22 suffered from progressive disease; and 5 died very early before complete assessment. Median follow-up time reached 23.5 months. Three-year overall survival (OS) was 43.7% and progression-free survival (PFS) was 43.3%. The maximum resection beside the delivery of radiation therapy was the most significant determinants of a better survival probability.

Conclusions: Management of pediatric ependymoma still represents a challenge in developing countries. Hindering factors included the ability to conduct gross total resection, and the limited availability of competent pediatric neurosurgeon and specialized pediatric cancer centers with modernized diagnostic, neurosurgical and radiation equipment. We believe that national networking can help to overcome such challenges.

V031 SIOP19-1537 | Clinical and Biologic Features Predictive of Survival After Relapse of Childhood Medulloblastoma

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Background/Objectives: Salvage therapy for recurrent medulloblastoma (MB) is not standardized. Factors associated with survival after recurrence have not been reported.

Design/Methods: Medical records were reviewed for 155 consecutive patients with newly diagnosed MB between 2007 and 2017, treated at Gustave Roussy and Hospital Necker. The following variables were collected for all patients: age at diagnosis, stage, histology (central review according to WHO 2016 classification), molecular subgrouping (DNA methylation), first line treatment modalities, time to relapse, pattern of recurrence and current status.

Results: A disease recurrence was observed in 47 patients (30%) at a median time of 15 months (range, 1-88 months). The 1-year survival after recurrence was 44% (CI 95%, 29.6 to 58.8). The pattern of recurrence was local in 9 patients, metastatic in 21 and combined local and metastatic in 17 patients. The time to first recurrence, less or more than 12 months from diagnosis, was a predictor of post-recurrence overall survival ($p < 0.0001$) after adjustment for age, treatment, MYC amplification and molecular subgroups. Twenty-seven patients (57%) experiencing recurrent or progressive disease more than 12 months after diagnosis, had an estimated 1-year survival after recurrence of 100% (CI 95%, 100.0 to 100.0) vs 30% (CI 95%, 12.2 to 50.1) with an earlier recurrence. Early relapse was more frequent in children younger than 5 years of age at diagnosis (75% vs 37%, $p = 0.009$), anaplastic/large cell MB (30% vs 3.7%, $p = 0.046$) and Group 3 tumours (76.5% vs 20.8%, $p = 0.003$). Other factors influencing post-relapse survival were metastatic disease and treatment modalities at diagnosis. Multivariable analyses will be presented.

Conclusions: The overall prognosis after relapse remains poor. Time to relapse is a significant prognostic factor for postrelapse survival and may help in the design of clinical trials evaluating new agents.

V032 SIOP19-0984 | Embryonal Tumors of Central Nervous System: Single Center Treatment Experience

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Background/Objectives: To evaluate clinical characteristics and treatment outcomes of central nervous system (CNS) embryonal tumor cases in our center.

Design/Methods: Medical records of patients diagnosed with CNS embryonal tumor between 1987-2018 were retrospectively evaluated. Patient characteristics, multimodal treatment details, treatment-related side effects, overall survivor (OS) and event free survival (EFS) rates were evaluated.

Results: Total of 77/1190 patients followed up with CNS embryonal tumor diagnosis in our center. The median age of diagnosis was 6 years (2months-17years), the M/F ratio was 1.3. Complaints at diagnosis as follows: vomiting (65%), headache (47%), dizziness (3%), unbalanced gait (34%), visual impairment (22%), neurological deficit (22%), personality change (4%), seizure (13%). In 68% of patients, the tumor diameter was >3 cm and the rate of spinal metastasis was 32%. 70/77 of the tumors were located in the posterior fossa. 44% of the cases were operated in our center. Tumor surgery resulted in 84% gross total and 16% subtotal excision. Hydrocephalus was detected in 90% of the patients. Rate of high-risk 66%, standard risk 34%. Craniospinal radiotherapy (RT) was applied in 77%, chemotherapy (CT) in 57% of the patients. Different CT protocols were used over the years, so CT schemas were heterogeneous; included platinum group, alkylating agents and etoposide combinations. Four patients had CCNU-containing schema. Median follow-up period was 13 months (1month-16 years), EFS rate was 53% in 5 years, 49% in 10 and 15 years, 14 patients had relapsed, refractory disease/progression. OS rate was 58% for 5 years, 54% for 10 years and 15 years. Only 1/24 patient had died due to treatment toxicity, two died in the early postoperative period due to sepsis, and others due to progressive disease. There was 1 patient with secondary malignancy.

Conclusions: Relapses and deaths may occur despite multimodal treatment regimens in CNS embryonal tumors. It is important to manage endocrinological, neurological, developmental late effects in long-term follow-up of survivors. In our series, anticancer chemotherapy was found to vary over the years. Despite the multimodal approach, 18% relapse/refractoriness developed and most of the deaths occurred with progression. When we look at living patients; neurological sequelae, neuropathy, ototoxicity, thyroid dysfunction and short stature, endocrinopathies were observed.

V033 SIOP19-1653 | Physical Functioning in Children Surviving a Brain Tumour

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Background/Objectives: Survival rates of children with brain tumours have largely increased over the past decades. Many long-term sequelae in these children are well known, but the physical functioning of these survivors is poorly described.

Design/Methods: In this cross-sectional study on paediatric survivors of a brain tumour, physical functioning was assessed in 48 patients who were treated at the University Hospitals of Leuven and were at least 6 months out of treatment. Median age at diagnosis was 6.10 years (range 0-14). Median age at testing was 14.0 years with a median follow-up time of 4.6 years. Pilocytic astrocytoma (52%) and medulloblastoma (19%) were the most common diagnosis. Overall motor function was evaluated using the Movement Assessment Battery for Children (MABC-2-NL) and/or Bruininks-Oseretsky Test of Motor Proficiency (BOT-2). Functional walking capacity was assessed with 6-minute walk test (6MWT).

Results: Median scores of MABC-2-NL components, i.e. manual dexterity, aiming and catching, balance and total score were below 1SD of the norm values in respectively 66.38%, 79.41%, 73.53% and 80% of patients. Median scores of fine manual control and body coordination of the BOT-2 were below 1SD in respectively 45.2% and 65% of patients. Fifty-eight percent of patients scored normal on the 6MWT while 33.33% showed a mild decrease and 4.44% a moderate or severe decrease. Patients with adjuvant treatment (66.67%; either chemo and/or radiotherapy) showed significant worse scores for both fine manual control ($p=0.007$) and body coordination ($p=0.021$) of the BOT-2. Age at diagnosis, follow-up duration and localization (infra- vs supratentorial) revealed no statistical differences.

Conclusions: The majority of survivors of a childhood brain tumour exhibits long-term decreased fine motor control and balance. Adjuvant treatment further impacts their physical functioning. Functional walking capacity was slightly better preserved. These results indicate that all paediatric patients with a brain tumour need a rehabilitation program.

V034 SIOP19-0308 | Low Grade Gliomas Treated at the University of Cape Town Academic Hospital Complex: 2001-2017

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Background/Objectives: The majority of central nervous system tumours in children are low grade gliomas (LGG). Long-term survival rates are high with a slow, progressive course. Tumour location and extent of resection affect outcome. Adjuvant therapy has an important role. This study evaluated the characteristics of LGG in our setting, the role of adjuvant therapy including more targeted, novel biologic therapy such as BRAF/MEK inhibitors, and the outcome of children with LGG in our institution.

Design/Methods: A retrospective analysis was performed on all children diagnosed with LGG at Red Cross War Memorial Children's Hospital (RCWMCH) between 2001 and 2017. Data were collected from patient hospital folders, as well as Paediatric Oncology records and Groote Schuur Hospital Radiotherapy records.

Results: Eighty-five children aged 0.10-13.76 years (median 4.74 years) were diagnosed with LGG between 2001 and 2017 at RCWMCH. Sixty-five patients (76%) were WHO Grade I, 18 patients were WHO Grade II (21%), and 2 patients' histology was indeterminate. Six patients had metastatic disease at presentation. The most common sites were the cerebellum (27%), hypothalamus (17%), optic nerves and cerebellum (11% each). Forty-three patients had surgery upfront (51%), of which 21 patients had a complete resection, and 22 patients had debulking surgery. Thirty patients had a biopsy only (35%), where definitive surgery was not feasible. Twenty-three patients (27%) received chemotherapy. All but two patients were treated with Vincristine/Carboplatin upfront. Twenty-two patients received radiotherapy (26%), of which 3 patients progressed. The estimated 5-year Overall Survival (OS) was 86.8% and the estimated 5-year Progression Free Survival (PFS) was 42.8%. BRAF status was evaluated in only 3 patients, all were negative.

Conclusions: Our outcomes are similar to those achieved in developed countries. Chemotherapy and radiotherapy are valuable adjuncts to treatment. BRAF status should be tested where possible to determine whether biologic therapies can be used.

V035 SIOP19-1580 | A Phase 0 Pharmacodynamic and Pharmacokinetic Study of Everolimus in Vestibular Schwannoma (VS) and Meningioma Patients

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Background/Objectives: Inhibition of mTORC1 signaling has been shown to diminish growth of NF2 deficient tumors in preclinical studies, and clinical data suggest that everolimus, an orally administered mTORC1 inhibitor, may slow tumor progression in a subset of adult and pediatric NF2 patients with VS. To assess the pharmacokinetics, pharmacodynamics and potential mechanisms of treatment resistance, we performed a pre-surgical (“phase 0”) clinical trial of everolimus in patients undergoing surgery for VS or meningiomas.

Design/Methods: Eligible patients with meningioma or VS requiring tumor resection received everolimus 10 mg daily for 10 days immediately prior to surgery. Everolimus blood levels were determined immediately prior to and after surgery. Tumor samples were collected intraoperatively.

Results: Ten patients completed protocol therapy, including 5 patients with NF2-related meningioma, 3 patients with sporadic meningioma, and 2 patients with NF2-related VS. Median pre- and post-operative plasma levels of everolimus were found to be in a high therapeutic range (17.4 ng/ml and 9.4 ng/ml, respectively). Median tumor tissue drug concentration determined by mass spectrometry was 24.3 ng/g (range 9.2–169.2), and median tumor tissue to post-operative plasma drug concentration ratio was 0.39. We observed only partial inhibition of phospho-S6 in the treated tumors, indicating incomplete target inhibition compared to matched control tissues from untreated patients ($p = 0.005$). Consistent with prior observations that inhibition of mTORC1 may lead to MAPK pathway activation through a PI3K-dependent feedback loop, we observed a statistically significant increase of phospho-ERK ($p < 0.03$) versus untreated controls.

Conclusions: In patients with meningioma or VS, treatment with everolimus leads to incomplete inhibition of mTORC1 signaling and upregulation phospho-ERK. These data may explain the limited anti-tumor effect of everolimus observed in clinical studies for pediatric and adult NF2 patients and identify upregulation of phospho-ERK as a likely resistance mechanism that could be addressed with combination therapies.

V036 SIOP19-0966 | Optic Pathway Gliomas in Children: A Single Center Experience

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Background/Objectives: Optic pathway gliomas (OPGs) are the most frequent tumors of the optic pathways. They can occur both in patients with NF1 and as well as without NF1. The aim of this study is to evaluate our patients with optic pathway gliomas.

Design/Methods: We reviewed the medical records of 72 patients treated between 1990 and January 2019.

Results: Thirty-nine females and 33 males with a median age of 60 months (1 mo. – 18 yrs) were diagnosed with OPG. Forty-eight patients (66%) had the diagnosis of neurofibromatosis type 1 (NF-1). Nineteen patients (%25) were classified as Dodge 1, 28 patients (%38.4) as Dodge 2 and 25 patients (%34.2) as Dodge 3. Mean follow up time was 8.75 yrs (2mo.-30 yrs). Sixteen patients (%22) had stable disease and were followed without treatment. Twelve patients underwent surgery. Primary radiotherapy (RT), was given to none of the patients in the last 15 yrs and only given to 6 patients. Forty four patients (%61) received chemotherapy due to presence of symptoms or progressive disease. All but one patients were treated with vincristine-carboplatinum chemotherapy. Two of 3 patients with leptomeningeal disease were lost despite treatment, one achieved complete remission in the spinal axis. While proptosis regressed in 10 patients, visual functions improved in 13 patients and were stabilized in 28 patients under chemotherapy. Magnetic resonance imaging findings remained stable in 42 patients.

Conclusions: OPG, particularly in NF1 patients are stable most of the time and remain indolent for many years after diagnosis. However these tumors may develop progressive characteristics and can cause visual disturbances, endocrine dysfunction, blindness and even death among some of the patients. In young children with progressive disease, chemotherapy with vincristine and carboplatinum seems to be effective and provides a good quality of life.

V037 SIOP19-1699 | Treatment Quality Score for Pediatric Medulloblastoma: Is There Room for Improvement?

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Background/Objectives: To design a prognostic score tool in Pediatric Medulloblastoma to evaluate the impact of treatment quality parameters on outcome.

Design/Methods: From 2000 to 2018, 62 patients with pediatric medulloblastoma, which received radiotherapy, were retrospectively analyzed. A Treatment Quality Score (TQS) proposal was developed including the extent of surgery and radiotherapy (RT) parameters such as timing and doses.

Results: Patient characteristics included 63% M0; 56% gross total resection; R0 56.5%, R1 24.2%, R2 19.3%, and 50% of the patients in the high-risk group. With a median follow-up of 48 months, 5-year overall survival (OS) was 59±6%. According to risk groups: 79±7% in standard and 37±9% in high-risk patients ($p=0.00$). OS was significantly better when total/near total resection was performed compared to subtotal resection (64% vs. 23%; $p=0.03$). Disease-free survival (DFS) for patients treated ≤40 days from surgery was 62±9% and 40±8% for those treated after >40 days ($p=0.24$). RT duration did not show differences in DFS (<45 days, 49±8% vs. >45 days 51±9%). Multivariate analysis identified high-risk group, subtotal resection, leptomeningeal disease and CSI dose <30 Gy as predictive of worse OS ($p=0.00$). We developed a TQS including: Residual tumor (R0/R1=0 points; R2=4 points); Surgery-radiotherapy interval (≤40days=0 points; >40days=2 points); Radiotherapy duration (≤45days=0 points; >45days=1 point). Score of 0-1 points revealed an OS of 61.4±10.2%; 2-3 points an OS of 44.9±10.7%, and a score of 4-7 points an OS of 16.7±10.8% ($p=0.005$).

Conclusions: Residual tumor >1.5 m2 after surgery remains the strongest risk factor with negative impact on survival. Within radiotherapy parameters, doses and timing altered outcome, with no significant differences in relation to RT duration or days from surgery to the start of radiation. The addition of these adverse treatment variables according to the TQS implies worse overall and disease-free survival.

V038 SIOP19-0299 | Identification of Ependymoma-B Subgroup by Transcriptional Profiling of Tumours from Formalin-Fixed Paraffin-Embedded Tissue Samples

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Background/Objectives: Infratentorial ependymomas include two molecularly distinct subgroups, ependymoma A (EPN-A) and ependymoma B (EPN-B), which differ in terms of survival rate for patients. DNA methylation-based approach is recommended for molecular classification of ependymoma, however alternative diagnostic methods would be helpful, where DNA methylation profiling is not available. We investigated expression level of marker genes at the RNA level from formalin-fixed, paraffin-embedded (FFPE) ependymoma tumours for identification of EPN-B using NanoString nCounter system analysis.

Design/Methods: Tumours from 30 paediatric patients diagnosed with infratentorial ependymoma (GII, GIII) were studied at diagnosis. Total RNA was extracted from FFPE tumour samples using RNeasy kits (Qiagen). For subgroup EPN-B detection a custom NanoString CodeSet was applied which consisted of 10 marker genes: NELL2, CEP83, NXNL2, DNAH1, C9orf72, LAMA2, CXorf67, IGSF, ALDH1L1 and SLC6A13. Tumours were analysed according to NanoString Technologies procedures for hybridization, detection and scanning. Raw counts for each gene underwent technical and biological normalization using nSolver software.

Results: Our analysis revealed that 5 tumours clustered separately from the remaining tumours and showed high expression of EPN-B signature genes: NELL2, CEP83, NXNL2, DNAH1 and C9orf72 as opposite to low expression of EPN-A signature genes: LAMA2, CXorf67, IGSF, ALDH1L1 and SLC6A13. Patients from this group were older from 7 to 15 years (median 11 years). None of them relapsed and all patients are alive. Therefore, clinical characteristics confirms the previous findings for this molecular type of tumours.

Conclusions: Results of analysis indicate that expression RNA profiling from FFPE tumour samples using NanoString nCounter system may be an useful approach for detection of EPN-B tumours which show favourable clinical behaviour.

V039 SIOP19-1249 | DTI-Fiber Tractography of Cerebellar Pathways can be Related to Neurocognitive Deficits in Children with Posterior Fossa Tumors

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Background/Objectives: Lesions of the cerebellum fibers may result in cognitive function impairments in brain tumor survivors. A more differentiated identification of neuroanatomical structures contributing to the extent of this damage is needed. We examined the relationship between long-term cognitive dysfunction and alteration of cerebellar pathways using diffusion tensor imaging (DTI) and tractography.

Design/Methods: DTI-based tractography was performed in patients with posterior fossa tumors. Spinocerebellar (SC), dento-rubro-thalamo-cortical (DRTC), fronto-ponto-cerebellar (FPC), parieto-ponto-cerebellar (PPC), occipito-ponto-cerebellar (OPC) and temporo-ponto-cerebellar (TPC) tracts were analyzed concerning fractional anisotropy (FA) and volumetric measurements. Cognitive outcome was assessed with the Developmental Neuropsychological scale (NEPSY). The correlations between NEPSY scores and fiber tracts were tested with linear regression analysis.

Results: Seven patients with cerebellar tumor were included (median age 63 months - IQR: 39-80). All children had complete surgery: 2/7 (29%) had medulloblastoma, and 5/7 (71%) pilocytic astrocytoma. Median IQ was 83.5 (74.75-83.87) and correlation was found with right SC (R2 for number of fibers 0.50; volume 0.90) and DRTC tracts (R2 for volume 0.58; FA 0.52). Patients showed worst performance in the following items: attention, correlated with right OPC (R2 for number of fibers 0.53; FA -0.86) and PPC tracts (R2 of number of fibers 0.59; volume 0.61; FA 0.52); memory for design, related to left FPC tract (R2 of number for fibers 0.63; volume -0.63); memory for names, correlated with right DRTC tract (R2 for number of fibers 0.85; volume 0.90); visuospatial function, inversely correlated with left OPC tract (R2 of number of fibers -0.81; volume -0.66); and social perception, correlated with left SC (R2 of number for fibers 0.55; volume 0.53) and right PPC tracts (R2 of number for fibers 0.90; volume 0.69).

Conclusions: DTI may be useful to identify relevant structures of the cerebellar pathway and possibly avoid surgically induced long-term neurological sequelae.

V040 SIOP19-1700 | Characterization of Pediatric Patients with Central Nervous System Tumors at a High Complexity Center in a Middle Income Country

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Background/Objectives: Malignant tumors of the Central Nervous System are the second most common childhood neoplasms and are the most common solid tumors among them

(20% of all childhood neoplasms), being the main cause of death by cancer in the pediatric population between 0 and 14 years. This research paper describes the demographic, clinical and treatment characteristics of pediatric patients diagnosed with central nervous system tumors at *Fundación Valle del Lili*, a high complexity hospital at Cali, Colombia between January 2011 and June 2017

Design/Methods: This was an observational descriptive research of a historical cohort. All patients between 0-17 years diagnosed at our hospital between January 2011 and June 2018 were included. They were evaluated through clinical history and institutional pathology results. Statistical package STATA was used. The results were presented as mean and standard deviation or median + RIC according to the distribution of the data.

Results: 160 patients were included; 56% male. The median age and IQR at the time of diagnosis was 8.6 years (4.4 - 12.9). 53% of the tumors had a supratentorial location and 47% were infratentorial. The predominant symptom was neurological deficit in 57% of the cases. 83% of patients received surgery within their treatment; 42% chemotherapy and 45% radiotherapy. The most commonly diagnosed tumor was Astrocytoma (30%), Glioblastoma (10%), Medulloblastoma (9.5%) and Ependymoma (7%) The overall survival of the patients was 82%, 80%, 79%, 77%, 75% and 62% at 12-24-36-48-60 and 72 months respectively.

Conclusions: The present research describes the sociodemographic and clinical characteristics of the pediatric population diagnosed with tumors of the central nervous system treated at our institution. This research shows the distribution of the illness in our country and may be comparable neighbor countries. Our results match with the worldwide literature in terms of tumor type and distribution by age and gender

V041 SIOP19-1728 | GNAS Expression Improves Survival Prognostication of SHH Medulloblastoma Molecular Subgroup

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Background/Objectives: Introduction: Medulloblastoma is the most frequent malignant brain tumor in children.

Currently, four distinct medulloblastoma molecular subgroups have been identified: MB SHH, MB WNT, MB GRP3 and MB GRP4. Although a 22-gene panel employing the NanoString technology was previously successfully developed for medulloblastoma molecular subgrouping, MB SHH may be sectioned into 2 distinctive subgroups according to clinical and molecular characteristics. Aim: To apply the 22-gene panel for medulloblastoma molecular subgrouping with further key cancer-related genes in order to improve classification and subclassification of Brazilian MB SHH using NanoString.

Design/Methods: Methods: FFPE samples from 131 medulloblastoma cases from four reference centers in Brazil were enrolled. Gene expression was assessed using the 22-gene panel previously developed by Dr. Taylor's group for medulloblastoma molecular subgrouping plus GNAS gene. Raw data was normalized by HK, followed by class prediction with Prediction Analysis of Microarrays (PAM). MB SHH subclassification was performed by GNAS expression. The molecular profile was associated with patients' clinical outcome.

Results: The medulloblastoma cases were distributed into MB SHH (n=61), MB WNT (n=21), MB GRP4 (n=26) and MB GRP3 (n=23). The lowest and the highest overall survival (OS) was found for MB GRP4 and MB WNT, respectively (mean of OS was 118.4 and 158.6 months, respectively). High and low expression of the GNAS tumor suppressor gene in MB SHH cases was associated with better and worse OS (p=0.02), respectively.

Conclusions: Conclusions: We implemented the NanoString platform for molecular classification of a medulloblastoma Brazilian series as an effective diagnostic tool for personalized medicine. The 22-gene panel for molecular classification of medulloblastoma associated with GNAS expression may improve the prognostication of survival in MB SHH patients.

V042 SIOP19-1732 | Lack of KBTBD4 Mutations in Molecularly Classified Brazilian Medulloblastomas

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Background/Objectives: Medulloblastoma is the most frequent malignant brain tumor in children, representing 20% of all childhood brain tumors. Currently, medulloblastomas

are molecularly classified in four subgroups that are associated with distinctive clinicopathological features. *KBTBD4* mutations were recently described in a subset of MB_{GRP3} and MB_{GRP4} medulloblastomas subgroups. However, no other studies reported *KBTBD4* mutations in medulloblastomas. Thus, our aim was to investigate *KBTBD4* mutations in a Brazilian series of medulloblastoma.

Design/Methods: We evaluated 128 medulloblastoma patients molecularly classified from four Brazilian reference centers. DNA from FFPE samples was screened for *KBTBD4* hotspot mutations by Sanger sequencing.

Results: Most of the patients were male, average age was 16.5 years old and average overall survival was 55.9 months. The most predominant histological subtype was the classic subtype, followed by nodular/desmoplastic, and the most predominant medulloblastoma molecular subtype was the MB SHH subgroup (46%), followed by MB GRP3 and MB GRP4 (19%/each), and MB WNT (16%). Among the 128 samples, 111 were successfully sequenced. No *KBTBD4* mutation were identified in 111 samples.

Conclusions: Concluding, our findings suggest that *KBTBD4* mutations are uncommon in Brazilian MB GRP3 and MB GRP4 medulloblastomas subgroups. Further studies in larger series of MB GRP3 and MB GRP4 are warranted to better assess role of *KBTBD4* mutations in medulloblastoma.

V043 SIOP19-1206 | Rare KIAA1549-BRAF Fusion Variants Characterize Spinal Low-Grade Gliomas in Children

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Background/Objectives: Gliomas are the most common CNS tumors in children and adolescents, however intramedullary spinal cord low-grade gliomas (sLGGs) are rare with scarce information about molecular background. Therefore, clinical and genetic single institutional study was performed to reveal sLGG-associated molecular alterations.

Design/Methods: Demographic data was collected and targeted genomic approach was employed to uncover known and novel alterations associated with sLGGs. Multiplex Ligation Probe Amplification (MLPA) and RT-PCR were used to screen for *KIAA1549-BRAF* fusion and direct sequencing for point mutations (*BRAF*, *H3F3A*, *HIST1H3B*, *FGFR1*).

Samples with no detected alteration were subjected to panel RNA-sequencing (FusionPlex Archer Diagnostics).

Results: Within 2000-2018 we diagnosed 22 patients (median age 6.7y, range 1.1y–17.5y) with sLGGs comprising predominantly of pilocytic astrocytoma, diffuse astrocytoma and ganglioglioma. sLGGs represented 5% of all our LGGs. RT-PCR revealed 10 tumours harbouring KIAA1549-BRAF. Interestingly, only three cases were identified with common 15-9 and one case with 16-9 fusion variants. Rare KIAA1549-BRAF variants were detected in 4 patients (one 16-11, one 15-11, two 13-11). Additional two patients harboured novel variant 10-9 which was specific for spinal gliomas with absence in any other anatomical locations (n=64). *CLIP2-NTRK2* fusion was detected using RNA-sequencing in one patient with intermediate grade glioma with multiple progressions. Surprisingly, we have not identified any BRAF V600E case in our cohort. No alteration was detected in 11 patients and therefore RNA-sequencing is being performed. Eight patients progressed after initial surgery and needed further therapy. Two patients (one with *KIAA1549-BRAF* 10-9 variant, one without known driver alteration) died of the disease.

Conclusions: This study provides important data on the molecular background of pediatric sLGGs. Rare *KIAA1549-BRAF* variants including novel variant 10-9 are more frequent in sLGGs compared to intracranial LGGs. Other drugable targets can be identified using RNA-sequencing as shown on our NTRK2 case.

V044 SIOP19-0145 | Racial/Ethnic Disparities in Survival for Children and Adolescents with Central Nervous System Tumours in the United States, 2000-2015

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Background/Objectives: Central nervous system (CNS) malignancy is the most common cause of cancer death in children in high-income countries. However, information on the association between race/ethnicity and survival from CNS tumours in children and adolescents is sparse.

Design/Methods: Children and adolescents (0-19 years) diagnosed with a primary malignant CNS tumour during 2000-2015 in the US were recorded by 18 population-based cancer registries and collated by the Surveillance, Epidemiology, and End Results programme. Overall survival was estimated using the Kaplan-Meier method. Hazard ratios (HR) and confidence intervals (CI) for association with race/ethnicity were estimated by Cox regression models adjusted for sex, age at diagnosis, diagnostic period, area-

based socioeconomic position (SEP) and tumour type. Insurance status data were available from 2007.

Results: In total 9,577 children and adolescents (62.5% non-Hispanic whites, 10.6% non-Hispanic blacks and 26.9% Hispanics) contributed 55,052 person-years of follow-up. On average, five-year survival was 74.5% [95% CI 73.6-75.5%]. Black and Hispanic children/adolescents tended to live in more deprived areas and to be more often diagnosed with high-grade astrocytoma. Survival was strongly associated with race/ethnicity: black and Hispanic children/adolescents were about 40% more likely to die than white children/adolescents, after adjusting for sex, age and diagnostic period, SEP and tumour type (HR 1.39 [95% CI 1.23-1.58] for blacks, 1.40 [95% CI 1.28-1.54] for Hispanics). For 5,429 children/adolescents diagnosed during 2007-2015, further adjusting for insurance status only partially attenuated the association with race/ethnicity (HR 1.25 [1.04-1.51] for blacks; 1.34 [1.17-1.54] for Hispanics).

Conclusions: Hispanic and non-Hispanic black children and adolescents with a CNS tumour had significantly worse survival than their white counterparts. This association was not fully explained by socioeconomic or clinical differences. These survival disparities may reflect racially/ethnically-driven barriers to optimal healthcare. Further research is needed to identify the reasons behind these disparities and guide policies aimed at reducing cancer survival inequalities.

V045 SIOP19-0389 | SPINAL CHANGE AFTER CRANIOSPINAL IRRADIATION FOR PEDIATRIC PATIENTS

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Background/Objectives: To analyze spinal change and the effect on future height after craniospinal irradiation (CSI) for medulloblastoma.

Design/Methods: Vertebral bones in 220 patients received CSI at ≤ 13 years with minimal follow up of 2 years with spinal MRI were analyzed. CSI dose ranged from 15Gy to 43.2Gy. Total of 896 vertebral body height were measured. Scoliosis, fatty marrow change, degenerative change of vertebral bones and disc, and wedging or vertebral height loss were also analyzed. Then impact of these changes on height was investigated.

Results: The bone growth rate (%/year) was significantly worse with the dose >38 Gy. The growth rates were similar for vertebral bodies treated with growth hormone (GH) compared to those in whom GH was not indicated (2.73% vs. 2.88%), but were significantly lower (1.38%) in those who refused or unable to receive GH, compared to those treated with GH

($p=0.0022$). Fatty marrow change, degenerative change of spinal bones and wedging or spinal height loss was observed in 83%, 13% and 17% of the patients, and 31% patients had disc degenerative change. Scoliosis was observed in 27% of the patients. Bone growth rates were significantly correlated to future height. Whereas, height growth was strong for patients with scoliosis ($p=0.0265$) and degenerative change ($p=0.0518$), and final height was tall for male ($p=0.0022$) and patients with disk change ($p=0.0086$).

Conclusions: Vertebral bone growth was significantly disturbed with the dose $>38\text{Gy}$, and adequate GH replacement was important for bone growth. Even with symmetrical irradiation, risk of scoliosis was high after CSI, and moreover, spinal demineralization and degenerative change frequently progressed after CSI. Moreover, degenerative change and scoliosis was frequent in patients with strong height growth. Therefore, careful attention should be paid for future spinal symptoms as the patients grow old even though their height growth was well.

V046 SIOP19-0073 | New Insights into Pediatric Low-Grade Gliomas in Saudi Arabia Revealed Through Genetic Profiling Single Centre Experience

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Background/Objectives: Gliomas account for $\geq 50\%$ of childhood central nervous neoplasms and can be subdivided into low-grade (LGG) and high grade gliomas (HGG). We performed comprehensive genomic profiling on 20 Saudi pediatric LGG (pLGG) patients to identify tumor associated genetic abnormalities. The identification of these events can inform prognostic, and therapeutic decision-making

Design/Methods: This retrospective study was performed on 20 children ($<16\text{ y}$) newly diagnosed with pathologically confirmed LGG. We reviewed the molecular, clinical and therapeutic aspects and the treatment outcome of pLGG patients. Next generation sequencing was performed using the OncoPrint Comprehensive Assay v3 system from formalin-fixed paraffin embedded (FFPE) tumor samples. Data were analyzed using the SPSS statistical package version 23.

Results: We detected genomic alterations (GAs) in all of the tumors, averaging 4.52 ± 2.11 GAs per patient. BRAF was the most commonly altered gene (75.0%, 15/20 cases). Other frequently mutated genes included ATM 15% (3/20), RNF43

15% (3/20), RAD51C 20% (4/20) and Notch2 20% (4/20). Casually altered genes (observed in less than 3 patients) included FANCD2, FGFR1, BRCA2, CDC4, KIF5B, RET, AKAP, SLX4, MSH6, NTRK, CCDC170, MLH1, AGK, PDGFRB, EIF3B, FGFR2, CDKN2A/B, PTCH1, SETD2, SLX4, MSH6 NTRK and CDK4. Interestingly, we identified a novel gene fusion of GOPC (Fig)-ROS1 in a 10-year old patient that lacked BRAF fusions. Midline tumor analysis revealed a left parietal mass with vasogenic edema. The patient received surgical resection with excellent post-operative recovery and no neurological deficit. No adjuvant chemotherapy or radiation therapy was required and the patient is stable with no tumor recurrence.

Conclusions: We provide comprehensive genomic profiling of Saudi pLGGs that promote diagnostic accuracy and enhance clinical decision-making. Additionally, GOPC1-ROS1 may be a biomarker to identify pLGG patients that will benefit from Target therapy.

V047 SIOP19-1319 | Chiasmatic-Hypothalamic Gliomas of the Child: Is There Still Room for Aggressive Surgery?

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Background/Objectives: Chiasmatic-hypothalamic tumors represent 2 to 7% of the brain tumors of the child. Their management remains difficult and the role of surgery is called into question. We report a series of patients who were treated in Lyon with wide surgery.

Design/Methods: Twenty-three patients have been treated since 2000 to 2017 for a chiasmatic-hypothalamic tumor: 12 girls and 10 boys. The age is between two months and 17 years. From the clinical point of view, 5 patients had visual disturbances (including 1 completely blind patient), 6 patients had intracranial hypertension, 6 had pluridirectional nystagmus, 1 patient had precocious puberty, and 4 had abrupt strabismus. Two patients had neurofibromatosis. All patients were studied with cranial spinal MRI. From the surgical point of view, 8 patients were treated with complete excision, 10 patients with partial resection and 4 patients had a simple biopsy.

Results: Forty-seven percent of patients have a good quality life with good schooling, 25% of patients have moderate sequelae with adequate schooling and 20% of patients have a life with severe sequelae. Three patients had visual worsening.

Conclusions: Chiasmatic-hypothalamic tumor surgery must respect patients' quality of life and is possible when

chemotherapy treatment does not allow the control of the disease. The surgical approach for wide resection is still relevant in cases with clinical and volumetric evolution and after failure of chemotherapy.

V048 SIOP19-1720 | Treatment Experience of Pediatric Low Grade Glioma in a Pediatric Hospital in Argentina

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Background/Objectives: To describe demographic characteristics, Event Free Survival (EFS) and Overall Survival (OS) in patients with Low Grade Glioma (LGGs) treated at Oncology Unit of Garrahan Hospital (HG), Argentina.

Design/Methods: Descriptive and retrospective analysis of medical records from patients with LGGs admitted between September 2003 to January 2019. Variables were: age, sex, localization, pathology, Neurofibromatosis (NF1) presence, relapse and death. First line treatment was SIOP-LGG 2004 protocol, with carboplatin, vincristine and actinomycin for allergic reactions (AR). For statically analysis SPSS (IBM) was used, for EFS and OS Kaplan-Meier and Long-rank test for significance.

Results: One hundred and sixteen patients were eligible. Median age 50 months, Ratio male:female 0,86:1. Patients present AR to carboplatin in 50% (n=59), whom switched to actinomycin. Eleven patients recived radiotherapy when relapsed. Localization was divided in Supratentorial (ST)(n=91) (cerebral hemispheres, optic path way, mid-line structures), Infratentorial (IT)(n=16) (cerebellum, caudal brainstem and crus cerebri), spinal canal (n=2) and disseminated (n=5). ST and IT localization were analysed. Median age for ST and IT was 73 and 62 months respectively, ST most frequent pathology was LGG while for IT pilocytic astrocytoma. No significative differences were found in OS at 5y between both groups (IT OS 77.9% vs ST OS 86% $p=0.69$ [CI95%0.2618-7.369]), nevertheless 5y EFS were significantly different (IT EFS 35.2% vs ST EFS 59% $p=0.04$ [CI95%1.015-9.375]). Global OS at 5 and 10y was 86.5% and 74% respectively (median survival >120 months), EFS at 5 and 10y was 54.3% and 74% respectively. At diagnosis 20 patients had NF1. No significant differences in EFS and OS were found between patients with or without NF1.(EFS 5y 60.3% vs 53.2% $p=0.55$ [CI95%0.3986-1.633]; OS 5y 88.4% vs 60.3% $p=0.4$ [CI95%0.4864-4.848] respectively).

Conclusions: Patients treated at HG have OS and EFS comparable with results of international cooperative groups. Even though LGG is a common feature in NF1, we did not find significant differences in survival rates between groups.

V049 SIOP19-0384 | Longitudinal Neurological Outcome in Pediatric Patients with Infratentorial Ependymoma Treated with Surgery and Radiation Therapy

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Background/Objectives: To evaluate neurological impairment and associated clinical factors in pediatric patients with infratentorial ependymoma treated with surgery and radiation therapy.

Design/Methods: Between 1997 and 2009, 102 patients were enrolled on a phase II trial of conformal radiation therapy (CRT) and prospectively followed with serial neurological exams for a minimum of 12 months. Impairment was classified by pattern of onset and recovery. Clinical (gender, age, CSF shunt) and treatment (target volumes and normal tissue doses, number and extent of surgeries, chemotherapy) factors were included in the analysis.

Results: The median follow-up was 137 months (range, 12-234 months) and total number of evaluations 991 (median 10, range 2-20). Impairment was observed prior to CRT and after CRT with eventual recovery in most cases. Impairment prior to CRT (331 findings) was associated with CSF shunt, surgery factors, chemotherapy and radiation target volumes. Impairment after CRT (126 findings) were most frequently nystagmus, hearing loss, involving cerebellar function and deep tendon reflexes (DTR). An association between impairment and radiation dose was found for hearing loss and DTR. The median time to onset of hearing loss was 67 months (range, 12-135 months) and associated with cochlear dose. Dose to brain sub-volumes was significantly associated with DTR impairment with time to recovery of 95 months and 126 months, respectively, according to onset before and after CRT.

Conclusions: With the exception of hearing loss, neurological impairment in pediatric patients with infratentorial ependymoma treated with surgery and radiation therapy recovers with time and is associated with clinical and treatment factors. The time to recover is long suggesting that long-term vigilance, support and perseverance is required in these patients.

V050 SIOP19-1075 | Sleep Disorder in Children Treated for Brain Tumour. A Polysomnography Study

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Background/Objectives: Few studies evaluated sleep disorder in children with brain tumours. We aim to characterize the sleep disorders in this population.

Design/Methods: Polysomnography study (PSG) was performed in our paediatric oncology centre from October 2017 to March 2019. Inclusion criteria: patients between 2-16 years old, affected by brain tumour, at least 6 months after the end of treatment. Children with seizure, taking sleep-interfering therapies and with adenotonsillar hypertrophy were excluded. We performed PSG following American Academy of Sleep Medicine (AASM) guidelines.

Results: We enrolled 16 patients (5 female, 11 male). Median age at the diagnosis was 9.3 years (IQR 25°-75° 3.5-11.5), and median age at PSG exam was 12.5 years (IQR 25°-75° 6.9-15.3). 8/16 patients had subtentorial tumour. The histologic distribution was: 31% pilocytic astrocytoma, 19% glioneuronal tumour, 12% choroid plexus papilloma, 38% other. Mean sleep record was 514 min (SD +/- 86 min). The mean oxygen saturation was 97% and mean FC was 71 bpm (SD +/-14). The respiratory record showed a CAI (central apnoea index) increased in subtentorial group with a median value 1.2 (IQR 25°-75° 0.85-1.45) compared with sovratentorial group with a median value 0.3 (IQR 25°-75° 0.2-0.5), $p = 0.0156$. We did not find any alteration related with radiotherapy treatment. The electroencephalogram record showed an alteration of night sleep organization: an increased N1 period, a shorter N2 period, and higher delta-sleep activity N3 period, compared with healthy populations.

Conclusions: We found an increased central apnoea index related with cerebellum localization, showing an impact of posterior fossa tumour on sleep and ventilatory control. Moreover, we described a sleep structure alteration. These modifications could determine consequences for the neurocognitive performance. We aim to highlight the role of sleep follow up in patients treated for brain tumour, to potentially set up a behavioural or pharmacological therapy to improve children's quality of life.

V051 SIOP19-1434 | Optic Pathway Glioma in Paediatric Regional Centre: A Retrospective Analysis

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Background/Objectives: The optic pathway glioma affected 15-20% of children with neurofibromatosis type 1 (NF-1), threatening vision function. The natural history of disease is

unclear. We aim to describe the incidence and outcome of children with NF1 referred to our regional centre.

Design/Methods: Retrospective case note review of 119 newly diagnosed NF-1 patients referred between 01.01.2008 and 31.12.2018 to the regional pediatric neuro-oncology service and rare disease center was carried out to determine the incidence, outcome and treatment of children affected by OPG. The descriptive analysis was used to determinate the populations characteristic. A p -value <0.05 was considered significant.

Results: We enrolled 119 patients: 58 were males (49%), and 12/119 presented OPG (10%). All children affected by NF-1 performed imaging (MRI), classified with modified Dodge Classification and visual exams as disease follow up. The mean age at diagnosis of OPG was 6.7 years old (SD +/- 5.3 years). The mean follow up was 106 months (SD +/- 69 months). 4/12 presented visual signs of OPG, whereas 8/12 were asymptomatic. Children with visual alteration presented at MRI PLAN 3/4 negative (2/4), and PLAN 3-4 positive: 2/4. The radiological progression was found on 5/12 patients, and only 1/5 patients received treatment. 3 patients received chemotherapy for the visual: 1 at the diagnosis for poor vision and the other 2 for progressive visual deterioration.

Conclusions: The OPG outcome remains unpredictable. Our cohort of NF-1 patients shows that the most important outcome for the choice of treatment is the vision function. The MRI could be useful at the diagnosis of disease, but not for the treatment choice.

V052 SIOP19-1475 | Prognostic Factors of Hydrocephalus in Children with Brain Tumors: A Retrospective Analysis

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Background/Objectives: Hydrocephalus is one of the main complications of brain tumors in children, involving about 50% of cases at diagnosis. It usually resolves with surgical tumor resection but could persist up to 10-40% of cases. The aim of this study is to identify prognostic factors associated with persistent hydrocephalus in a pediatric population of patients with brain tumors.

Design/Methods: Retrospective case note review of 56 newly diagnosed brain tumour patients referred between 04/2012 and 01/2018 to our regional paediatric neuro-oncology service was carried out to evaluate preoperative and postoperative Magnetic Resonance Imaging (MRI) and to determine Evans' Index (EI) and fronto-occipital horn ratio (FOHR) for

each scan. Chi-square and Fischer test were used to analyze categorical variables as appropriate. Mann-Whitney analysis was used for the evaluation of continuous variables. A p-value <0.05 was considered significant.

Results: Data on fifty-six children were analyzed: 30 males (54%), mean age at diagnosis 9.03 (SD $\pm$ 4.11 years). Anatomical distribution was sovratentorial 21/56 (37.5%), subtentorial 35/56 (62.5%). MRI reported the presence of radiological hydrocephalus in 25/56 children (45%) at diagnosis; 9/25 children (36%) had persistent hydrocephalus in the post-operative phase. The previous presence of an external ventricular drain (p: 0.028) and a FOHR > 0.46 at diagnosis (p: 0.042) were related to a higher prevalence of persistent hydrocephalus and therefore to the need for a cerebrospinal fluid drain device.

Conclusions: Identifying pre-operatively patients at risk for developing persistent hydrocephalus would avoid delays in the execution of interventions for the placement of permanent cerebrospinal fluid drain devices. This study finds that a FOHR > 0.46 at diagnosis could impact on the therapeutic management of children with hydrocephalus and brain tumors. Prospective and large-scale studies are needed in order to standardize this approach.

V053 SIOP19-0287 | Evaluation of the Post-Operatory Period in Neurosurgical Pediatric Patients with Central Nervous System Tumor: A Single General Center Experience

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Background/Objectives: Morbidity following tumor surgery is greater than other types of neurosurgery. Accurate data collection allows comparison between institutions and quality improvement. The aim was to analyze the 30-day or inpatient outcome of pediatric patients with central nervous system (CNS) tumors in terms of significant adverse events (SAE) in our general institution in the post-operative (PO) period.

Design/Methods: AE of children 0-16 years operated at our institution (2009-2018) for CNS tumors were prospectively registered and retrospectively analyzed with consensus definitions.

Results: Seventy-eight procedures were performed in 65 patients (54% male, mean age 9.1 years). Tumors were supratentorial in 59% children and Astrocytic tumor was the most frequent diagnosis (55%). Fifty-eight percent underwent gross total resection, 31% partial removal and 11% biopsy.

Six percent developed Hydrocephalus in the PO period, 5% maior CSF-leakage and 8% pseudomeningocele. Nineteen percent developed new moderate-severe neurological deficits (73% infratentorial tumors), 5% seizures and 6.4% a CNS infection. We recorded 5 ischemic events (6.4%) but no hemorrhages. Mortality was 0% while 30.1% procedures were linked to at least one SAE; in these children the mean Hospital and ICU length of stay were significantly longer (p< 0.00001-p<0.005). Using a *logistic regression model we found* no association with sex (p=0.17), age at the onset (p=0.21) and histology (p=0.19) while we found that total resection had a 79% lower risk (OR=0.21; 95%CI=0.06-0.68) of SAE in comparison with partial removal-biopsy (p=0.009) and that sovratentorial tumors had a 87% lower risk (OR=0.13; 95%CI=0.03-0.49) of SAE in comparison with infratentorial-spinal tumors (p=0.003).

Conclusions: SAE rate in a general tertiary hospital is high but comparable to published data of international pediatric institutions. Recognition of adverse events is fundamental for appropriate patient management and could affect long term outcome therefore continuous surveillance is needed. Infratentorial and not completely resectable tumors are independent risk factors for SAE.

V054 SIOP19-0896 | Validation of EZH2 Protein as Therapeutic Target for Infiltrating Glioma of the Brainstem: Pharmacological and Genetic Approaches

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Background/Objectives: Diffuse Intrinsic Pontine Glioma (DIPG) is a rare and highly aggressive pediatric tumor with one year survival time after diagnosis. Currently, there are no effective treatments. DIPG is characterized by a mutation in histone H3 leading to a substitution of Lysine 27 to Methionine (H3K27M) which deregulates Polycomb Repressive Complex 2 (PRC2), including enzymatic activity of EZH2. It has been shown that EZH2 inhibition decreases cell proliferation and inhibits tumor growth in vivo. This project aims to confirm that EZH2 could be a therapeutic target using pharmacological and genetic approaches and to determine the underlying molecular mechanisms of action

Design/Methods: Efficacy of EZH2 inhibitors and protein down-regulation were evaluated in DIPG cell lines by proliferation and cell death assays, Western blot. A knockout (KO) of EZH2 gene was also realized and validated using the CRISPR/Cas9 system. A proteomic analysis is underway to determine molecular changes occurring in tumor cells under EZH2 inhibition. In vivo tumor growth study was performed on chick embryo chorioallantoic membrane (CAM).

Results: GSK126 is an efficient inhibitor with consistent anti-proliferative and pro-apoptotic effects in DIPG cell lines. Inhibition of EZH2 using siRNAs also showed decrease in proliferation after 18 days; however, EZH2 KO cells exhibited cell growth deficits. Combination treatment of tumor cells with GSK126 and siEZH2 leads to an increase in the expression of EZH2, pointing to a compensatory system. CAM model demonstrates an anti-tumor effect of GSK126 on tumor formation.

Conclusions: EZH2 remains a challenging target in DIPG tumors. Proteomic analysis is underway to identify these novel targets that can be inhibited by chemical blockade. Inhibitory effects will be further confirmed using murine DIPG tumor models. Vectorization of anticancer agents is a promising concept that could improve the effectiveness of chemotherapy and significantly reduce its toxicity, currently being studied.

V055 SIOP19-1343 | *MSI2* Gene is Aberrantly Expressed in Ependymoma: In Silico and RNA-SEQ Analyses

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Background/Objectives: Introduction: The Ependymoma (EPN) is the third most common childhood cancer which comprises nine distinct molecular subgroups. ST-EPN-ReIA and PF-EPN-A exhibit a more aggressive tumor and poor outcome. The Musashi-2 (*MSI2*) is a RNA-binding protein which act as a regulator of translation and, when aberrantly expressed, is associated with worst prognostic of some tumors. **Aim:** Analyze the transcriptional profile *in silico* and by RNAseq of *MSI2* in Ependymoma.

Design/Methods: Methodology: Public database of ependymoma GSE64415 (only pediatric samples was selected, n=116) was used to perform the *in silico* analyzes through R plataform DESeq2 package. RNA-seq data (n=17) from a brazilian EPN cohort was analyzed and statistic was performed using the non-parametric Mann-whitney test by the SPSS 20.0 program.

Results: *In silico* analyses (GSE64415) of *MSI2* gene showed a highexpression in ependymoma when compare with pediatric normal brain samples (n=22). When analyzed EPN strata, *MSI2* is higher expressed in PF-EPN-A ($p=0.0001$), PF-EPN-B ($p=0.0001$) and ST-EPN-ReIA ($p=0.0001$). RNA-seq results from 17 pediatric brazilian samples showed a similar pattern of expression as observed for *in silico* analysis,

although not reaching statistical differences because of the small number of samples.

Conclusions: These results demonstrate and validate the overexpression of *MSI2* in Ependymoma. Future studies are necessary to better understand the role of this gene in Ependymoma.

V056 SIOP19-1573 | Step-Wise Diagnostic Approach and Treatment Outcome in Low Grade Gliomas (LGG) in Pediatric Patients

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Background/Objectives: Low-grade-gliomas (LGG) encompass a diverse group of tumors of different histologies. They are the most common type of pediatric brain-tumors accounting almost for 30-50% of them.

Design/Methods: A retrospective review of newly-diagnosed patients with LGG, treated in our unit between 2015-2018, was performed. Gender, age, symptoms, location, leptomeningeal infiltration, histological type, BRAF-status, NF-status, management and outcome were analyzed.

Results: During the study period, 61 patients with LGG (26females) were diagnosed out of 133 patients with primary brain tumors. Median age was 6.3years (range: 40days-15.8years). Nearly 80% of the patients had symptoms of raised intracranial-pressure (headache/vomiting). The most common locations were: posterior-fossa (45.1%) followed by optic-pathway (22.5%). Surgical intervention was possible in 42patients (34 subtotal/total excision, 5 partial excision, 4 biopsy). Leptomeningeal infiltration at diagnosis was detected in 2patients. Histological type was mostly astrocytoma (33pts, 76.8%), especially pilocytic type (78.7% of astrocytomas). NF1 was genetically confirmed in 26.2% of the patients (16pts). In 37patients without criteria or genetic confirmation of NF1, Real Time-PCR was performed for KIAA1549/BRAF-fusion and was positive in 15patients (40.5%) and BRAFV600Emutation was detected in 3 patients (8.1%). Treatment according to LGG2004-protocol was administered in 19patients, of which 11 needed treatment-modification (6 due to carboplatin allergic reaction and 5 due to progressive disease). Radiotherapy was administered in 3patients. One patient had a malignant transformation to glioblastoma multiforme, 16 months after initial diagnosis

and died. One patient with optic pathway glioma was biopsied after progression of disease and an anaplastic astrocytoma GrIII was found. At the end of treatment, visual and mobility problems were noted in two and one patients respectively.

Conclusions: Our findings agree with those of internationally published studies. The most common histologic type was pilocytic astrocytoma. Even though overall survival is good (95.1%), progression cannot be excluded. Further studies for the molecular classification of those patients with negative NF1 or BRAF status are needed.

V057 SIOP19-0888 | Metronomic Maintenance with Weekly Vinblastine After Induction with Bevacizumab-Irinotecan in Children with Low-Grade Glioma Prevent Early Relapse

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Background/Objectives: Low-grade glioma (LGG) represents the most common brain tumor in childhood. Previous studies have reported that a therapeutic strategy based on the association of bevacizumab-irinotecan (BI) could produce rapid tumor response & clinical improvement in children with LGG. Nevertheless, a majority of patients relapse shortly (median of 5 months) after stopping bevacizumab/irinotecan. We proposed a 12 months metronomic maintenance with weekly vinblastine added after 6 months induction to prevent early relapse.

Design/Methods: This is a monocentric retrospective analysis of patient with LGG treated with Bevacizumab (10mg/kg) and Irinotecan (125mg/m²) for 6 months followed by maintenance with weekly vinblastine (6mg/m²) from October 2012 to April 2019 in our institution.

Results: 18 patients (7 males and 11 females), 5/18 NF1 were analyzed, with a median age of 10 years (range: 1-16 months). 16 patients received therapeutic strategic based on the association with BI and 2 patients received bevacizumab only. Mean duration of induction was 6.2 months (range: 2-12 months). 14 children received total duration of vinblastine treatment, 3 patients are still “on-therapy” and 1 patient had not started maintenance therapy. Mean duration of maintenance was 8.3 months (range: 3-12 months). During induction, clinical improvement was noted in 7 patients, 7 patients have stable symptoms and 4 patients have progression. With a median follow-up of 26 months after beginning of maintenance, 17/18 patients are alive (range: 3-78 months). 15 patients had stable disease, 3 patients progressed after vin-

blastine maintenance and 1 during vinblastine maintenance. This treatment was well tolerated in line with previous reports of good safety of both BI and vinblastine.

Conclusions: We report here, the potential benefit and the improvement of progression-free survival by adding metronomic maintenance with weekly vinblastine after initial induction with BI in children with LGG.

V058 SIOP19-0441 | Pediatric Non-Pontine Diffuse Midline Glioma H3K27M Mutant: A Monoinstitutional Experience

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Background/Objectives: The new entity “diffuse-midline-glioma H3K27M-mutant”, recently specified in the 2016 WHO revision, is characterized by an aggressive clinical behavior and poor survival as DIPG, receiving a WHO grade IV designation regardless of tissue histological features. No prospective studies have been so far published. We report our experience between 2016-2018 in treating patients with “diffuse-midline-glioma H3K27M-mutant” with radiotherapy (RT) and Nimotuzumab/Vinorelbine chemotherapy, as already published for DIPG's patients (DOI10.1007/s11060-014-1428-z). All patients provided written informed consent.

Design/Methods: We treated 9 patients: 7/9 females, median age at diagnosis 13 years (range 1-26), median onset of symptoms 1,5 months, 3 thalamic (1 bi-thalamic), 2 pontocerebellar, 1 pineal and 1 with leptomeningeal dissemination. Two patients were biopsied, 6 received partial resection, 1 subtotal resection. In all cases a central pathology review was performed: 4 patients had morphologic grade IV glioma, 1 grade III, 1 grade II, 1 glial tumor with oligodendroglial aspects, 2 midline glioma H3K27M mutant at the first local pathological evaluation. Eight patients received focal radiotherapy (total dose 54 Gy), and 1 patient craniospinal irradiation (39.6 Gy).

Results: Six patients had progressive disease with a median time to progression of 9 months (range 6-13); 2/9 had partial response (11 and 15 months after diagnosis) and 1 had pseudoprogression at the first MRI after RT. Two patients with local progression (5 and 6 months after RT) were reirradiated; they died 8 and 6 months after the end of re-RT respectively. One patient with leptomeningeal dissemination 3 months after RT received craniospinal re-irradiation with no evidence of response. Median observation time from diagnosis is 12 months (range 4-15).

Conclusions: The clinically/molecularly defined setting of this tumor provides a rationale for therapies directed against the effects of the H3K27 mutation and suggests, until now, inclusion of this entity in DIPG treatment registry/protocols or in larger prospective trials.

V059 SIOP19-1621 | Zinc Enhances Temozolomide Cytotoxicity in Pediatric Glioblastoma Multiforme Model System

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Background/Objectives: Temozolomide (TMZ) is an alkylating agent that has become the mainstay treatment of the most malignant brain cancer, glioblastoma multiforme (GBM). Unfortunately only a limited number of patients respond to it positively. We have shown that zinc metal reestablishes chemosensitivity in adult GBM in vitro and also in vivo but this effect has not been tested with pediatric GBM.

Design/Methods: Using Human pediatric glioblastoma cell lines- KNS42 (mutant p53/ MGMT [+]) and SF188 (mutant p53/ MGMT [-]), we investigated whether addition of zinc to TMZ enhances its cytotoxicity against GBM.

Results: *In vitro* cell viability analysis showed that the cytotoxic activity of TMZ was substantially increased with addition of zinc and this response was accompanied by an elevation of p21, PUMA, BAX and a decrease in growth fraction as manifested by low ki67. Beta gal analysis showed that most of the remaining cells after the combination therapy are in senescence state. In order to eliminate the senescent population created as a result of the combined treatment of TMZ and Zinc, we decided to use a senolytic agent Navitoclax (ABT-263) that was demonstrated to be effective in reducing senescent cells by specific inhibition of Bcl-2, Bcl-XL and Bcl-w. Following the addition of Navitoclax to the combined treatment, SF188 cells, but not KNS42, show a significance reduction in viability compare to the combination treatment.

Conclusions: Our results suggest that zinc may serve as a potentiator of TMZ therapy in pediatric patients with GBM and using a second hit with senolytic drug in some cases may be even more beneficial.

V060 SIOP19-0138 | Survival and Prognosis of Patients with Pilocytic Astrocytoma and Piloxyoid Astrocytoma: A Single-Center Study in the Korean Yeungnam Region

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Background/Objectives: Pilocytic astrocytoma (PA) and pilomyxoid astrocytoma (PMA) are brain tumors that are relatively more common in children and young adults. Long-term data pertaining to PA/PMA in the Korean Yeungnam region are limited.

Design/Methods: We retrospectively reviewed the medical records of patients with PA/PMA treated in Keimyung University Dongsan Medical Center between 1988 and 2018.

Results: We included 33 subjects with PA/PMA. The median age at diagnosis was 13.3 years, and the median follow-up duration was 9.9 years. The ratio of PA/PMA to the total number of primary brain tumors was higher in the patients aged <20 years (22.9%) than in those aged ≥20 years (1.2%, $P<0.001$). The total PA/PMA group had a 10-year disease-specific survival rate (DSS) of 93.1% (95% confidence interval [CI]: 83.9–100) and 10-year progression-free survival rate (PFS) of 52.7% (95% CI: 32.9–72.5). In the patients aged <20 years, tumors were more likely to be located in sites where gross total resection (GTR) could not be performed. No statistically significant difference in 10-year DSS was found between the GTR (100%) and non-GTR groups (90.7%, 95% CI: 78.4–100; $P=0.398$). However, a statistically significant difference in 10-year PFS was found between the GTR (100%) and non-GTR groups (38.1%, 95% CI: 16.1–60; $P=0.013$). In the non-GTR group, no statistically significant difference in 10-year DSS was found between the patients who received immediate additional chemotherapy and/or radiotherapy (Add-Tx group; 93.8%, 95% CI: 81.8–100) and the non-Add-Tx group (83.3%, 95% CI: 53.5–100, $P=0.504$). No statistically significant difference in 10-year PFS was found between the Add-Tx group (32.1%, 95% CI: 6.4–57.8) and non-Add-Tx group (50%, 95% CI: 10–90, $P=0.814$).

Conclusions: The PFS of the patients with PA/PMA only depended on the degree of surgical excision associated to the tumor location. This study has limitation due to the small number of patients and the retrospective data.

V061 SIOP19-1610 | Use of Bevacizumab in Pediatric Low-Grade Gliomas: Ten-Year Experience of a Single Center

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Background/Objectives: Pediatric low-grade gliomas (PLGGs) are challenging tumors to treat, especially when unresectable. A strategy combining systemic therapy with close observation when stable has become the standard of care in the last few years. The excellent overall survival of

these tumors and chemotherapy side effects have led clinicians and investigators to look for better-tolerated regimens and more durable tumor control. Bevacizumab, a humanized monoclonal antibody directed against vascular endothelial growth factor, has been used in a number of studies and reports.

Design/Methods: We present a retrospective institutional observational study between 2008-2018 on the safety and efficacy of bevacizumab in the treatment of PLGGs.

Results: Twenty-six patients were identified treated with bevacizumab. Mean age was 4.5 years-old (0.4-16.58 years). Nineteen had optic pathway and chiasmic-hypothalamic gliomas (73%). Nine (35%) patients had neurofibromatosis type 1, 9 (35%) harbored BRAF-KIAA1549 fusion transcript and 2 (8%) the BRAF V600e mutation. We could evaluate toxicity and efficacy of 35 treatment courses. In sixteen (46%) courses bevacizumab was administered in combination with chemotherapy. Responses were assessed at 3 months of treatment, when 13 (37%) had partial response and 21 (60%) stable disease. Treatment response was maintained during the treatment, progression free survival at 12 months was 94% (CI 86.3-100%). Only one patient progressed and died of disease. There was not any severe adverse effect due to bevacizumab treatment. Limiting toxicities included proteinuria and hypertension grade 2 in 4 and 2 patients, respectively. Fourteen cases (40%) presented tumor progression with a median of 25 months from the end of therapy. Eleven patients (42%) had radiologically stable disease with a follow-up of 33 months.

Conclusions: Bevacizumab in PLGGs appears to be clinically advantageous with minimal risk of toxicity. Larger prospective studies are required to determine whether the response is conditional upon different histological and molecular characterization.

V062 SIOP19-0601 | Utility of Bone Marrow Evaluation Prior to Stem Cell Harvesting in Paediatric Brain Tumour Patients Undergoing High-Dose Chemotherapy with Autologous Stem Cell Rescue

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Background/Objectives: High-dose chemotherapy with autologous stem cell rescue (ASCR) is becoming more prevalent in the treatment of malignant paediatric brain tumours. Metastatic spread in paediatric brain tumours is often through leptomeningeal seeding or direct extension. Extraneural metastasis is rare, though brain tumours such as medulloblastoma have been reported to be associated with

metastases outside the central nervous system. It raises questions as to whether documentation of absent bone marrow (BM) metastasis prior to stem cell harvesting is necessary.

Design/Methods: A retrospective study of 22 paediatric brain tumour patients undergoing peripheral blood stem cells harvesting in preparation for high-dose chemotherapy with ASCR was carried out. A majority (n=16) had medulloblastoma. The remaining patients had relapsed suprasellar germ cell tumour (n=2), relapsed primitive neuroectodermal tumour (n=2), pineoblastoma (n=1) and embryonal tumour with multi-layered rosettes (n=1).

Results: Of the 22 patients studied, 11 had a BM biopsy done either at the point of diagnosis or prior to stem cell harvesting. Out of those who were not tested for BM involvement, 1 was subsequently found to have early disease relapse with BM involvement post stem-cell harvesting—it is uncertain if bone marrow involvement was present from diagnosis or only at relapse. All of the patients who underwent a BM biopsy at the time of initial diagnosis did not have BM involvement. In this group, 1 patient developed early and widely disseminated disease progression including BM metastasis, after stem cell harvesting and prior to high-dose chemotherapy.

Conclusions: The study population size is unfortunately small and further studies are recommended to conclude on the utility of BM evaluation prior to stem cell harvesting. Extraneural metastasis can occur in paediatric malignant brain tumours. An index case of bone marrow involvement post-stem cell harvesting suggests benefit of documenting absent BM metastasis prior to stem cell harvesting.

V063 SIOP19-0060 | Optic Pathway Tumor in Children: Toward a New Classification for Neurosurgical Use

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Background/Objectives: Optic pathway tumors (OPT) still represent a challenging topic for the pediatric neurosurgeon. Role of surgery in such lesions is still debated and protocols about therapeutic strategy have not been established yet. During the last decades, therapeutic attitude changes in favor of chemotherapy, as surgery carries a high risk of iatrogenic damage, with reduced QOL status for the patient. However, in some cases, none of the available therapy provides alone a satisfactory result. Considering the complexity and the unpredictability of OPT natural history, each case has to be evaluated individually by pluridisciplinary panel of experts to offer a tailored protocol of care.

With the aim to clarify the place of neurosurgery for OPT, we propose a new, simple and practical classification.

Design/Methods: We analyzed the data of 38 patients with OPT treated in the same institution. Lesion's anatomy and behavior, clinical aspects, treatments and outcome, are discussed. The new classification is based on radiological and anatomical aspects, and it divides OPT in five groups.

Results: Among the 17 children operated on for OPT (large biopsy, debulking, partial or subtotal resection), 11 (68%) presented a PFS superior to 18 months, ranging from 1 to 108 months. Outcome data after surgery showed visual improvement in 1 patient, iatrogenic visual impairment in 2 patients and diabetes insipidus in 3, with an overall complication rate of 29%. There is strong correlation ($p = 0.0002$) between new classification groups and decision of surgical treatment in first instance. Only 1 patient in our series died, with 100% overall survival rate at 5 years and a mean follow up of 8 years.

Conclusions: Surgery can offer a valuable therapeutic complement for OPT, above all in case of refractoriness to chemoradiotherapy, stabilizing tumor without major risk of iatrogenic damage. Eligibility of patients to surgery can be based on a new classification system.

V064 SIOP19-0876 | Single Drug Bevacizumab is Effective in Children with Visual Impairment due to Optic Pathway Glioma: A Retrospective Study

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Background/Objectives: Despite a multidisciplinary therapeutic approach, the visual prognosis of children with optic pathway glioma (OPG) remains poor. Bevacizumab, a monoclonal antibody that inhibits the activity of vascular endothelial growth factor and irinotecan have been used with success.

Design/Methods: We performed a retrospective monocentric study of single drug Bevacizumab in children with OPG and visual impairment. Patients had visual and imaging assessment before and during treatment. For each patient, treatment with Bevacizumab was decided due to visual impairment after collegial discussion.

Results: Twenty children were treated with intravenous Bevacizumab at 10 mg/kg every 2 weeks. Twelve patients (60%) were naive, and 8 patients had received 1 (25%) or 2 (15%) lines of chemotherapy (vincristine/carboplatin, vinblastine or

both). Median age at diagnosis and at Bevacizumab were 3.2 years (range: 0.4-15.7) and 3.9 (0.4-15.8) respectively. A biopsy or subtotal resection was performed in 9 patients. Pathology was pilocytic astrocytoma in all cases (KIAA1549-BRAF fusion in 7). No tumor harbored BRAF V600E mutation. Eight patients (40%) presented with neurofibromatosis type 1. Patients received a median of 16 (4-54) weeks of Bevacizumab treatment, then switched to chemotherapy. First visual and imaging assessments were performed after a median of 4 (2-6) infusions. MRI showed 7 (37%) objective response, 11 (58%) stable disease, 1 (5%) progressive disease, and 1 not evaluable. Functional visual evaluation showed 10/18 and 7/7 patients with visual acuity or field improvements respectively. Only one evaluable patient presented with visual acuity worsening while MRI showed a stable disease. Visual acuity or field improved in all patients with MRI objective response and in 5/10 patients with stable disease.

Conclusions: Bevacizumab without irinotecan is effective in patients with OPG and visual impairment and should be discussed as first line treatment in these patients.

V065 SIOP19-1598 | microRNA-182 Enhances Invasion and Migration in Pediatric Glioblastoma Model

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Background/Objectives: Glioblastoma multiforme (GBMs), the most aggressive malignant primary brain tumors and associated with poor prognosis. The pediatric GBM virulence is mainly due to infiltrative and proliferative characteristics of the malignant tumor cells. In contrast to adults, pediatric GBM cannot be explained only by genetic instability, due to lower number of chromosomal imbalances and much fewer DNA copy number alterations. Expression data of tumors from pediatric patients with GBM revealed that mir182 is overexpressed in these samples. mir-182 is known to be a promoter of migration, invasion, cell survival or proliferation in many cancers.

Design/Methods: We used KNS42 cell line as a model for pediatric GBM. Mir182 expression was inhibited in the pediatric GBM cell line KNS42 using mir182 complimentary oligonucleotide and the effect on migration, invasion, cell survival.

Results: Inhibition of mir182 decreased cell migration, cell invasion and upregulated the expression of mir34 family members, in KNS42 cells. Mir182 inhibition also shifted the conformation of p53 from mutant to wildtype conformation.

Conclusions: Mir 182 may have a role in the virulence of pediatric GBM by enhancing migration and invasion

capabilities. Inhibition of mir-182 also activates the p53 which is important for the success of chemotherapy treatment.

V066 SIOP19-0409 | Clinical Outcomes of Children with Primary Brain Tumors Treated with Pencil Beam Scanning Proton Therapy

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Background/Objectives: Brain tumors affect 11,000 children <19 years in Western Europe yearly. The long-term treatment-related toxicity burden is significant in these cancer survivors. Strategies to reduce toxicity include the use of highly conformal radiotherapy techniques such as Pencil Beam Scanning (PBS) proton therapy (PT). The aim of this study is to report late clinical outcomes in children with brain malignancies treated with PBS.

Design/Methods: We retrospectively reviewed data from 222 patients diagnosed at <18 years of age with primary brain tumors, treated with PBS PT, and with >12 months of follow-up (FU). Overall survival (OS), disease-free survival (DFS) and local progression-free survival (LPFS) were calculated using Kaplan Meier estimates. Median FU was 51 months (range, 4-222; 12 deaths <12 months after PT).

Results: The cohort contained 130 males (59%) and 92 females (41%). Median age at diagnosis and at PT start were 3.1 and 4.1 years, respectively. The most common histologies were Ependymoma (n=88;39.6%), Low-grade glioma (n=30;13.5%), Craniopharyngioma (n=22;9.9%), Atypical Teratoid/Rhabdoid Tumor (n=21;9.5%) and Medulloblastoma (n=15;6.8%). Tumor resection status before PT was total, subtotal or biopsy only in 80 (36%), 111 (50%) and 20 (9%) patients, respectively. Overall, 161 patients (72.5%) received chemotherapy; in 61 (17%) cases concomitantly with PT. Median PT dose was 54Gy (RBE) (range, 18-64.8). The 4-year OS, DFS and LPFS (95% CI) were 85% (+/-5.0), 68% (+/-6.7) and 75% (+/-5.9), respectively. Late neurological toxicity data was available for 199 patients. Late grade 3, 4 and 5 events occurred in 16, 2 and 1 patients, respectively. Radiation-induced grade 2 pituitary disorder occurred in 40 (18%) cases. There were 5 (2.3%) secondary malignancies.

Conclusions: Survival/disease control outcomes reported in this PBS series compare well to previously published data from children with brain tumors treated with other irradiation modalities. The observed toxicity was acceptable and manageable. Of note, secondary malignancies occurred in approximately 2% of children.

V067 SIOP19-1345 | Anti-PD-1 Treatment in a Family with Constitutional Mismatch Repair Deficiency Syndrome with Multiple Cancers From Turkey

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Background/Objectives: Constitutional mismatch repair deficiency (CMMRD) a rare childhood cancer predisposition syndrome resulting from biallelic germline mutations of MMR genes. We present affected children of consanguineous parents dx with CMMRD syndrome of germline bi-allelic MSH6 mutations with multiple cancers, mimicking NF1 in a family with 6 children from Turkey

Design/Methods: 8-yr-old female, referred with brain tumor w follow up NF1& FMF. One of the female siblings died of aggressive brain tumor at 4yrs of age, one male siblings due to medulloblastoma, followed by dx of a metachronous metastatic colonadenoca at 15yrs of age. Family cancer history included colorectal ca, brain tumor, papillary thyroid ca. On PE 8-10 cafe-au-lait spots and hypodense macules were found. Lab tests were normal w low IG G2 levels. Cranial MRI a mass in the left cerebellar region, subcortical hyperdense lesions in fronto-parietal area. She underwent near-total resection, histopathology revealed classic desmoplastic medulloblastoma. Postoperative craniospinal MRI showed no residue or metastasis. Craniospinal RT and CT of CCNU, cisplatin, VCR were given. Because of colon adenoca history in her family, the colonoscopy was performed, with no polypoid lesions

Results: Genetic analysis disclosed a novel homozygous single base insertion mutation in exon 5 of the MSH6 gene (c.3261dupC/ p.Phe1088Leu). Five cycles of chemotherapy & Nivolumab was commenced at 3 mg/kg/dose in every 2wks as new polyps detected. After 10th dose, 9 polyps were removed of tubular adenoma. She is still on antiPD1 tx (18th dose in remission. Last colonoscopy revealed only one polyp 6mm size. One female sibling 24mos old w multiple cafe-au-lait spots to be homozygous, under FU with screening tests of possible neoplasms. The parents & 2 siblings (11 and 6 yrs old boys) are heterozygous, male sibling, died of medulloblastoma and colorectal ca had the same homozygous mutation.

Conclusions: As the use of immune modulation for cancer prevention rather than therapy has gained considerable attention, we wonder if 24-mos-old female sibling with homozygous mutation will be a candidate for cancer immunoprevention with AntiPD1 drugs.

V068 SIOP19-0440 | Clinical Outcome and Quality of Life of Children and Adolescents/Young Adults with Craniopharyngioma Treated with Proton Therapy

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Background/Objectives: The current study aims to report the clinical outcome and quality of life (QoL) of children-adolescents/young adults (AYAs) with craniopharyngioma (CP) treated with proton therapy (PT).

Design/Methods: A total of 16 CP children/AYA (median age, 9.5 years) who underwent PT (54 GyRBE) at the Paul Scherrer Institute between 2008 and 2014 were analyzed. Thirteen (81%) patients had hypopituitarism prior to PT. Twelve (75%) had visual defect prior to PT. QoL data were prospectively collected using questionnaires which are established, multidimensional instruments that covers 8 domains and is available as proxy-rating version for the parents (PEDQOL- & PedsQL-proxy) and self-rating version for children older than 4 years (PEDQOL-self).

Results: After a median follow-up time of 48.5 months, tumor size decreased for 3 (19%) patients and remained stable for 13 (81%) other patients. One patient with visual defect had improved visual function and 3 patients with partial visual defect prior to PT had a decline in visual function. The estimated 3-year vision preservation rate was 92.8%. The 3-year survival without new anterior pituitary deficit was 77.3%. Two (12.5%) radiation-induced cerebral vasculopathies (RICVs) were observed 14 and 24 months (median, 19) after PT. A total of 14/16 patients were analyzed for QoL. At baseline (E1) and two months after PT (E2), the QoL was globally lower when compared to the normative cohort but not significantly so (E1: 66.7±18.3 vs. 81.5±17.9; E2: 64.3±15.0 vs. 81.5±17.9). Two months after PT (E2), the QoL scores continue to significantly decrease for cognition, physical functioning and social functioning/peers when compared to the normative population, whereas for self-esteem, emotional, social functioning/family and body image the scores increased non-significantly when compared to E1.

Conclusions: Tumor control of recurrent or residual CP treated with PT was good. Two RICVs were observed. Two months after PT, some QoL domains are increased others are still decreasing.

V069 SIOP19-0320 | Identification of Molecular Targets in Pilomyxoid Astrocytoma

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Background/Objectives: Pilomyxoid astrocytoma (PMA) is a recently recognized variant of pilocytic astrocytoma (PA) with more aggressive clinical behavior, but ultimate WHO grading has been deferred pending further clinical studies. We report our experience with PMA, including results of tumor whole exome sequencing.

Design/Methods: Between 2002 and 2017, 12 children were diagnosed with PMA, and 5 were referred following surgery elsewhere. Outcomes were recorded for time from diagnosis to last follow-up or death. Tumor whole exome and transcriptome sequencing were performed in a CLIA-certified laboratory.

Results: Patient age range was 3 months to 10 years 10 months (median 3 years 9 months). Primary site was optic nerve (1), suprasellar (4), hypothalamus (1), 3rd ventricle (1), thalamus (2), temporal lobe (1), pineal (1), cerebellar (3), and cervicomedullary (3). Leptomeningeal dissemination occurred in 1 patient. Surgery was gross total resection in 6, subtotal resection in 6, and biopsy in 5. Pathology showed predominantly solid circumscribed lesions with myxoid matrix. Ki67 proliferation index ranged from 2 to 11.6% (median 5%). Intratumoral hemorrhage was noted in 7 cases. Tumor whole exome and transcriptome sequencing in 4 patients showed KIAA1549-BRAF fusion in 3, with potentially targetable high expression outliers noted in one case. Treatment included chemotherapy in 14 patients, with 7 requiring additional chemotherapy at disease progression. Two patients received radiation therapy. One patient died of multiply progressive tumor. Overall survival was 94%, median survival 7.5+ years, and median progression-free survival 5.2+ years.

Conclusions: PMA differed from PA by younger age, higher Ki67 proliferation index, more frequent intratumoral hemorrhage, and decreased progression-free survival, but not decreased overall survival. Results of tumor sequencing confirm a potential therapeutic role for MEK inhibitors, with possible additional targeting of tumor-specific high expression outliers to circumvent resistance.

V070 SIOP19-0031 | Prognostic Factors in Children with Atypical Teratoid Rhabdoid Tumors (AT/RT) of the Central Nervous System

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Background/Objectives: Evaluation the prognostic factors in children with AT/RT of central nervous system.

Design/Methods: Analyzed the prognostic factors in 72 patients treated from 2003 to 2018. The median age was 22 months (2 months-15 years old), 35 (48, 6%) boys, 37 (52, 4%) girls. Tumor location supratentorial-55, 5%, infratentorial-40, 2%, multifocal-2, 7%, 1, 4%-in the spinal cord. 56, 9%-M0, 30, 6%-M+ or a multifocal tumor, the stage was not evaluated in 12, 5%(Mx). All the patients underwent initial surgery: total in 24 (33.3%), subtotal in 30 (41.7%), partial in 15 (20.8%), biopsy in 3 (4.2%). 52 (72,2%) patients got chemoradiotherapy by protocol ATRT-2006; 6 (8,3%)-CWS; 6 (8,3%)-EU-RHAB; 5 (7%)-HIT-SKK; individual treatment-3 (4,2%) patients.

Results: 34 patients (47,2%) are alive, 38 (52,8%) died. 30 deaths were due to progressive disease, 4-to chemotherapy complications. Progression-free survival (PFS) was 34%±0.06; 5-year overall survival 43%±0.06. The median survival was 28 months, the median PFS was 15 months. The median time of observation was 23 months (2 to 161 months). PFS was higher in patients above 2 years old compared to those younger than 2 years (45% and 24%, p=0.01), in girls compared to boys (48% and 18%, p=0,04). In the cases of total tumor removal, the survival was better compared to subtotal, partial removal and tumor biopsy (50%, 38%, 0%, 0%, respectively, p=0,02). Radiotherapy improved the survival compared to those who did not get it (craniospinal 62%, local 58%, without radiotherapy 0%, p=0,000). PFS of M0 stage was better compared to M+/multifocal tumors/Mx (43%, 18%, 38%, respectively, p=0,001). The PFS higher in the cases of supratentorial location compared to infratentorial: 42% and 23%, p=0,036. 5-year survival was better in patients treated according to ATRT-2006 (40%) compared to CWS (17%); 2-year survival was better in the patients treated by EU-RHAB compared to ATRT-2006, individual schemes, CWS and HIT-SKK (50%, 42%, 34%, 17%, 0%; p=0,009). The survival was higher for intraventricular/intrathecal administration of Methotrexate/Ara-C/Prednisolone compared to use only Methotrexate or no drugs at all: 40%, 20%, 12%, respectively; p=0,01.

Conclusions: Survival patients depended on the age, sex, localization, presence of metastases, extent of surgery, chemotherapy protocol, use of radiotherapy and regional chemotherapy.

Childhood Cancer International (CCI)

V071 SIOP19-0267 | Parental Perception of Severe Acute Malnutrition in Children with Cancer in Malawi

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Background/Objectives: The risk for severe muscle wasting in children with cancer in resource-limited countries is high as malnutrition is prevalent. Little is known about patient family perceptions regarding cancer-related severe acute malnutrition (SAM). The objectives of this study were to assess the perception among guardians of children with cancer-associated severe malnutrition and to identify barriers to improving care and management in these settings.

Design/Methods: This qualitative pilot study was conducted on the Pediatric Hematology-Oncology ward at Kamuzu Central Hospital (KCH) - a tertiary level health facility serving the Northern and Central regions of Malawi. Guardians were consented for the study. The study population included primary caretakers of children (< 19 years) with cancer and SAM. And secondly English/Chichewa as primary language, stable clinical condition, and availability for interviews at the time of the study. Using a purposive sampling method, we enrolled patients until thematic saturation was reached. Data was collected using a semi-structured interview tool and conducted in Chichewa, recorded using a phone, and translated into English using a forward and back process. Data were coded to identify themes, anonymized, and confidentiality secured.

Results: Eleven primary care givers were interviewed (10 females, 1 male). Diagnoses included Burkitt lymphoma (n=4), neuroblastoma (n=3), Wilms tumour (n=1), Hodgkin lymphoma (n=1) and acute lymphoblastic leukemia (n=2). Themes included awareness of cancer-related SAM, inadequate communication with health professionals, social isolation, loss of control of child's illness, and insufficient social support. Identified barriers to improving management of these patients and their families included the pressure of social stigma, different belief systems about the cause of illness, and inadequate knowledge sharing by health professionals.

Conclusions: Our results suggest that qualitative methodology is a useful approach for engaging caregivers. Next steps could include developing interventions in this population or testing the generalizability of this methodology elsewhere.

V072 SIOP19-0517 | Pediatric Oncology Implementation Strategies in Low to Middle Income Countries. Sustainability: A Criterion, A Measure Or An Objective?

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Background/Objectives: The Sanofi Espoir My Child Matters Programme (MCM) aims to contribute and promote initiatives in Low-to-Middle-Income Countries to reduce the pediatric cancer burden worldwide. Since 2006, MCM has called for proposals from the pediatric-oncology healthcare community. In 2019, MCM received a number of submissions from institutions that had been previously granted. We noticed that sustainability applied to these projects, tends to shift from an eligibility criterion, to a measure or to an objective.

Design/Methods: "A health care is considered sustainable when operated by an organizational system with the long-term ability to mobilize and allocate sufficient resources" (Olsen, 1998). In principle, sustainability is the carrying ability of the organization promoting activities and services. Pediatric oncology-related sustainability depends on the existing ability of the country to deliver at least essential care to their citizens, which is intrinsically connected to the income level. Using these concepts, we performed a descriptive analysis of how sustainability plays a role according to the profile of the interventional strategy proposed by candidates.

Results: Among 197 concept-notes, 57 underwent full-review. Among these 57, 24 were a continuation of a previous grant. This result raised the question on their sustainability. Sustainability was considered an eligibility criterion whenever the project disclosed an upstream strategy. This was the case of proposals focusing on training since human investment has lasting impact in the community. In the case of projects proposing an innovative solution, sustainability was considered a measure for evaluating the degree of strategy implementation. For the projects demanding a renovated effort for pursuing the same initiative, sustainability was considered the objective.

Conclusions: Sustainability as an integrator of social and financial performances should be an eligibility criterion in projects with an upstream strategy. Sustainability as an objective should be addressed as routinization/institutionalization.

To this purpose, the alliance of local governments and health authorities is crucial.

V073 SIOP19-0755 | Impact of Second Opinion Using Telepathology to Support Diagnosis in Paediatric Oncology in Africa

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Background/Objectives: In order to improve diagnosis accuracy in paediatric oncology, to report paediatric tumours according to the SIOP protocols in Africa and to involve African pathologists in research and publications, a GFAOP pathologist panel including 10 French-speaking African Sub Saharian countries and 2 Maghreb countries was created in 2017 in order to develop south to south collaboration.

Design/Methods: The 5 aims of this committee are: (i) to promote telepathology in Africa, (ii) to train African pathologists, (iii) to review paediatric tumours, (iv) to propose research projects, (v) to publish. With the NGO, AMCC (Alliance Mondiale Contre le Cancer), microscopes with a digital camera were set up and connected to the internet INCTR i-Path platform in 11 French speaking African Countries.

Results: Between 2015 and 2018, 79 cases from 6 countries were reviewed using the i-Path platform, mostly for a second opinion (97%) or teaching (didactic cases) (3%). Diagnosis was performed in 73% of cases whereas diagnosis was partially or not feasible in other cases (27%) due to poor technical quality. In 70% of cases, diagnosis was made in less than 1 day underlining the efficiency of telepathology. All the paediatric cases (29 cases, 30%) were represented by malignant tumours: Burkitt lymphoma (6), leukaemia (4), lymphoma (2), soft tissue tumour (5), Wilms tumour (4) and others (2).

Conclusions: Telepathology is a useful tool to improve communication between European and African pathologists in order to accurate diagnosis in paediatric oncology and treat African children according to the SIOP protocols.

V074 SIOP19-1495 | Anticipatory Guidance in Pediatric Oncology: Art–Therapy Based Supportive Intervention During A Diagnostic and First Treatment Phase

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Background/Objectives: Time frame surrounding diagnosis and first chemotherapy is an overwhelming experience loaded with uncertainty, which determinates child and family's compliance and adaptation process. Within days parents receive extensive cancer information, make important treatment related decisions, giving at the same time emotional containment to their child, who concurrently faces painful diagnostic procedures, diagnosis communication and first chemotherapy. It is a challenge to help a frightened child and his family as they have different needs for information and reassurance. We use structured art-therapy based approach to set an individual, supportive intervention.

Design/Methods: The art-therapy trained psychologist follows the family since their first steps into the unit: during medical interviews, diagnostic procedures, diagnosis communication and treatment. Since the very beginning offers expressive activities, stimulating the child to find proper inner 'safe place'. Activities are conducted in child-friendly deliberately designed space in the unit. Psychologist prepares for and assists during diagnostic painful procedures through imagery stimulation and recalling the 'safe place image', helping the child to face the experience and to express preferences for pharmacological support. During age appropriate diagnosis communication reassuring reality-based cartoon style images are recalled to contrast fearful fantasy-based images of cancer. Expressive laboratories are offered to the caregivers as well apart from clinical dialogue.

Results: The Arts Observational Scale (ArtsObs) was used to evaluate the intervention. Art-therapy facilitates the treatment compliance and helps to stimulate the child when overwhelmed by cancer experience, restoring sense of normality. Art becomes important clinical tool helping to assess individual's elaboration process and coping.

Conclusions: All families should receive support attuned to their specific needs since the first hospitalization. Art therapy becomes an important allied creating a respectful space, where an individual needs can be embraced. It helps to elaborate emotional burden of the diagnosis, promoting growth and development.

V075 SIOP19-1701 | Improving Survival Rates in All Patients in Clinica Angloamericana, Peru

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Background/Objectives: The cure rates in children with cancer in public hospitals in Peru are not as good as those in European or US countries. We believe that this can change by improving the hospital infrastructure and the care that these children receive.

Design/Methods: This is a retrospective and descriptive study. Patients with diagnosis of acute lymphoblastic leukemia between the ages of 0 and 17 years were admitted at our place between 2010-2019. For analysis we only include patients that have complete treatment in our center and have complete data. Epidemiological, clinical, laboratory and treatment results were recorded. Survival analysis was performed using Kaplan-Meier method.

Results: 70 patients with ALL diagnosis were admitted at our place, 57 were evaluable for analysis. Median age of the 57 evaluable patients was 5.6 years, male to female rate was 1.59. 51 patients had precursor B cell ALL, 2 of them were Down Syndrome patients and other 2 were less than 12 months, the other 6 had precursor T ALL. Of the B ALL patients, 25 had high risk (53.2%), 14 had intermediate risk (29.8%) and 8 had low risk disease (17%). 31.9% of B ALL patients were ETV6/RUNX1 (+) and 6.4% were BCR/ABL (+). Event free survival for the entire cohort was 91% at 5 years, 89% for high risk, 83% for intermediate risk and 100% for low risk B ALL patients. The 2 patients with infant ALL and the 2 patients with Down Syndrome are alive and free of disease after completing treatment, as well as the 6 T ALL patients.

Conclusions: Good survival rates for pediatric ALL patients can be achieved in a country like Peru, similar to developed countries, improving care of these children like in Clinica Angloamericana.

V076 SIOP19-0251 | An International Collaborative Effort to Treat Children with Acute Lymphoblastic Leukemia/Lymphoblastic Lymphoma in Belize

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Background/Objectives: Pediatric acute lymphoblastic leukemia (ALL) has excellent outcomes in high-income countries, with 5-year survival approaching 90%. This success has not been replicated in low-income countries such

as Belize because of multiple barriers. Belizean children seeking treatment for ALL must travel out of the country for care, posing significant financial and familial challenges that result in abandonment of treatment or a decision not to treat newly diagnosed patients.

Design/Methods: In 2008, Belize Cancer Center-Dangriga (BCCD) was established as the only cancer treatment center in Belize. This center functions as an ambulatory chemotherapy unit with a staff of two oncology nurses and a clinic coordinator. Periodic visits are conducted by a US-based adult hematologist/oncologist; otherwise, treatment is guided via telemedicine.

Since opening, BCCD established a twinning program with pediatric oncologists at Hospital O'Horan (HOH). Upon diagnosis, children are evaluated at HOH, where initial, high-intensity and intrathecal treatment is provided. Lower-intensity treatments are given at BCCD.

We retrospectively reviewed results of this 10-year experience.

Results: Since 2008, 52 Belizean children with cancer have been referred to HOH, of which 19 received treatment for ALL or stage IV lymphoblastic lymphoma (mean age 5.1 years, 12 male). The treatment schema was based on Total XV for ALL. Children received most of post-consolidation chemotherapy at BCCD. Intrathecal chemotherapy was given at HOH. Six patients remain on treatment. Five-year overall survival for this cohort was 67%; event-free survival was 58%.

Conclusions: The creation of BCCD and the BCCD-HOH twinning program has offered the possibility of cure for children with ALL. BCCD has improved access to care by providing in-country access to chemotherapy, thereby eliminating cost and other burdens associated with frequent out-of-country travel to obtain care. This model can be replicated in other resource-limited settings, but it requires a dedicated team and strong collaborative efforts

V077 SIOP19-0406 | Cancer in Refugee Children in Turkey

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Background/Objectives: Treatment of cancer in refugees 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 treated in Turkey between 2016-2018 and to evaluate the problems encountered and to compare the results with those obtained between 2013-2015.

Design/Methods: The records of refugee children with cancer treated in five centers in two cities in Turkey, Adana (in the southeast, close to the border) and Istanbul, between 2016-2018 were evaluated retrospectively.

Results: The median age of 214 children (male:female, 1.8:1) with cancer was 5 years (1-17). Most (75%) had advanced disease. The diagnosis were acute leukemia in 18%, lymphomas 18%, brain tumors 14%, neuroblastoma 8%, bone and soft tissue sarcomas 14%, Wilms tumor 11%, retinoblastoma 4%, and other 13%. Forty-one additional patients underwent hematopoietic stem cell transplantation. All treatment was reimbursed by the government, 64% patients are alive, 16% have died, 20% were lost to follow up. The most frequent problems encountered in centers in Adana were accommodation (92% lived outside camps in the current study), social and psychological problems, hygiene, language barriers, compliance with therapy, some similar to the previous study; in centers in Istanbul, there was improvement in housing conditions, hygienic measures in the family, compliance with treatment.

Conclusions: The frequency of the most common three types of pediatric cancer and the outcome according to stage was similar to that of Turkish children, male-to-female ratio and the percentage of lost to follow up was higher. It was encouraging to observe that in Istanbul, in those living in Turkey for a longer time, there was improvement in problems encountered. These results may help to inform future responses in children with cancer who are forced to migration.

V078 SIOP19-1153 | Mental Wellbeing Screening Tool for Family Support Coordinators to Assess Counselling Needs For Parents and Caregivers

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Background/Objectives: To create a screening tool that can be used by non-clinical professionals to accurately determine the counselling needs for a parent or caregiver during the course of the professionals interactions with the families.

Design/Methods: A tool has been developed in conjunction with the Cancer Psychology Service at Massey University. The tool has been adapted so that Family Support Coordinators, who work with families in the community. can safely

use the tool, with the permission of the parent or caregiver, to gauge their level of mental wellbeing at points along the childhood cancer journey and determine whether additional counselling support is needed that cannot be funded through government agencies or the medical institutions. Mental wellbeing is becoming an increasing important area of concern in New Zealand and government agencies cannot meet the demand or needs of all potential beneficiaries.

Results: The tool has been adapted from clinical tools and built in conjunction with the Family Support coordinators to use in the field. It is being piloted as this submission is being written and it is intended to put into general practice in our service by the end of this year. Results of the pilot will be shared with the Congress participants.

Conclusions: As yet undetermined.

V079 SIOP19-0456 | The “Golden-Hour” Intervention to Improve Time to Antibiotics in a Resource-Constrained Setting: Application of Health System Strengthening Principles to Achieve its Successful Implementation and Sustainability

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Background/Objectives: Febrile neutropenia (FN), an oncologic emergency, requires timely antibiotics administration. Health System Strengthening (HSS) includes actions to ensure sustained improvements in the provision, utilization, quality and efficiency of health services, including clinical interventions. We applied the HSS principles during implementation and sustainability phases of the “Golden Hour” intervention, aimed at decreasing time to antibiotics (TTA) in patients with FN at the Hospital General-Tijuana.

Design/Methods: We conducted a 5-year prospective study (2014-2018) in patients with FN at our pediatric oncology unit. HSS principles of *holism, context and collaboration, social mobilization, capacity enhancement, equity, financial protection and evidence-informed action* guided our implementation and sustainability planning.

Results: *Holism:* we improved processes systemically, at multiple levels (hospital/unit/provider and patient/family), and procured mentorship from external advisors. *Context and*

collaboration: through capacity-building, engagement and adaptation, staff, patients and caregivers engaged themselves during implementation. *Social mobilization:* with the support of our grass-roots foundation, we ensured the long-term sustainability of the “Golden Hour”. *Capacity enhancement:* nursing staff achieved autonomy upon patient arrival to start antibiotics. *Equity:* TTA was reduced from a mean of 68.9 minutes to 44.34 minutes ($p=0.001$) and intensive care admission rates dropped from 45% to 9% ($p=0.009$). We successfully achieved equity in clinical outcomes in an underserved population equivalent to outcomes in high-income countries. *Financial protection:* local foundation, extramural grant funding and government support have assured long term financial sustainability. *Evidence-informed action:* the “Golden Hour” was designed based on baseline data from 2013, which showed high rates of septic shock due to prolonged TTA.

Conclusions: In a resource-constrained setting, we demonstrated that the application of HSS principles in a multilevel intervention, such as the “Golden Hour”, facilitates successful implementation and long-term sustainability. The “Golden Hour” is now a recognized clinical intervention in Mexico and is being implemented in 7 pediatric oncology units nationally.

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V080 SIOP19-0419 | Broad Cancer Alliances – The Power of Collaboration

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Background/Objectives: Before 2010 cancer in South Africa was voiceless and didn’t have a significant impact on change for the treatment and care of cancer patients. Individuals advocated for cancer through their own experiences and some even started their own NGO’s. Over the past decade the power of collaboration brought change and political will when Alliances and Networks were officially formed.

Design/Methods: In 2010 a cancer survivors summit were held in Cape Town (SA). In this call to action survivors were asked to break the silence, stand up and speak. Cancer organisations and healthcare professionals were asked to be active in advocacy collectively. The Cancer Alliance SA was formed and provides a joint platform for 30 cancer related non-profit organisations and advocates to work together on issues of national importance. Members agree to be governed by the Membership Agreement and associated Code of Ethics.

Results: Cancer in SA became a national priority and the National Department of Health and started to listen and

consult with the Cancer Alliance. During the President's speech of the nation he launched a national cancer awareness campaign. A ministerial advisory cancer committee on cancer prevention and control were appointed and several cancer policies were written and approved by Government. Advocacy Toolkits for the plans were written and are being used with great success.

Conclusions: It is only when the cancer community in SA began to collaborate the imbalances; inequity and disparities could be addressed. Powerful advocacy requires organizing and organization, a strategy and actions to influence the decisions, practices and policies.

V081 SIOP19-0421 | Research Priorities for Brain Tumours from Families' Point of View

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Background/Objectives: Georgia Bain, aged eight was diagnosed with a brain tumour and after 30 radiation sessions, had cognitive and motor challenges to integrate back into the mainstream school system in South Africa. After a lengthy search and many disappointments, the Bain family met with CHOC to discuss how we could work together as an NGO and the family to develop resources to assist other families that experience the same challenges.

Design/Methods: It was important not to reinvent the wheel; however resources available had to be adapted to the SA context. Funds were raised to support the new programme; contacts were made with the other NGOs, international partners, parents of brain tumour children and experts with specialized academic background. This working group will assist CHOC to design resources according to the new strategy for the programme. CHOC was invited to do an advocacy workshop for brain tumour patients at the Society for Neuro Oncology of Sub-Saharan Africa Conference during August 2019. The findings from the workshop will assist us to enhance and develop our new programme of support.

Results: CHOC now has a new programme called Cognitive Support Services assisting patients with cognitive challenges beyond treatment. We are expanding our offer to fund neuro assessments nationally. Our aim is to have material available by end December 2019 to give parents guidance and resources on the best opportunities for their children's academic and social future.

Conclusions: CHOC is a support organisation and do not have the resources to provide other specialised services, however we can develop resources that we can share with other NGOs and parents on different media platforms to support and assist parents that experience mutual problems. As an NGO we listen to our parents, work with them and the medi-

cal teams to assist the children post treatment to become socio economic independent adults.

V082 SIOP19-0239 | The Perceptions of Children / Adolescents with Cancer Regarding Their Experiences of Reflexology or Sham Reflexology as Part of a Randomised Controlled Trial

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Background/Objectives: The aim of this presentation is to discuss the perceptions of children/adolescents with cancer regarding their experiences of reflexology or sham reflexology.

Children and adolescents with cancer are at risk of experiencing distress as a result of their cancer diagnosis, treatment and treatment-related procedures. Pain, sadness, worry, lack of appetite, fatigue and vomiting have been found to cause the most significant distress. Reflexology involves the stimulation of predefined pressure points on the feet and hands. This controlled pressure is believed to correspond to specific body organs. Despite previous findings highlighting the popularity of reflexology among children with cancer, there is a dearth of research on the impact of reflexology on children and adolescents with cancer.

Design/Methods: Ethical approval was granted from the corresponding hospital's Research Ethics Committee. Children and adolescents aged between 7 and 18 years attending a national children's hospital for cancer treatment were invited to participate in a randomised controlled trial using a Mixed Between Group Repeated Measures design. In total, 75 children/adolescents either consented or assented to take part in the study. Of these, 39 were randomized to the intervention group (reflexology) and 36 to the control group (sham reflexology). Semi-structured interviews were undertaken with children/adolescents using an interview guide. Interviews were analysed using Braun and Clarke's (2006) thematic analysis.

Results: The main finding which emerged from the interviews was that the children/adolescents experienced a sense of wellbeing following both reflexology and sham reflexology. This central theme is discussed under a number of subthemes, namely, psychological benefit, perceived physiological impact, a 'different space' and relationship with the therapist.

Conclusions: Children and adolescents with cancer reported positive experiences following both reflexology and sham reflexology. The implications of the study findings and the future delivery of the complementary therapy service will be discussed.

V083 SIOP19-1202 | “Hayim for Children with Cancer in Israel” Association - in the Service of Children with Cancer in Israel

D. Orren¹

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Background/Objectives: The Hayim Association was founded by parents of children with cancer in 1984. Active in most Children's Oncology wards throughout Israel with the goal of assisting and reducing the suffering of children and their families, and improve the quality of health care.

The association is a member of CCI.

The association's achievements include: Assistance in establishing the first night care ward for children with cancer, and later setting up a children's bone marrow transplant ward.

Main activities: Supporting the Israel Medical Association for Pediatric Hematology and Oncology in gathering and coordinating medical information on child cancer.

Purchase of sophisticated equipment for improving diagnosis and treatment.

Funding studies and development of sophisticated methods for improving Diagnoses and optimal care and medical staff participation in conventions and seminars.

Supporting families with financial problems due to their child's disease, including funding support groups, trips and fun days.

Design/Methods: Unique activities: A program with the Israeli Air Force to empower and entertain children with cancer. Groups of children, (Jews and Arabs alike) visit a base, receive flight suits, are shown the fighter planes, seat in the cockpit, each child is accompanied by a pilot. Getting the feeling of being a pilot and in control makes wonders with their self-esteem.

Results:

Conclusions: Another involvement in a project is named “Surgical 3Dprinting lab” in the Tel-Aviv Medical Centre which develops an innovative platform for 3D surgical planning and execution of malignant bone tumor resections and complex osteotomies. The project introduced a new innovative platform for 3D surgical planning and execution of bone tumor resections and complex osteotomies in the Israeli Orthopaedic-Oncology. Basically it enables creating 3D com-

puterized and printed models of tumor, and 3D planned and printed Patient Specific Instruments (PSI), to assist in conducting accurate surgical procedures with final aim of accurate and controlled histological margins.

V084 SIOP19-1102 | Impact of a Latin America-Wide Teleconferenced Brain Tumor Board

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Background/Objectives: Pediatric-cancer cure rates are ~80% in high-income countries (HIC) however, 80% of children with cancer live in low-to-middle income countries (LMIC) where chances for cure are much lower. Pediatric neuro-oncology requires a multi-disciplinary effort challenging to achieve in LMIC. We started a pediatric neuro-oncology teleconference to help improve healthcare disparities for children in Latin America with brain tumors. We summarize our efforts.

Design/Methods: Utilizing a web-portal provided by cure4kids.org we connect HIC-global-pediatric neuro-oncologists with pediatric subspecialists in Latin America. Weekly, real-time, 60-minute sessions are held in Spanish. Minutes are sent in Spanish with pertinent literature after each meeting to solidify recommendations and education.

Results: In 2013, we started with one country and 6 members. Substantial growth and data acquisition occurred to include 20-countries throughout Latin America with growing membership- 2015: 44, 2016: 121, 2017: 199, and 2018: 275; and participation- median of 17 (range: 9-22) in 2016 to 25 (range: 11-40) in 2017 ($p=0.0005$), and median 31 (range: 14-44) in 2018. This required more sessions 2015: 13, 2016: 34, 2017: 47, and 2018: 43. The total number of cases reviewed were- 2015: 22, 2016: 73, 2017: 132, 2018: 143; demonstrating 2017 and 2018 had statistically more cases per session, on average, than 2016 ($p=0.004$) and 2015 ($p=0.007$).

Conclusions: The growing size of our program demonstrates a reassuring response by Latin America. We provide systematic and effective communication among providers in their language. We succeeded in connecting institutions of differing resources and experience with global-pediatric neuro-oncologists from leading cancer-centers in HIC to help improve the care of children with brain tumors in Latin America and promote continuing education for their providers.

V085 SIOP19-1696 | Building International Pediatric Cancer Data Commons: The Pediatric Acute Leukemia (PEDAL) Initiative

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Background/Objectives: The paucity of pediatric cancer cases makes consortium-based studies necessary to collect sufficient sample sizes. The University of Chicago's Pediatric Cancer Data Commons (PCDC) group supports these research programs by creating disease-specific consortium-based collections of harmonized clinical trials data that can be connected to genomic, proteomic, and other data sources. The data commons underlying the Pediatric Acute Leukemia (PedAL) initiative must support internationally-balloted data standards, disparate data sources, and robust governance. Here we describe the process of designing and implementing the PedAL data commons. The platform described here can be extended to other diseases and should serve as a paradigm for general data commons development.

Design/Methods: Prior data commons design and architecture were reviewed. Stakeholders were interviewed and retained as consultants for PedAL efforts. Previous neuroblastoma and soft-tissue sarcoma data commons were leveraged to identify the opportunities and challenges in developing international consortia and creating and balloting data standards. The international AML community was engaged to generate interest and to assist in identifying research questions best enabled with a data commons. The results of these inquiries have been synthesized into a best practices document for data commons construction.

Results: We have identified the main components of data commons development as stakeholder engagement, data governance, data standards and harmonization, infrastructure selection and implementation, and sustainability. We show that data governance, including data contributor and use agreements, is one of the most critical early steps in data commons development. We have chosen the Gen3 infrastructure, supported by the NCI's Cancer Research Data Commons program. Finally, we propose several models for sustainability, including public-private partnerships and researcher-supported models.

Conclusions: Data commons are critical to research into pediatric cancer. Keeping data standards, infrastructure, stakeholder support, governance, and sustainability at the forefront is critical to new research paradigms and will be transformative for pediatric cancer.

V086 SIOP19-1726 | Clinical Adverse Factors for Central Nervous System Relapse at Primary CNS Infiltration in a High Risk all Pediatric Hispanic Cohort. National Institute of Pediatric, Mexico

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Background/Objectives: Introduction: In Mexico, pediatric cancer went from the 13^o place as a cause of death in 1971, to 2nd place among the population from 1 to 14 years after the year 2000 after accidents. ALL is the malignant pathology that involves the central nervous system, for that reason still an important clinical problem. Clinical features in our institution is different.

Objective: Describe clinical factors to predict relapse to central nervous system in the Hispanic population.

Design/Methods: Methods: A cohort study was conducted in patients with Acute Lymphoblastic leukemia from January 2012 to October 2018, at National Institute of Pediatrics.

Results: We included 184 patients, 105 male, 27 had primary central nervous system infiltration (PCNS) in a very high proportion (14.7%). Only 63% were diagnosed with blasts in cerebral spinal fluid. 96.2% were B cell leukemia, 7.1% had t (1;19), 3% t (12;21), 0.5% t (4;11) and 3.3% t (9;22). All patients received St Jude XV at first line of treatment. 44 patients (23.9%) had a systemic relapse, for these patients, 66% was a central nervous system relapse. From 157 with no PCNS, 22 had SNC relapse and from 27 with PCNS only 7 had a relapse (p=0.11). The t (1;19) (p=0.03) and male sex (p=0.04) are adverse prognosis factors to relapse. Steroid response, immunophenotype, blasts in spinal fluid were not prognosis factors; 37.5% of dead patients were patients with CNS relapse.

Conclusions: Conclusions: Male sex and t (1; 19) confer significant statistical evidence as risk for relapse to CNS, so in these patients prophylaxis therapy must be intensive to avoid relapse; infiltration at diagnosis, mediastinal mass and ALL of T precursors are not prognostic factors for relapse. In low and middle income countries protocols must be adapted in our patients who has a very high proportion of PSNC compared to the rest of the world.

V087 SIOP19-0610 | Effects of a New Method of Video Publicity for Improving the Perception of Childhood Cancer

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Background/Objectives: The appropriate understanding of society on childhood cancer as well as the patient or caregiver is an important key to improve the success rate of the patient and to optimize the treatment environment. The way to achieve the goal has been mainly through the Internet or a booklet, but it's not enough to provide sufficient data in Korea, which is the strongest country with its fastest desire for knowledge. The Korean Society of Pediatric Hematology-Oncology (KSPHO) and Korean Association for Children with Leukemia and Cancer (KACLC) have jointly conducted a series of videos and spread them through social network services as a way of improving the perception of childhood cancer.

Design/Methods: The theme of the video was the contents of the questionnaires of the patient's caregivers achieve institutional improvement for the optimal treatment environment, and global treatment using an international network. The video was screened for 3-5 minutes, and it was produced as a series. The publicity evaluation was conducted by the number of views, event comment induction (YouTube, Facebook, Instagram) and the number of times the press was exposed.

Results: The perception of childhood cancer were improved through an interview expert and quiz events. The number of people who viewed the spreading SNS was 2,319 times and the number of participations (sympathy, comment and sharing) was 1,760 times. There were 12 articles in the press. More than 99% of the responses to the images are left with the following remarks: 'I have solved my misconceptions about childhood cancer' and 'I hope it becomes a society that does not misunderstand about childhood cancer'.

Conclusions: Improvement of the perception in pediatric cancer through communication of the general public and medical staff by using the production of promotional videos that have been escaped from the existing methods, improved the quality of life of patients and their families.

Epidemiology - Pathways of Care

V088 SIOP19-1198 | Exploring the Process of Developing a Wearable Vital Monitor for Pediatric Cancer Patients in Low-Resource Settings: An Interdisciplinary Approach Using Design Problem-Solving Theory

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Background/Objectives: Of the 300,000 children diagnosed with cancer worldwide each year, 80% live in low-and middle-income countries (LMIC) of which 20% or less survive. One of the leading causes of pediatric cancer mortality is infection and sepsis. This project examines and documents the way that an interdisciplinary team in engineering, public health, and medicine collaborated to tackle disparities in global childhood cancer survival by developing a technological solution to aid sepsis and infection detection.

Design/Methods: Design problem-solving theory was used as the theoretical framework. A thorough literature review, over 8 brainstorming sessions with diverse users, and over 10 consensus-building exercises were performed to hone the solution concept. Additionally, 7 interviews with pediatric oncology experts (clinicians, nurses, nutritionists, psychosocial providers, administrators, and global health leaders) and 3 interviews with pediatric oncology clinicians and nurses from 4 LMIC countries were conducted to incorporate applicable feedback and experience. Design process balanced trade-offs to achieve highest impact for the most striking need.

Results: Three design phases were implemented: a. investigate (problem exploration, identification, definition), b. ideate (concept selection, design specification), and c. create (prototyping, testing, feedback). The final solution, a wearable vital monitor that measures heart rate, respiratory rate, and body temperature, was chosen and refined through 5 iterations of feasibility analysis and was presented with quantifiable design specifications and preliminary data on prototype accuracy. Feedback from all team members was continuous to ensure viability and applicability, and increase buy-in.

Conclusions: Collaboration within medical, public health, and engineering disciplines is essential in designing devices to address global health issues. This device holds potential to improve the quality and treatment of pediatric cancer care in LMIC by providing technologically-independent and affordable vital monitoring. Next steps include refinement and piloting the device, and continuation of the interdisciplinary partnership.

V089 SIOP19-0266 | Adolescent and Young Adult Oncology Care in the Asociación de Hemato-Oncología Pediátrica de Centro América

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Background/Objectives: There are over 1 million new cancer diagnoses in adolescent and young adults (AYA: ages 15-39) worldwide annually, the majority of which occur in low-and-middle-income countries. However, little is known about the current landscape of AYA oncology care in these settings. We aimed to begin to fill this gap in knowledge by identifying where AYA patients are treated and the barriers and facilitators encountered in providing care for these patients in Central America.

Design/Methods: This cross-sectional study involved an online self-administered survey, conducted among physicians from the Asociación de Hemato-Oncología Pediátrica de Centro América. Descriptive statistics characterized the respondents and evaluated survey responses. The survey had a 60% response rate.

Results: Respondents were primarily pediatric hematologist/oncologists (84%), working for ≤ 10 years (60%), in a public children's hospital (52%), with >100 new diagnoses per year (52%). Thirty percent of physicians reported the maximum patient age at their institution was 18 years, followed by 17 years (33%), and as low as 12 years by 4.5% of physicians. These ages were mostly dictated by government (23%) and hospital (45%) regulations. Only 32% percent of the physicians felt comfortable treating patients >18 years old. Half of the physicians reported having collaborated with an adult hematology/oncology colleague to take care of an AYA patient. In addition, 17% of physicians reported availability of AYA-specific services in their center; most common were social work, mental health and transportation. Mental health and reproductive services were identified as the greatest areas of opportunity to improve care for AYA patients.

Conclusions: Age limits, restricted exposure and experience among providers, and limited availability of AYA specific services are prevalent and limit comprehensive care of AYA patients in Central America. Addressing the challenge requires a health-systems approach; explicit inclusion of AYA patients in national cancer control plans could help.

V090 SIOP19-0294 | Brain Tumors in Children and Adolescents: Waiting Times of Brazilian Health Care System

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Background/Objectives: Early diagnosis and survival of Central Nervous System (CNS) tumors is still a challenge. Treatment requires a specialized center with a multidisciplinary team. Knowledge about delays in health care system is important to build improvements in early diagnosis and treatment.

The aim of this study was to identify delays in the Brazilian health care system among children and adolescents (aged 0-19 years) with CNS tumors.

Design/Methods: This retrospective study included 2,339 cases of CNS tumors from 145 Brazilian Hospital-Based Cancer Registries (2007-2011). The term "delay" was used to designate the time interval. Delays were analyzed in two groups of patients: Group1 - without a previous histopathological diagnosis - 1,513 pts (64.7%) and Group 2 - with a previous histopathological diagnosis - 826 pts (35.3%). Referral, hospital, health care, treatment and diagnosis delays were calculated in days, as well as the median and 25th and 75th percentiles among categories. Mann-Whitney and Kruskal-Wallis was used to test differences (SPSS-20.0). Significance was considered as $p < 0.05$.

Results: Male gender was predominant (54.6%). Astrocytoma was the commonest tumor (36.2%). More than half of patients came from the Southeast region (57.7%). Most of delays increased with age. Patients with 'other gliomas' had the shortest diagnosis, health care system and referral delays and the longest treatment delay. Patients from the North region had the longest diagnosis and hospital delays while from South region had the shortest. Delays varied between Brazilian geographic regions, patients from the North and Northeast regions had the longest delays.

Conclusions: Important regional disparities were seen across Brazilian regions. Adolescents had the longest delays. The diagnosis and referral delays can be a major issue to improve care of patients with CNS tumors.

V091 SIOP19-0619 | Time to Diagnosis of Pediatric Cancer in an Oncology Unit of a Country with Limited Resources

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Background/Objectives: Early diagnosis is fundamental in pediatric oncology because it allows treatment at an early stage of the disease with less toxicity, lower cost and better outcome. Some studies have assessed the factors associated with the time-to-diagnosis of cancer for children but they are rare in Africa. Our objectives are to identify the diagnostic delays in pediatric cancer and analyze risk factors for diagnostic latency.

Design/Methods: We performed a study of 80 cases of childhood cancer referred to the Pediatric Hematology and Oncology department of Rabat Children's Hospital between January and August 2017. We recorded patients' data through parents' interview and review of the medical records. We studied the time intervals between onset and final diagnosis and start of treatment; and investigated associated factors with shorter intervals.

Results: The median latency to diagnosis in our study was 37 days. The median physician interval was higher than the median patient interval (24 vs. 7 days). The gender, the family size, the place of residence and the type of health insurance had no significant association with the diagnostic latency. There was no significant association between physician lag time and tumor type or health care system. Misdiagnosis was recorded in 35% of patients, ten of them had steroid intake prior to diagnosis of cancer. Factors associated with a significantly shorter patient interval ($P < 0.05$) were mother's high level of education, age at presentation (between 5 and 10 years) and parents' employment (both parents working).

Conclusions: Our findings show that the index of suspicion for childhood cancers remains low in our country. Mother's education level, age at presentation and parents' employment were factors of shorter consultation delay. Thus, increase in public awareness, continued medical education for general practitioner and pediatricians would reduce pediatric cancer diagnostic delays.

V092 SIOP19-1050 | The Adapted Resource and Information Application (ARIA) for Pediatric Oncology Guidelines: A Clinical Decision Tool for Pediatric Oncology Care in Low- and Middle-Income Countries

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Background/Objectives: Clinical decision tools are needed in settings where trainees and general pediatricians without

formal pediatric oncology training are tasked with providing care to children with cancer. To support healthcare workers in low- and middle-income countries (LMIC) where staffing is limited, we developed a prototype computer application to facilitate easy access to relevant guidelines.

Design/Methods: A prototype clinical decision tool, ARIA, was designed using a design-based approach consisting of three steps: definition of content, prototyping and testing. The underlying design principles were simplicity of use and rapid access to evidence-based information. Content requirements were determined using data output from a multistage peer-reviewed comprehensive adapted treatment guideline initiative coordinated by members of the St. Jude Global Sub-Saharan Africa Regional Program. The prototype program was developed using Microsoft Access 2012. Testing was conducted in two phases: content review from a panel of pediatric oncologists and regional review by trainees, pediatricians and pediatric oncologists in Zimbabwe and Zambia.

Results: ARIA is a scalable program that architecturally includes 19 tables and 15 forms linked together through 78 query-based reports and can run on any Windows-based computer. The database currently includes a total of 17 pediatric oncology guidelines and 72 treatment bundles. To facilitate user navigation, the program has a front-end menu with clickable categories. Based on user selection, curated forms provide detailed information on diagnostic evaluations, treatment summaries, roadmaps, dosage calculators for chemotherapy and antibiotics, local control guidelines for surgery and radiation oncology, toxicity monitoring/modifications and other supportive care guidance. Users can also directly print guideline-specific roadmaps and chemotherapy calendars from the program.

Conclusions: We have created a prototype decision aid application for healthcare workers in resource limited settings designed to make clinically relevant evidence-based information rapidly accessible. Next steps include development as a mobile-friendly health application and adding additional guidelines to the database.

V093 SIOP19-1076 | A Structured Approach to the Development of Comprehensive Resource Adapted Treatment Guidelines for Childhood Cancers: Rhabdomyosarcoma as an Initial Case Example

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Background/Objectives: Published adapted treatment regimens are critically important but lack detailed guidance for physicians taking care of children with cancer in resource-limited settings. In response to needs at Cancer Diseases Hospital, Zambia and Parirenyatwa Hospital, Zimbabwe, we designed a novel approach to comprehensive, resource adapted treatment guideline (ATxG) development.

Design/Methods: A two-phase approach to maximize simplicity, ensure evidence-based decision-making and generate multi-stakeholder consensus was framed. First, a three round modified Delphi was conducted to identify appropriate circumstances for early palliative referral. Thirty-three cancer sub-groups, defined using the International Classification of Childhood Cancer-3 and Toronto Staging System (TSS), were scored by treatment intention: curative intent, palliative-metronomic therapy, or palliative-symptomatic care only. Simultaneously, a scoping review of protocols/guidelines/regimens from the International Society of Paediatric Oncology, International Network for Cancer Treatment and Research, St. Jude (SJ), Children's Cancer and Oncology Groups, and other published country/regional regimens was completed. Using abstracted treatment data, fixed doses and cytotoxic drug schedules were standardized across solid tumor categories. Second, a three-tier review process was conducted: primary development by a SJ team; secondary review by a physician panel with regional and multi-disciplinary (pediatrics, pediatric oncology, surgery, radiation oncology, palliative care) representation; tertiary review by external content experts.

Results: The approach was piloted with the development of a rhabdomyosarcoma ATxG. As both hospitals have access to radiation, surgery, and chemotherapy, all treatment modalities were included. Cytogenetics were assumed unavailable. During the review process, the TSS rhabdomyosarcoma categories of local/metastatic were further refined into six strata through inclusion of the Oberlin clinical scoring system. The final rhabdomyosarcoma ATxG includes 16 sections with appendices representing a standard ATxG template.

Conclusions: With multi-stakeholder input, we successfully piloted a structured approach for ATxG development. Ongoing work includes development of 16 additional guidelines, monitoring ATxG implementation outcomes, and refinement of a clinical decision tool for mobile devices.

V094 SIOP19-1107 | Development of Pediatric Cancer Registry Standards and a Cloud-Based Tool for Hospital-Based Cancer Registration in Low- And Middle-Income Countries (LMIC)

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Background/Objectives: Hospital-based pediatric cancer registration is incomplete to non-existent in many LMIC. Where it does exist, limited guidance is available for what types of data these cancer registries should collect. To address this critical gap in cancer control efforts, we developed a registry tool with associated standards optimized for pediatric cancer in LMIC.

Design/Methods: The registry was created using an iterative approach consisting of defining requirements, prototyping and testing. The underlying design principle was to capture only relevant data needed for stakeholders to make decisions and monitor outcomes. Content, software and security requirements were independently defined. Potential data elements and variables were first identified through a scoping review and subsequently finalized for prototyping following two rounds of input by a panel of pediatric oncologists and registry directors. Concurrently, requirements for software platform selection and security compliance were completed with input from information technology and legal specialists. Alpha (internal) and Beta (external) testing were conducted by global collaborators with pediatric cancer registration expertise. At each stage, users were asked to sequentially review the registry and, following applied revisions, provide further feedback following the data processing of ten anonymized patients.

Results: Six adaptive electronic forms capturing essential information, demographics, diagnosis, staging, treatment and follow-up were developed. The number of elements captured per form varies from 2 to 40 dependent on previous answers. Data collection standards with definitions, values and logic attached to each data element were compiled and are publicly available. Security measures such as sandboxing and multifactor authentication were incorporated to ensure compliance with American, European and Chinese data

privacy laws. Language support includes English, Spanish, Portuguese, French, Russian, and simplified Chinese.

Conclusions: We have field tested a cloud-based pediatric cancer registry tool optimized for LMIC. The registry includes data collection standards for hospital-based registration. Free access is available through the St. Jude Global Alliance.

V095 SIOP19-0232 | Access to World Health Organization Essential Medicines for Childhood Cancer Care in Trinidad and Tobago: A Health System Analysis of Barriers and Enablers

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Background/Objectives: The burden of childhood cancer is greatest in low- and middle-income countries (LMICs), where unreliable access to essential cancer medicines is a critical barrier to providing effective care. A lack of context-specific data on the determinants of drug access in many LMICs hampers efforts to efficiently and reliably procure essential childhood cancer medicines, and ensure they reach the children who need them. This is relevant in the English-speaking Caribbean, where childhood cancer outcomes lag behind those achieved in most high-income countries.

Design/Methods: We conducted a case study of the barriers to and enablers of access to World Health Organization (WHO) essential medicines for childhood cancer care in Trinidad and Tobago. Stakeholders (n=9) were interviewed across the pharmaceutical supply system using a novel analytic framework and qualitative interview guide. Interviews were recorded, transcribed and coded to capture emergent themes. Quantitatively, we compared alignment of the 2017 WHO Essential Medicines List for Children (EMLc) and the essential medicines list in Trinidad and Tobago. National buyer prices were compared against median international prices, with calculation of median price ratios (MPR) to assess procurement efficiency.

Results: Principal barriers of access to essential childhood cancer medicines included a lack of data-driven procurement, low supplier incentive to engage in tenders, reactive processes in response to stockouts, and siloed information systems. While the essential medicines list in Trinidad and Tobago had 90.9% alignment with the WHO EMLc, 46.4% of procured medicines had a MPR greater than 1, suggesting inefficient public sector procurement. Overall, regionalization, standardization, and proactivity were identified as key themes relevant to policy reform.

Conclusions: Our novel analytic approach identified pliable areas for policy change sensitive to local health system and sociopolitical realities. It provides a framework for similar studies of drug access in other jurisdictions and contributes to global efforts to improve childhood cancer outcomes.

V096 SIOP19-1450 | Evaluation of UK National Advisory Panels for Childhood Cancer

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Background/Objectives: In the UK, there has been a recent rise in national advisory panels (NAPs) composed of professionals with tumour-specific expertise who make recommendations for individual patients. The role is advisory and the final decision remains with the treating clinician and family. The selected NAPs for this evaluation include sarcoma, ependymoma, leukaemia, neuroblastoma and renal tumours. The NAPs do not receive funding and there are no formal guidelines to define standards. We present an interim evaluation of selected NAPs in terms of the service they provide, their value and impact.

Design/Methods: Methodology was mixed and included NAP chair interviews, activity reports including process and structure, formal documentation review and retrospective analysis of discussed cases.

Results: Eight hundred and fifty-six referrals have been made to date. For sarcoma, 155 referrals were received (61 meetings over 6.4 years); ependymoma had 311 (129 meetings over 3.1 years); leukaemia 234 (46 meetings over 2.1 years); neuroblastoma 70 (19 meetings over 1.7 years) and renal 86 (30 meetings over 1.4 years). For all NAPs, treatment advice was the commonest referral theme. Specific tumour-type questions included local control options, nephron-sparing surgery, neurosurgery and treatment options at relapse. Additional NAP roles included stratification of trial patients, advice regarding complex neuroradiology, optimisation of bio-banking and specialist therapy recommendations such as CAR-T and proton beam. Only 20% of cases had recorded follow-up data regarding recommendation implementation

Conclusions: The NAPs make recommendations for a significant number of patients in time that is currently not commissioned. Further clarity is required in terms of the impact and value of the panels for patients. Themes identified for focus in the next phase include systems for robust data collection

including follow-up information, adherence to recommendations and exploring the role of the patient voice.

V097 SIOP19-0485 | The Suspected Cancer Pathway; A 5-Year Analysis of Urgent Referrals to a UK Paediatric Oncology Shared Care Centre

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Background/Objectives: The National Institute for Health and Care Excellence (NICE) introduced the suspected cancer referral pathway in England (2000, updated 2015) to facilitate early diagnosis. This includes 'urgent' referrals (for specialist assessment within 2-weeks) or 'very urgent' (within 48-hours). This study evaluates the effectiveness and diagnostic yield of the urgent suspected cancer (USC) pathway in children.

Design/Methods: The case notes of 274 patients referred by the USC pathway to a UK paediatric oncology shared-care centre were retrospectively reviewed over a 5-year period (2014-2018). Recorded information included; suspected cancer type, clinical evaluation, investigations, referrals and outcome. A local cancer database was analysed to identify the referral route of confirmed cancer cases in the same period.

Results: 1.82% (5/274) of patients referred by the USC pathway had cancer. Two new patients were diagnosed following referral from primary care (0.73%). The other three patients were referred by other hospital specialists or diagnosed abroad. Suspected lymphoma/leukaemia was the most common reason for referral (51.9%). Of the 44.8% referred with lymphadenopathy; no child with lymphadenopathy alone had haematological malignancy. 19.8% were referred with a suspected brain tumour; none were diagnosed. There were 52 new confirmed cancer cases in the same time-period. The majority were referred from the Emergency department (63.5%) and 25.0% from other hospital specialists.

Conclusions: The diagnostic yield of childhood cancer by the USC pathway was <2%. Although the pathway expedites referral to a paediatric specialist, when suspicion of malignancy is low, alternative urgent referral routes should be explored. The NICE pathway was not strictly adhered to as many 'very urgent' presentations, as stated in the referral letter, were classified as 'urgent'. We would advise same-day discussion by telephone with a paediatrician when childhood cancer is suspected to ensure appropriate and timely referral.

V098 SIOP19-0739 | The Value of Naming Software in Allocating Ethnicity in a Specialist Children's Cancer Registry

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Background/Objectives: Ethnic group has been collected as part of the minimum data set for childhood cancer registration in the UK since the 1980s. Despite this, deficiencies in the data still exist and alternative methods for allocating ethnicity are being developed. We compared ONOMAP naming algorithm software, which derives an ethnic subtype from a combination of surname and forename, against over 12,000 patients within a Children's Cancer Registry to examine the accuracy of the software in allocating ethnic group to missing cases and enrich the quality and value of the data.

Design/Methods: The West Midlands Regional Children's Tumour Registry holds population based data on children diagnosed with cancer from 1957 onwards. Ethnic group, where available, is ascertained from childhood cancer registration forms or hospital data systems. Ethnicity coding for 12,585 patients was examined for completeness and compared with the ONOMAP generated subtype, which was used to allocate missing ethnicities by the 2001 Census ethnic group.

Results: Complete ethnicity data existed for 78.6% of patients. Missing data were more common in earlier decades of diagnosis: 1950s (61.2%), 1960s (55.8%). Agreement between the known and ONOMAP generated ethnicities were: White 99.4%, Mixed 0%, Asian or Asian British 72.6%, Black or Black British 11.9% and Other Ethnic Groups 27.6%. Ethnicities generated by ONOMAP for the missing cases were: White 98.2%, Asian or Asian British 0.8%, Black or Black British 0.1%, Other Ethnic Groups 0.8%, Unclassified 0.1%.

Conclusions: ONOMAP is a good predictor of White and Asian ethnic group membership, but less so for Black, Other and Mixed ethnicities. The high concordance rate between our known and computer generated 'White' ethnicities leads us to cautiously accept the ONOMAP output for our missing patient cohort. In the absence of alternative data sources, naming algorithms can provide valuable ethnicity data, but the results must be applied carefully.

V099 SIOP19-0295 | Where Children with Cancer are Dying in Brazil?

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Background/Objectives: Place of death (PoD) has become increasingly important during the process of end-of-life care. The aim of this study was to describe the PoD of children with cancer in Brazil.

Design/Methods: Population-based study using information from Brazilian Mortality Information System. We selected data from 1996-2014; death's age under 15 and cause of death coded as C00-C97 and D46 (ICD-10th). Variables included: gender; death's age; geographic region of residence (North, Northeast, Midwest, Southeast and South); city of residence (capital; non-capital); year of death, type of tumor, PoD was analyzed as home vs. hospital and Geographic Place of Death (GPoD) (geographic region; capital, non-capital). Analyses were performed using SPSS 20.0 (p-value < 0.05).

Results: The dataset comprises 38,050 records. Male gender was predominant (55.2%). Leukemia was the major cause of death (34.6%), followed by central nervous system (CNS) tumors (25.4%). Most of deaths has occurred in hospitals (94.1%). There was a decrease in home deaths across periods (1996-2002-8.0%; 2003-2008-5.4%; 2009-2014-3.8%). Home deaths were more frequently between patients from Northeast region; living on non-capital cities; children older than 4 years and with solid tumors. GPoD differ among Brazilian regions, 14% of children living on the North region had migrated to others regions while less than 10% of children living on others regions died at their residence's region. When children lived on non-capital cities located on the South and Southeast regions they died more often on their city of residence and among the others regions children living in non-capital cities died more often on capital.

Conclusions: There were major differences between Brazilian regions regarding where children die. Patients from North migrated to others regions probably seeking for treatment and died far from home. Hospital was the major PoD increasing during the period.

V100 SIOP19-0380 | Access to Who Essential Medicines for Childhood Cancer Care in Ghana: A Health System Analysis of Barriers and Enablers

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Background/Objectives: Inadequate access to essential medicines is a major contributor to poor childhood cancer survival in low- and middle-income countries (LMICs). We studied the availability and determinants of childhood cancer drug (CCD) access in Ghana to inform national health policy and facilitate public procurement efforts.

Design/Methods: We employed a mixed-methods case study approach to analyze the determinants of CCD access in Ghana, comprised of a scoping literature review, in-depth qualitative interviews (n=21) with key health system stake-

holders, and prospective collection and quantification of drug availability and price. Interviews were recorded, transcribed, coded both deductively and inductively, and analyzed to capture emergent themes. We determined alignment of cytotoxic and adjuvant medicines between the World Health Organization Model List of Essential Medicines for Children (WHO EMLc) and Ghana's Essential Medicines List (NEML), and compared national buyer prices against median international prices to assess procurement efficiency.

Results: Encouraging generic substitution, removing taxes on imported drugs and strategic national drug procurement are among the government cost-saving strategies that address the issue of affordability. The lack of public procurement of CCD renders Ghana reliant on the private sector and highly susceptible to stock-outs. Other barriers include drug quality concerns, low childhood cancer awareness and limited financing options for medicines. Overall, there is a 65.2% alignment between the WHO EMLc and the NEML. However, the NEML only lists nine out of the 19 cytotoxic medicines on the WHO EMLc. Approximately 59.7% of the NEML drugs had a median price ratio greater than 3 which indicates inefficiency in procurement by the private sector, especially for adjuvant medicines.

Conclusions: Rigorous evidence on health system determinants of CCD access in Ghana can inform policies to improve childhood cancer outcomes in Ghana. Our findings yield transferable insights into drug access dynamics for children with cancer and other non-communicable diseases in comparable health system settings.

V101 SIOP19-0144 | Political Priority and Pathways to Scale-Up of Childhood Cancer Care in Five Nations

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Background/Objectives: The factors that determine whether and how childhood cancer is prioritized in national health agendas and integrated into health systems remain poorly understood. We investigated the political, social, and economic factors that influence health system priority-setting on

childhood cancer care (CCC) in a range of low- and middle-income countries (LMIC).

Design/Methods: Based on in-depth qualitative case studies, we analyzed the determinants of priority-setting for CCC in El Salvador, Guatemala, Ghana, India, and the Philippines using a conceptual framework that evaluates the impact of political contexts, actor power, ideas, and issue characteristics on political prioritization. Data derived from interviews ($n=68$) with key informants involved in CCC policies and programs, supplemented by academic literature and policy documents.

Results: Political priority for childhood cancer varies widely across the countries studied and is most influenced by political context and actor power dynamics. Ghana has placed relatively little national priority on CCC, due to competing priorities and a lack of stakeholder cohesion. In El Salvador and Guatemala, actor power has played a central role in generating national priority for CCC, where civil society organizations have disrupted legacies of fragmented governance to shape policy agendas. In India, an empowered private actor was instrumental in establishing priority and sustained channels of financing for CCC. In the Philippines, the childhood cancer community capitalized on a window of opportunity to expand access to CCC through the political prioritization of UHC and NCDs in health system reforms.

Conclusions: Actor power emerged as a critical enabler of CCC prioritization in LMIC. Responsiveness to political contexts – in particular, priority placed on NCDs and UHC – is also crucial to place CCC firmly on national health agendas. Governments must be convinced of the potential for health system strengthening and the capability of networked actors to amplify public sector investments and catalyze change on the ground.

V102 SIOP19-1545 | Informatics Methods for Early Case Capture of Pediatric and Young Adult Cancer Cases

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Background/Objectives: Population-based cancer surveillance data are essential to monitoring incidence trends and the planning, implementation and evaluation of cancer prevention and control initiatives. Registry data also have the potential to play a greater role in clinical trial recruitment and cancer survivorship initiatives, particularly for pediatric and young adult cancer (PYAC) patients (ages 0-19). Rapid identification of PYAC cases is needed, yet current reporting practices require approximately 19 months to achieve complete, population-based data. We describe the development of informatics methods for early case capture (ECC) of PYAC cases

within 30 days from the date of diagnosis in the state of Kentucky from 2012-2018.

Design/Methods: We utilized a prospective population-based study design with support from the U.S. Centers for Disease Control and Prevention's Pediatric and Young Adult Early Case Capture Program. Our approach relied heavily upon informatics methods and electronic reporting sources, such as electronic pathology reports, electronic health records and the novel use of a state health information exchange network. A variety of data sources, innovative software applications and registry workflows were evaluated to achieve complete reporting within the minimum amount of time.

Results: Our results show that the majority (>90%) of pediatric cancer cases can be successfully identified by a population-based central cancer registry within 30 days of diagnosis. Natural language processing of electronic pathology reports was demonstrated to be the most productive method to identify the greatest proportion of cases. Limitations arose from Kentucky cases diagnosed and treated out-of-state.

Conclusions: Our study demonstrates that early case capture of PYAC cases is both feasible and practical for population-based cancer registries. However, significant investments in electronic reporting infrastructures are required. In addition, ECC efforts also led to the development of new data dissemination tools that have informed public policy and revealed a high burden of brain and central nervous system tumors in Kentucky.

V103 SIOP19-1029 | Development of a Web-based Curriculum for Novice Clinical Research Professionals in Low- and Middle-Income Pediatric Oncology Centers

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Background/Objectives: The mission of the Department of Global Pediatric Medicine at St. Jude Children's Research Hospital is to provide education, improve capacity, and expand research opportunities within collaborating institutions in low- and middle-income countries (LMIC). The role of the clinical research professional is not well established in LMIC, and no training courses currently exist which target a novice study coordinator working in the pediatric hematology-oncology setting.

Design/Methods: A survey of data management capacity was administered to 24 medical directors at pediatric oncology centers in LMIC which identified a gap in training resources. Through collaboration with educational design leaders and

subject matter experts, learning objectives were written and content was generated. Lessons were storyboarded prior to implementing animations and audio in Storyline 360.

Results: This online curriculum entitled “Clinical Data Abstraction in Pediatric Oncology” is presented as two coordinating courses: “Introduction to Pediatric Oncology” and “Introduction to Clinical Data Abstraction”. The courses are divided into 5 interactive modules which include 14 lessons and 4 case studies. Over 60 annotated fictitious medical documents were created and incorporated into the exercises and case studies. The combined courses require about 8 hours to complete; learners must complete pre- and post-tests to receive a certificate of completion. Feedback from internal and external testing was incorporated into the final product which was then translated into Spanish. Additional languages may be offered in the future.

Conclusions: We produced a stand-alone web-based course in pediatric oncology clinical research which is suitable for novice personnel and meets programmatic priorities with consistent, reproducible, and scalable curriculum in 2 languages, is self-paced, and carries no cost to the learner. This curriculum will serve as the foundation for newly hired research professionals prior to receiving project-specific training as new data projects are mounted by collaborating sites.

V104 SIOP19-0304 | How Well are Clinical Processes of Care Documented for Teenagers and Young Adults with Cancer Treated in Specialist and Non-Specialist Centres: Brightlight Study Findings

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Background/Objectives: BRIGHTLIGHT is the national prospective cohort study of teenagers and young adults (TYA) receiving specialist cancer services, followed for up to three years from diagnosis.

Objectives: To use data from medical records to examine the association between documentation of clinical processes and the three levels of specialist TYA care provided: none, some or all.

Design/Methods: Data were analysed from the BRIGHTLIGHT Clinical Report Form (CRF), completed after diagnosis and included: histological diagnosis; molecular diagnosis (where relevant); cancer stage/prognostic group; initial treatment plan; multi-disciplinary treatment (MDT) communication; assessment by supportive care services (contact with clinical nurse specialist and at least one other MDT professional i.e. social worker/psychologist); fertility discussion; and potential clinical trial entry.

Results: 1,114 participants (aged 13-24) were recruited between October 2012-April 2015, CRFs were available for 1,078 of which 1,009 were assigned to: ‘no TYA specialist Care (SC)’ (none, n=333); ‘Some TYA-SC’ (some, n=409) and ‘all TYA-SC’ (all, n=267).

Documentation of histological diagnosis, cancer stage/prognostic group, initial treatment plan and MDT communication was high ($\geq 88\%$) and similar across levels of care (Chi test: $p > 0.1$).

Those receiving some/all SC had a higher frequency of documented molecular diagnosis, (none 26%; some 35%; all 44%, $p = 0.002$), assessment by supportive care services (none 38%; some 61%; all 60%, $p < 0.001$) and fertility discussion (none 54%; some 69%; all 75%, $p < 0.001$) with significant trends towards more documentation for those having all treatment in SC ($p < 0.02$). There was also some evidence of a trend for better documentation of the initial treatment plan (88% none; 91% some; 94% all, $p = 0.04$).

Conclusions: BRIGHTLIGHT findings indicate that processes essential for good clinical care are frequently documented for young people with cancer. Molecular diagnosis, fertility and holistic support for young people are more likely to be recorded for those treated in specialist TYA centres.

V105 SIOP19-1019 | Self-Reported Presenting Symptoms and Timeliness of Help-Seeking Among Teenagers and Young Adults with Cancer: Findings from the Brightlight Cohort

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Background/Objectives: Improving the diagnostic experience of Teenagers and Young Adults (TYA) with Cancer is a priority. Greater understanding of presenting symptoms could inform early diagnosis strategies.

We aimed to examine the nature/frequencies of presenting symptoms in TYA and their association with diagnostic timeliness.

Design/Methods: Data were collected from the BRIGHT-LIGHT cohort about their diagnostic experience. Participants responded yes/no to 16 pre-specified symptoms before diagnosis, or other symptoms (free-text responses). We calculated symptom frequency, and the ensuing ‘symptom signatures’ of lymphoma, germ cell tumours, leukaemia, carcinoma, bone tumours, soft tissue sarcomas, brain tumours and melanoma. We then examined how these relate to diagnostic timeliness.

Multivariate logistic regression was used to examine variation in the help-seeking interval by presenting symptom, categorised as ≤ 1 month versus more than 1 month.

Results: Eight hundred and thirty TYA completed a face-to-face interview, 14 reported no specified symptoms, 10 had missing data and 3 were invalid. Of 803 TYA with symptom/s, lump or swelling was most common (52%), followed by extreme tiredness (38%), unexplained pain (35%), lymphadenopathy (24%), and night sweats (24%). Most patients (59%) reported more than one symptom. Symptom signatures varied by cancer type.

Over a quarter (27%) reported patient intervals longer than 1 month. This varied by 3-fold after adjustment for multiple symptoms. After adjustment for sociodemographic factors and cancer-type, night sweats was associated with greater odds of a patient interval greater than 1 month compared to lump or swelling alone (OR (95% ICI): 2.06 (1.27–3.34)) while rash/itching was associated with lower odds (OR (95% ICI): 0.52 (0.27–0.98)).

Conclusions: Young people experience a range of non-specific symptoms in combination before diagnosis, in frequencies greater than those previously reported. Variation in time-to-diagnosis by symptoms, demonstrates an association between symptoms and help-seeking and may lend itself to the design of symptom awareness campaigns.

V106 SIOP19-0995 | Design-based Research Approach to the Development of a Scalable, Asynchronous Training Curriculum for Pediatric Cancer Registration

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Background/Objectives: Pediatric cancer registration in low- and middle-income countries (LMICs) is often processed by staff with little to no formal training. To provide a scalable solution for initial and continuing education, we developed a customized pediatric cancer registry curriculum for personnel in this setting.

Design/Methods: A design-based research approach to allow for iterative cycles of revision and refinement of instructional materials was used. As a first step, a scoping review of available cancer registration training materials was conducted. Using available data, a team consisting of cancer registry directors, pediatric oncologists and clinical research associates (CRA) formulated a list of core-competencies and learning objectives during two in-person sessions. Learning objectives were then grouped together hierarchically as modules and lesson plans to form a syllabus. Next, course content, study guides and assessment questions were developed using a three-stage iterative process of peer review. Initial content was developed by a CRA. Second review included input from educators and a pediatric oncologist. Third, feedback for accuracy and completeness from a global panel of pediatric cancer registry experts was used to finalize content. To allow for asynchronous training, lectures were recorded for production on www.Cure4Kids.org.

Results: A competency-based curriculum consisting of seven modules, 20 lessons and 59 learning objectives, with topics including principles of registration, classification and coding, staging, treatment, follow-up, and epidemiology was developed. Four modules have undergone the full peer review process, two were recorded and one edited for production. In parallel, an internet-based registry environment was created for practical training opportunities.

Conclusions: We developed an asynchronous, competency-based educational curriculum designed for learners in LMIC settings who work on pediatric cancer registries. Ongoing next steps include finalizing peer reviews and recordings, developing dummy-patient charts for the practical learning component, field testing, and translating content into additional languages.

V107 SIOP19-0432 | Adolescents with Cancer in Italy: Access to Pediatric Oncology Centers

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Background/Objectives: Adolescents with cancer may have difficulties in accessing optimal cancer services. Various projects were developed in Italy under the guide of the national pediatric haematology oncology association AIEOP (Associazione Italiana Ematologia Oncologia Pediatrica). In this study, we evaluate the number of observed (O) cases, comparing them to the numbers of expected (E) cases. In addition, we analyse the proportion of children and adolescents in the different AIEOP centers.

Design/Methods: The hospital-based Model 1.01 database registers all the patients diagnosed within AIEOP centres. In Italy, all the pediatric oncology units are affiliated to AIEOP. All malignant tumors were considered for the study. The period considered for the analysis was 2015–2017. Expected cases were calculated on the basis of the incidence rates derived from the population-based Italian Network of Cancer Registries AIRTUM.

Results: The estimated annual expected cases were 2,402, i.e. 1,542 in the 0–14 years (64%) and 860 in the 15–19 years group (36%). Observed cases per year were 1,935, i.e. 1,623 between 0–14 years (84%) and 312 between 15–19 years (16%). The overall O/E ratio was 0.80, i.e. 1.05 for children and 0.36 for adolescents. The relative proportion of children/adolescents varied in the different AIEOP centers. The percentage of adolescents was higher than 20% in 10 out of the 43 enrolling centers.

Conclusions: The proportion of adolescents seen in AIEOP centers increased significantly over the years: in previous studies the O/E ratio was reported as 0.10 (1989–2006) and 0.28 (2007–2012), and it was 0.36 in the current study (2015–2017). This result suggests the efficacy of local and national programs dedicated to adolescents.

V108 SIOP19-1254 | Scaling-Up Effective Interventions in Global Pediatric Oncology: Mexico in Alliance with St Jude, a Breakthrough Model

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Background/Objectives: Scaling-up effective interventions remains a major challenge in health service delivery; accomplishing it in global pediatric oncology is no exception. While twinning has created frameworks for successful capacity-building, it has not conquered the challenges of scale. Mexico in Alliance with St Jude (MAS) aims to improve quality of care and survival for children with cancer in Mexico favoring a scalable alliance-building model. We report results after 3 years of collaboration.

Design/Methods: A stakeholder focus group of about 20 experts convened in April of 2016 to, utilizing a structured tool, prioritize 3–5 common challenges amenable to improvement through multi-site collaboration to be further developed and implemented over the subsequent 2 years. Upfront, the goal was to maximize equity, collaboration, and measurable, multi-site, integrative, and innovative impact, through the development of an alliance. Structured in-person working meetings continued every 6 months, and weekly online meetings were organized for monitoring and evaluation of implementation.

Results: The three pre-existing twinning collaborations were quickly transformed into an eight-center alliance. By the start of year 2 a “package” of interventions was developed, consisting of 4 pillars (collaboration, modernization, quality, and evidence) and 15 core interventions, which received peer-reviewed external funding for implementation. By year 3, three new sites were incorporated. By year 4, 68% (81/120) of interventions were implemented across the 8 initiating centers, a handful of centers documented progress on all fronts, and an additional 14 centers joined the alliance and began implementation, totaling 25 centers. Interventions are beginning to show an effect on treatment-related mortality for children with ALL, the main cause of preventable deaths in participating centers.

Conclusions: The alliance-building model has leveraged the strengths of member institutions and St. Jude programs, allowing shared decision-making and building of experience

regarding challenges, opportunities, and prioritization. This is a promising model for addressing challenges of scale.

V109 SIOP19-1279 | Development and Validity Testing of Profile: An Assessment Tool for Pediatric Hematology and Oncology Facilities in Low- and Middle-Income Countries

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Background/Objectives: In global pediatric oncology, the influence of non-biologic factors on outcomes is frequently more prevalent and actionable than biologic factors. To capture the impact of non-biologic factors, we developed the Pediatric Oncology Facility Integrated Local Evaluation (PrOFILe) tool. This self-assessment tool allows Pediatric Hematology and Oncology (PHO) facilities and associated stakeholders comprehensively evaluate and monitor these factors.

Design/Methods: PrOFILe's was developed and tested in three phases. First, several existing tools were consolidated, with final domains and questions verified by 6 internal and 3 external PHO experts. The second phase (pre-alpha testing) focused on software selection and interface, workflow, and data collection forms development. During the third phase (alpha testing), 93 international PHO experts were invited to assess clarity, user-friendliness, relevance, and the scoring system. After each phase, the tool was iteratively modified based on feedback.

Results: The score-based, 12-module tool, comprehensively captures the patient-care continuum in 5 sections. The "Context" section assesses national context, local context, and finances. "Workforce" focuses on personnel, service capacity, and service integration. "Diagnostics" evaluates laboratory, pathology, and imaging capabilities. "Therapy" gathers information about chemotherapy, supportive care, surgery, and radiotherapy capabilities. "Patients and Outcomes" assists in identifying the PHO case mix and their outcomes. Each PrOFILe "module" consists of: (1) electronic forms that collect objective and end-user data from multiple stakeholders, (2) educational modules to provide technical guidance, (3) online mentoring sessions on standards of PHO care, and (4) quality improvement exercises to identify and prioritize areas amenable for improvement. Alpha testers agreed the tool was

user-friendly (91%) and would be helpful to assess improvement overtime (95%).

Conclusions: We have developed a tool that assists PHO teams and institutions identify improvement strategies and visualize the path for optimal PHO care delivery. PrOFILe will begin end-user pilot testing (beta-testing) soon; free access is available through the St. Jude Global Alliance.

V110 SIOP19-0180 | The Cost and Cost Effectiveness of Childhood Cancer Treatment in Low- and Middle-Income Countries: A Systematic Review

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Background/Objectives: A major barrier to improving childhood cancer survival is the perception that pediatric oncology services are too costly for low- and middle-income country (LMIC) health systems. We conducted a systematic review to synthesize existing evidence on the costs and cost-effectiveness of treating childhood cancers in LMICs.

Design/Methods: We searched multiple databases from their inception to March 2019. All studies reporting costs or cost-effectiveness of treating any childhood cancer in an LMIC were included. The quality of included articles was evaluated using the CHEERS checklist. Where possible, we extracted or calculated the cost per disability-adjusted life year (DALY) averted using reported survival and country-specific life expectancy. Cost/DALY averted was compared to per capita gross domestic product (GDP) as per WHO-CHOICE guidelines to determine cost-effectiveness.

Results: Of 2,802 studies identified, 30 met inclusion criteria. Studies represented 22 countries and 9 different malignancies. The most commonly studied cancers were acute lymphoblastic leukemia (N=11), Wilms tumour (N=4), and Burkitt lymphoma (N=4). The mean CHEERS Checklist score was 17.5 of 24. Only 7 studies included at least 10 of the 14 key inputs necessary for comprehensive cost analysis. For example, healthcare worker salaries were included in only 11 studies. Cost/DALY averted was extracted or calculated for 12 studies and ranged from USD\$22 to \$4,475, although the lower-end costs were from studies that omitted key cost components. In all 12, cost/DALY averted through treatment was substantially less than country per capita GDP, and therefore considered very cost-effective.

Conclusions: Many included studies did not account for key cost inputs, thus underestimating true treatment costs.

Costs/DALY averted were nonetheless substantially lower than per capita GDP, suggesting that even if all relevant inputs are included, LMIC childhood cancer treatment is consistently very cost-effective. While additional rigorous economic evaluations are required, our results can inform the development of LMIC national childhood cancer strategies.

V111 SIOP19-0244 | SIOP Maps Paediatric Oncology Services in Africa to Address Inequalities in Childhood Cancer Services

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Background/Objectives: Most children with cancer in Africa go undiagnosed, and those diagnosed have significantly inferior chances of survival when compared to high-income countries. To complement the WHO's mission to increase survival rates of children with cancer, this project creates a baseline of paediatric oncology resources across Africa.

Design/Methods: The project was launched at the SIOP annual congress, 2018. An extensive search for contacts in Africa was performed by the SIOP PODC Education and Training Working Group, supported by a My Child Matters grant from Sanofi Espoir Foundation. A 55-question survey in English, French and Portuguese was published online; links emailed, and printed copies completed at the SIOP Africa conference, March 2019. Parameters included location, staffing, equipment, specialised medical, surgical and psychosocial services.

Results: From November 2018 to March 2019, 537 responses were received: 293 were evaluable—192 from African respondents. Responses were predominantly in English (154), followed by French (36), and Portuguese (2); 46/52 African countries were represented. Twenty countries reported having no full time paediatric oncology physicians. Median annual number of new patients reported from each centre was 120 (IQR 45-300); median number of dedicated paediatric beds/centre was 22 (IQR 10-48). Multidisciplinary services across countries included radiotherapy (22/46), palliative care (15/46) and psychosocial (36/46). Only three countries (Egypt, Kenya, South Africa) have centres with complete haematopathology services. Six countries have

acceptable nursing ratios while the majority have only 1-5 nurses for the entire centre.

Conclusions: This study provides the most comprehensive overview of paediatric oncology services in Africa to date and highlights marked disparities between countries. The data constitutes a baseline against which to measure efforts to improve comprehensive care for children with cancer and their families in the region. This data will be available to assist other childhood cancer stakeholder groups in lobbying for more resources

V112 SIOP19-1022 | SIOP Mapping of African Paediatric Oncology Services: Implications for Training and Education

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Background/Objectives: The World Health Organisation (WHO) estimates a shortage of 4.3 million healthcare workers worldwide and a mismatch of skills, competencies, clinical experience, and expectations. WHO's call for increased medical faculty, quality education, certification and competency maintenance, directly influences the quality of global childhood cancer care. In 2018, SIOP with the PODC Education and Training Working Group (ETWG) initiated a situational analysis by a Global Mapping of Paediatric Oncology Services survey, starting with Africa, supported by a Sanofi Espoir Foundation My Child Matters grant.

Design/Methods: A 55 item electronic (and paper) survey was based on the SIOP Framework for Adapted Treatment Regimens and was made available in English, French and Portuguese. The survey was distributed (snowball methodology) in October 2018 to March 2019 to known SIOP and SIOP Africa members, conference attendees and paediatric oncology (PO) groups to document centres and professionals treating children/adolescents with cancer.

Results: As of April 1st, responses from 45/52 African countries and 150 individual PO units were received; 192/240 (80%) responses were evaluable. Most responses (159; 83%) were from government/faith-based hospitals. One-third (61;

32%) had an established PO programme with basic services (few state-of-the-art services) while one fifth (40; 21%) had all essential services (most state-of-the-art services). One quarter (49; 26%) had severely limited PO inpatient facilities, impacting on training of healthcare workers.

Conclusions: Results show significant gaps in healthcare and facilities, and marked inequities in access to adequate PO training. The initiation and continuation of appropriate PO specialised education programmes within African academic and healthcare settings remain challenging and will require support and commitment from Ministries of Health, Education and Finance across the region. The WHO Global Childhood Cancer Initiative will provide regional advocacy to reinforce the PODC ETWG's efforts to improve access to specialised PO education and training for all health professionals in low- and middle-income settings.

V113 SIOP19-0577 | Establishing an NGO-based Pediatrics Oncology Unit in Syria: Challenges and Lessons Learned During Humanitarian Crisis

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Background/Objectives: Establishing specialized pediatric oncology units has contributed to the significant improvement of childhood cancer outcomes over the past years. During humanitarian crisis in developing countries, multiple challenges arise and may affect multiple aspects of the unit function.

Design/Methods: In 2006, BASMA Association was established, with a mission to improve the health and social conditions of Syrian children with cancer through multiple programs. In 2009, BASMA established the first dedicated pediatric oncology unit in the country through a special agreement with the government to be located in the Governmental Oncology Hospital in Damascus, but to be fully operated by BASMA Association. The unit provided free treatment to all enrolled patients. This abstract aims at studying the effect of humanitarian crisis in Syria on unit function, number of newly enrolled patients, and loss to follow-up rate.

Results: Between April 2009 and March 2019, 1017 patients were enrolled. During the most intense period of war between April 2011 and May 2018 (period I), the mean number of newly enrolled patients per month was lower compared to the period between June 2018 and March 2019 (period II) (7.7 vs 16, P : 0.0005). There was a trend toward higher loss to follow-up rate in (period I) compared to (period II) (5% vs

1.8%, P : 0.09). Between February 2018 and July 2018, the unit has moved from its original location to a temporary safer location in another governmental hospital, however, the unit did not stop its daily function since 2009 until this date.

Conclusions: The humanitarian crisis in Syria has led to a significant decrease in the number of newly enrolled patients and increase in lost to follow-up rate in an NGO-based dedicated pediatric oncology unit in Damascus.

V114 SIOP19-0450 | Association Between Pediatric Leukemia Incidence and National-Level Improvement in Human Development Index

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Background/Objectives: Pediatric leukemia incidence has been steadily increasing without a clear understanding of etiology. This study evaluated whether changes in national developmental status were associated with pediatric leukemia incidence in children <5 years of age.

Design/Methods: Incidence data for acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) from 1988-2012 were extracted from *Cancer Incidence in 5 Continents* (CI5) volumes VII-XI. Incidence rates were aggregated based on human development index (HDI)— a statistical index of economic growth, educational attainment, and lifespan. Countries were categorized as low, medium, high or very high HDI with changes categorized as movement in HDI from 1990-2012. Crude average annual percent change (AAPC) was estimated using Poisson regression.

Results: During the study timeframe, 26 countries changed HDI category. Among the 4 countries that moved from low to medium HDI, no change in ALL or AML incidence was observed. Of the 17 countries that moved from low or medium to high HDI, incidence of ALL increased from 29.9 to 42.5 per million [AAPC of 1.44% (95% CI 0.24-2.65)]. AML incidence was unchanged. In the 5 countries (Bulgaria, Uruguay, Belarus, Croatia, and Saudi Arabia) that moved from medium to very high HDI, ALL incidence increased from 22.8 to 56.3 per million [AAPC of 3.84% (95% CI 2.28-5.41)] and AML incidence increased from 3.4 to 8.1 per million [AAPC of 4.29% (95% CI 3.47-5.11)].

Conclusions: We identified a significant positive association between change in HDI to high or very high and pediatric leukemia incidence, suggesting a role for improvements in economic growth, educational attainment, and lifespan in leukemogenesis. This may be biologic (e.g. rising parental age) or related to altered environmental exposures. The five countries that moved from medium to very high HDI

are geographically and demographically diverse, suggesting universal factors related to development underlie our findings.

V115 SIOP19-0663 | Global Problem of Hospital Detention Practices

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Background/Objectives: Hospital detention practices (HDP) are defined as: “refusing release of either living patients after medical discharge is clinically indicated or refusing release of bodies of deceased patients if families are unable to pay their hospital bills.” Reports of HDP are very scarce and lack consistent terminology. Consequently, the problem’s scale is unknown. The aims of this study are to find evidence of HDP worldwide, to explore characteristics of HDP reports, and to compare countries with or without HDP reports.

Design/Methods: We searched evidence of HDP worldwide, explored characteristics of HDP reports, and compared countries with or without reports. PubMed and Google were examined for relevant English, Spanish and French publications up to January 2019.

Results: Of 195 countries, HDP reports were found in 46 countries (24%) in Africa, Asia, South-America, Europe and North-America. Most reports were published by journalists in newspapers. In most countries reports concern living adults and children who are imprisoned in public hospitals for months. Almost all countries, with or without HDP reports, have signed UN Human Rights Declaration ($P=1.000$). Countries with reported HDP have larger population size ($P<0.001$), worse Corruption Perception Index score ($P=0.025$), higher out-of-pocket expenditure ($P=0.024$), lower Universal Health Coverage Index score ($P=0.015$), and worse Press Freedom Index score ($P=0.012$).

Conclusions: HDP are more widespread than currently acknowledged. Urgent intervention by stakeholders is required to stop HDP.

V116 SIOP19-1640 | Childhood Cancer Survival in Morocco: Report from the Pediatric Oncology Unit of Rabat

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Background/Objectives: In 2008, My Child Matters experts estimated the childhood cancer survival rate in Morocco to 30%. In absence of accurate data about survival rate we conducted a study on the demographics and outcome of childhood cancer in the pediatric oncology unit of the Ibn Sina university Hospital - Rabat Morocco

Design/Methods: We included in the study all the patients aged less than 15 years old referred for malignancies from January 2012 to December 2014. The study was performed retrospectively using medical charts. We reviewed age at diagnosis, gender, parent social and economical Characteristics, distribution by type of cancer and outcome. Kaplan Meier’s method was used to estimate Overall Survival.

Results: Data about 803 cases of childhood cancer were collected. The female/F ratio was 1.2 and median age at diagnosis was 4.5 years. Parent economical status was low in 77% of cases and 63% had the government medical coverage for needy patients. About 89% of the cases were cytological or histological proven. Hematological malignancies accounted for 45% of cases (leukemia 30.6% and Lymphomas 13%). Among the Leukemia’s patients, 2/3 were acute lymphoblastic leukemia (ALL) and 55% of the lymphomas were non-Hodgkin’s lymphoma. Solid tumors accounted for 55%, mainly Central Nervous System (CNS) (11%), Renal (10.3%) and Neuroblastoma (9.3%). The 5 years overall survival rate was 63% and 50% of death were non documented and considered initially as abandonment. The survival rate was higher for nephroblastoma (84%), Hodgkin’s disease (81%), retinoblastoma (78%), Burkitt lymphoma (73%) and lower for Ewing sarcomas (46%) and neuroblastoma (37%). The 5 years OS rate in ALL was 67%. Difference in survival according to gender, age and economical level was not significant.

Conclusions: These results constitute a baseline for a strategy to improve the outcome of childhood cancer in Morocco and emphasize the need of a better documentation of death causes.

V117 SIOP19-0252 | Pediatric Oncology Outreach: First Step to Care

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Background/Objectives: Numerous barriers exist in the optimal management of children with cancer in low- and middle-income countries. Education and beliefs of parents, distance from the health care facilities, lack of family and psycho-social support, the absence of insurance schemes, and lack of trained personnel and infrastructure to name a few. Improvement in mortality is feasible only through early and accurate diagnosis followed by effective treatment. Can a pediatric oncology outreach clinic eliminate the barriers to optimal care.

Design/Methods: A pediatric oncology outreach clinic was started at Advanced Cancer Institute, Bathinda from February 2019 onward in association with CanKids, the National Society for a change in childhood cancer. Patients with suspected cancer referred from surrounding areas were evaluated by a visiting pediatric oncologist in collaboration with an in-house team of the radiation oncologist, pathologist and onco-surgeon. The family of the patients was counseled regarding the disease, treatment modalities available and prognosis. The social worker appointed by CanKids extended psycho-social and financial support to the family. The data from these clinics were collected.

Results: A total of 67 new patients attended the clinic. Forty-one were diagnosed to be suffering from childhood cancer and 26 had non-oncological conditions, immune thrombocytopenia being the commonest. The most common childhood cancer diagnosed in the clinic was Acute lymphoblastic leukemia followed by Hodgkin lymphoma. Five (12%) patients refused treatment and 1 was lost to follow up. Twenty-seven (66%) patients were offered curative treatment, 3 palliative and 4 were given both curative and palliative treatment. Monitoring for long term complications was done in two patients. Seven patients have completed the treatment protocol, 2 patients expired due to complications and 18 are still on treatment.

Conclusions: Outreach pediatric oncology in association with the government set up and non-governmental organization can bridge the gaps in pediatric oncology services.

V118 SIOP19-0745 | Childhood Central Nervous System Tumors: 10 Years Experience from a Tertiary Care Cancer Hospital in Bangladesh

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Background/Objectives: Childhood Central Nervous System Tumors (CCNSTs) is the most common solid tumor in children and leading cause of cancer related mortality and morbidity. There is no population based cancer registry in

Bangladesh so exact incidence of CCNSTs is unknown. Even hospital based studies are very few. The aim of this study is to describe the characteristics of CCNSTs treated at the National Institute of Cancer Research and Hospital (NICRH), only tertiary care cancer hospital in Bangladesh.

Design/Methods: Ten years hospital records of patients who presented at paediatric haematology and oncology department of NICRH between 2009 to 2018 were reviewed. The data were collated and analyzed using SPSS software.

Results: During the study period a total 368 cases were evaluated. Among these primary and metastatic were 343 (93.2%) and 25 (6.8%) respectively. CCNSTs were more common in males 283 (76.9%) compared to females 85 (23.1%), with a with male to female ratio of 3.33:1. Mean age was 8.98 years, minimum 7 months to maximum 18 years. Most commonly affected age group was 5-11 years 187 (50.8%), followed by 12-18 years 113 (30.7%) and < 5 years 68 (18.5%). Location were recorded in 272 (73.9%) cases, among them supratentorial 131 (35.6%), infratentorial 128 (34.8%) and spinal 13 (3.5%). Most Common types were astrocytomas 84 (22.8%), medulloblastoma 72 (19.6%) and ependymoma 64 (17.4%), brainstem glioma 22 (6%). Pineoblastoma, chrinopharyngioma, meningioma and other tumors including spinal and metastatic contributing 109 (29.5%), remaining 17 (4.6%) were not specified. Yearwise distribution shows there is an increasing trend only 5 (1.4%) cases in 2009 and 91 (24.7%) in 2018.

Conclusions: Number of CCNSTs (368) over ten years at a key tertiary referral center potentially indicates serious under-reporting of CCNSTs. Related health professionals should be made aware about early referral to make positive change for CCNSTs in Bangladesh.

V119 SIOP19-1626 | Resource Mapping in Low- and Middle-Income Countries as a Tool for Further Improvement of Paediatric Cancer Care: Eurasian Experience

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Background/Objectives: Mapping of resources for pediatric oncology in Low- and Middle-income Countries (LMICs) is crucial for healthcare planning, improvement of referral pathways, workforce training, and resource mobilization. The

Eurasian Alliance in Pediatric Oncology (EurADO) is a collaborative to improve childhood cancer outcomes in the 11 countries of Eurasia (Armenia, Azerbaijan, Belarus, Kazakhstan, Kyrgyzstan, Moldova, Mongolia, Russia, Tajikistan, Ukraine, and Uzbekistan). No prior mapping of pediatric oncology resources have been conducted in this region. We describe a coordinated, comprehensive mapping of pediatric oncology resources in the Eurasia.

Design/Methods: Resource mapping was conducted using methodology developed in Dmitry Rogachev Center for Pediatric Hematology, Oncology and Immunology (Russia) and with support from St. Jude Children's Research Hospital (USA). A questionnaire was developed collecting data on cancer diagnoses, workforce, facilities and equipment in each country. Details collected included research protocols, collaborating centers and palliative care resources. Project timeline was: mapping of resources in Russia (January – August 2018), modification of process for EurADO, pilot country (Uzbekistan) completed in December 2018, mapping of remaining 10 countries (January – April 2019).

Results: Mapping of pediatric oncology resources was successfully completed in the 12 countries of EurADO. The Russian resource map included details of 82 sub-regions; all country maps include visual data on pediatric oncology resources available in each country/region. Maps are presented using an infographic format making them easy to use and understand. This visual resource has been utilized to modify referral pathways, workforce training algorithms, and to create plans for future capacity growth.

Conclusions: We describe the development of comprehensive resource mapping in the Eurasian region, creating a resources that can be used to improve daily childhood cancer care and for future planning of healthcare services improvement. We hope these tools will help for EurADO collaborators to achieve the overall goal to improve childhood cancer care in the region.

V120 SIOP19-1246 | Sexually Transmitted Diseases Among Childhood Cancer Survivors - A Population-based Register Study from Finland

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Background/Objectives: Childhood cancer survivors have been reported to be prone to late psychiatric morbidities and risky health behavior. Chronic diseases in general have been

shown to be associated with risky sexual behavior in adolescence. We studied the risk for sexually transmitted diseases (STDs) among childhood cancer survivors in Finland.

Design/Methods: Combining data from national cancer and population registries, we identified 5,590 persons diagnosed with cancer under the age of 20 years between 1971 and 2009, and 27,558 age- and sex -matched population comparisons. Survivors and comparisons were included if they were alive at 13 years in 1995. The cohorts were linked to the Infectious disease register to identify laboratory verified sexually transmitted infections. Rate ratios (RR) were estimated using a Poisson regression model, adjusting for age and diagnostic period.

Results: We found that 7% of survivors and 9% of comparisons had a sexually transmitted infection at some point during follow-up. The overall risk for STDs was not increased among childhood cancer survivors as compared to population comparisons (RR 0.84 [95%CI; 0.76-0.93]). The risk seemed to be elevated among females when compared with males in both groups (RR 1.52 [95%CI; 1.42-1.63]). Survivors with CNS tumors were least likely to have an STD (RR 0.49 [95%CI; 0.37-0.64]).

Conclusions: Our preliminary results show that childhood cancer survivors are as likely to have a sexually transmitted disease as population-based comparisons. It is important to integrate sexual education in the follow-up care to reduce risky sexual behavior in this vulnerable group of patients.

V121 SIOP19-1174 | Paediatric Cancer European Reference Network (ERN PAEDCAN) – Report on the Efforts and Achievements Towards Increasing Childhood Cancer Survival and Quality of Life

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Background/Objectives: The ERN PaedCan network aims to improve outcomes and to increase childhood cancer survival and quality of life by linking pre-existing reference centres inherent to the established European Clinical Trial Groups, fostering cooperation, research and training, with the ultimate goal of reducing current inequalities in childhood cancer survival and healthcare capabilities in EU Member States. The main objective is to provide cross-border best care to rare childhood cancer populations.

Design/Methods: In line with the SIOPE Strategic European Cancer Plan for Children and Adolescents, ERN PaedCan focuses on patient groups with conditions requiring a particular concentration of resources and expertise, especially where the expertise for certain cancer diagnoses is rare. The innovative contribution is a Roadmap summarizing briefly cancer entity background, standard treatments and identifies entity specific conditions prone to approved expert referral sites and virtual tumour advisory boards. The network intends to establish mechanisms to facilitate movement of information, guidelines and knowledge rather than patients.

Results: ERN PaedCan continues to build the Roadmap. Entities covered so far: Retinoblastoma, Wilms Tumours, Hepatoblastoma, Langerhans Cell Histiocytosis, Very Rare Tumours, Brain Tumours and Parents and patients survivor organisation. Best practice meetings facilitate these developments (i.e. recent topics were aspects in neuro-oncology and long-term follow-up). Twinning programmes (training fellowships) were set up for oncologists from widening countries, education webinars and films were produced, and key achievements have been broadly disseminated.

Conclusions: ERN PaedCan will increase access to medical expertise and facilitate information sharing for specific/rare conditions beyond national borders, will establish a cross-border dimension for long-term follow-up, implement a virtual tumour board network, develop and publish standardised treatment guidelines and involve an active community of parents and patients.

The ERN PaedCan received funding by the European Union's Health Programme (2014-2020), grant agreement nr. 768967.

V122 SIOP19-0692 | Comparison of Cases Captured in the Singapore Childhood Cancer Registry with the National Population-based Cancer Registry

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Background/Objectives: The Singapore Childhood Cancer Registry (SCCR) is a hospital-based registry, which has been systematically collecting information on malignant childhood cancers and benign brain tumours diagnosed and treated in Singapore since 1997. The cases registered in SCCR are notified by the paediatric units from two public hospitals in Singapore, KK Women's and Children's Hospital and National University Hospital. We compared the number of cancer cases in the SCCR with the Singapore Cancer Registry (SCR), a national population cancer registry.

Design/Methods: All local residents (Singapore Citizens and Permanent Residents), aged 0-14 years, diagnosed with cancers between 1997 and 2014 were included. The cancers were classified according to the International Classification of Childhood Cancer (ICCC). The number of cancer cases registered in SCCR was compared with the number of cancer cases in SCR.

Results: In 1997-2014, 1,508 cases (91.3%) were registered in SCCR compared to 1,651 cases in SCR. The average number of cases captured in SCCR and SCR per year was 83.8 and 91.7, respectively. Comparing by cancer type, the lowest coverage by SCCR was found for the carcinoma and melanoma group (49.1%), followed by lymphoma group (64.6%), other malignant neoplasms (75.0%) and soft tissue tumour group (84.6%). By age group comparison, the coverage by SCCR for 0-4 years, 5-9 years and 10-14 years were 99.9%, 95.0% and 76.3%, respectively.

Conclusions: Overall, the SCCR captured majority of the childhood cancer cases in Singapore. Hence, it serves as a valuable data source for research and clinical management. A notable gap between SCCR and SCR in patients aged 10-14 years old suggests that these patients were treated at the private hospitals or adult oncology units in Singapore. Strategies in capturing of childhood cancer cases need to be evaluated further to improve the completeness of SCCR.

V123 SIOP19-0187 | Validation of a Questionnaire Symptoms and Signs Addressed to the Timely Detection of Childhood Cancer in Mexico Through a Digital Platform

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Background/Objectives: In Mexico, the diagnosis and referral for pediatric cancer is late, with high mortality. We need easy, accessible tools that allow early detection of childhood cancer in our country, through the use of digital platforms.

Objective: To elaborate and validate a questionnaire aimed at the timely detection of childhood cancer

Design/Methods: We designed a questionnaire of 20 items addressed to parents about the main symptoms of the most frequent malignancies in children and applied it in 60 patients with cancer, we evaluated appearance, content and construct validity. The internal validation was performed with the version obtained and applied in a digital platform to 100 patients and 20 negative controls. For external validation we analyzed the predictive power by applying Machine Learning Methodology and we obtained a second digital version of 23 dichotomous questions, which was applied to 686 patients and 99 negative controls in 25 regions of Mexico, we used Random Forest method to evaluate the predictive value of the questionnaire.

Results: We included the digital questionnaires that responded family members of 785 patients, 416 men, 369 female, 40% adolescents. Diagnoses 442 leukemia, 160 lymphomas, 29 bone tumors, 39 germinals and others. The questions related with weight loss, change in skin tone, fatigue, fever, pain and level of it, and adenopathies were positive in the most of cancer patients. The ROC and AUC matrix yielded a value of 0.8995 for the prediction of cancer allowing to correctly classify true negatives in 70%.

Conclusions: The diagnosis and timely reference of patients with childhood cancer will allow to raise the survival in our country above the 50% to 3 years. Although this questionnaire presents some biases, it will be part of a smart tool, available online which will include the social accompaniment of patients with high-risk questionnaires, until the diagnosis of cancer is confirmed or discarded.

V124 SIOP19-1458 | Global Trends in Childhood Cancer Mortality Worldwide, 1990-2017

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Background/Objectives: To examine childhood (0-14 years) cancer mortality trends worldwide.

Design/Methods: We derived population and mortality data for all cancers, and cancers of the liver, bone, connective and soft tissue, kidney, brain and nerves, Non-Hodgkin lymphomas and leukaemia from the World Health Organisation mortality database, for the age groups 0, 1-4, 5-9, 10-14 years, between 1990 and the most recent available year (2017), for all countries with sufficient data quality and over 5 million population. We calculated 0-14 years age standardised rates

for quinquenniums 1990-94, 2000-04 and 2010-14, as well as yearly rates, by sex and country. We applied joinpoint regression models to pinpoint changes in trends and calculate annual percent changes (APC).

Results: Mortality from all neoplasms declined between 2000-04 and 2010-14 in most countries. In the EU rates fell from 3.9 to 3.0/100,000, -23% in males and 3.2 to 2.5, -21% in females, in the US gains were about 15%, with lower rates (2.6 and 2.3/100,000 in 2010-14), Russia showed greater gains (28 and 30%), but had higher rates 4.3 in males and 3.7/100,000 females. The highest rates were in Cuba, Colombia, Mexico, Venezuela and Ukraine (5.4 to 6.2/100,000 males and 4.2 to 5/100,000 females) and the lowest rates were in the USA, Japan and several Western and Northern European countries, including the UK, with rates between 1.8 and 2.7/100,000 males and 1.8 and 2.3/100,000 females. All cancer APCs were generally favourable, with exceptions in a few Latin American countries. Some falls in mortality were registered in neuroblastomas, though smaller than for leukaemia and most other lymphoid neoplasms.

Conclusions: Favourable trends and rates were confirmed in most areas. However, selected areas of Latin America and Eastern Europe had higher rates and smaller gains. This highlights the opportunity for improvement through more widespread and better adoption of adequate and newer treatments.

V125 SIOP19-0523 | Report on the 6 Year Experience of the DAJAC: The Adolescent and Young Adult (AYA) Program in Lyon

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Background/Objectives: In 2012, the French INCA (Institut national du cancer) launched a program to structure and improve the management of AYAs (aged 15-25) with cancer.

The cancer Centre Léon Bérard (CLB) and the Pediatric Hemato-Oncology Institute (IHOP) implemented a dedicated program (DAJAC), in 2012. This program is based on a multidisciplinary team: 4 medical doctors (an “adult” oncologist, an “adult” haematologist, a paediatrician and a medical gynaecologist), two nurses, two psychologists and a social worker.

We report on the first 6 years of this program.

Design/Methods: A database of the patients managed within the DAJAC was created in 2012. An analysis was performed to describe the population and outcomes.

Results: Between June 2012 and June 2018, 635 AYAs were treated for cancer in our institutions and managed within the DAJAC. There were 270 females and 365 males. The great majority of patients were enrolled in the DAJAC at initial diagnosis. Median age of our cohort was 19.3 years (range: 11.4–29.3 years). Fifty two percent were managed in the CLB (median age = 22.3 years) and 48% in the IHOP (median age = 16.8 years).

Overall, 30% had sarcoma, 23% lymphoma, 13% leukaemia, 11% testicular germ cell tumours, 9% brain tumours, 3% ovarian tumours and 10% another tumour type.

From June 2012, at initial diagnosis, every case was discussed at a multidisciplinary tumour board meeting with at least one “adult” oncologist and one paediatrician. One hundred and thirty nine patients were enrolled in a clinical trial. Multidisciplinary supportive care including psychological and social support, fertility preservation advice, adapted physical activity, educational support, and support from charities... is now offered to every AYA patient.

Conclusions: The implementation of a specific program to manage AYAs with cancer is feasible and has led to improvement of care, both in medical and psychosocial terms. Our future aim is to address the survivorship needs.

V126 SIOP19-1602 | Systematic Review of Childhood Solid Tumor Survival in Low and Middle Income Countries

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Background/Objectives: Observed population-based global survival estimates of childhood hematologic and central nervous system cancers were recently reported by the CONCORD Programme, but estimates of childhood survival of solid tumors in low and middle income countries (LMICs) are

lacking. The goal of this systematic review was to assemble the current literature.

Design/Methods: PubMed/Medline, EMBASE, Web of Science, CENTRAL, IMEMR, SciELO, and LILACS were searched from 01/01/11 to 12/19/16 for clinical trial and sequential case series reports from LMIC of survival of children age 0–14y with a childhood cancer.

Results: The search identified 4,695 articles; only 59 fulfilled the inclusion criteria during the 5y period. Among these publications, 11 upper middle income countries, 9 lower middle income countries, and 4 low income countries were represented. China contributed the most studies (13); reports from low income countries Malawi (4 studies), Botswana (1 study), Senegal (1 study), and Uganda (1 study) were included. The distribution of articles by disease was as follows: retinoblastoma (17), germ cell tumors (2), hepatoblastoma (3), rhabdomyosarcoma (7), osteosarcoma (5), Ewing sarcoma (2), Kaposi sarcoma (3), neuroblastoma (6), soft tissue sarcoma (2) and Wilms tumor (12). Inconsistent methodology governing censoring, minimal follow-up times, and only reporting results by risk group made overall survival estimates difficult to summarize but estimates varied greatly from 10% at 5 years in soft tissue sarcoma (Cambodia) to 98% at 5 years in retinoblastoma (China).

Conclusions: A paucity of published data on the survival of children with solid tumors in LMICs exists. A meta-analysis of the published estimates was hampered by errors in reporting, few articles in any one disease category, and inconsistent methodologies. Support of clinical databases with standardized outcome reporting is necessary to understand the current situation of survival of children in LMICs and to serve as a benchmark against which to compare future results.

V127 SIOP19-1112 | Predictors of Clinical Trial Enrollment in Adolescent and Young Adult Cancer Patients

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Background/Objectives: Despite upward trends in U.S. cancer survivorship over the past few decades, children under 15 and adults over 40 enjoy greater rates of improvement than the 15–39 year-old (Adolescent and Young Adult or AYA) demographic. This survivorship discrepancy coincides with a drop-off in clinical trial enrollment for AYA patients. Multiple studies have associated increased survival rates with clinical trial enrollment in this population. This study evaluates possible predictors of clinical trial enrollment including cancer type, pediatric v. adult oncologist care, ethnicity, sex and age at diagnosis.

Design/Methods: Data collection entailed retrospective chart review of electronic health records for patients diagnosed with any malignancy from 2014-2016 who were 15-39 years old at diagnosis within a large county-based public health system in South Texas: University Health System (UHS). Clinical trial enrollment data were acquired through the UHS Cancer Center Clinical Trials Office. STATA 15.1 statistical software was used to run multinomial logistic regressions and create frequency tables.

Results: Patients with Leukemia and Osseous and Chondromatous Neoplasms had significantly greater clinical trial enrollment than those with other cancer types. Furthermore, when stratified by cancer type, patients who had Leukemia, Osseous and Chondromatous Neoplasms, Lymphoma or Germ Cell Tumors who were treated by a pediatric oncologist were significantly ($p < .05$) more likely to be enrolled in a clinical trial. Ethnicity and sex were not significant predictors of enrollment.

Conclusions: Adult oncologist treatment of AYA patients with classically pediatric cancer types predicted decreased clinical trial enrollment. These results suggest that pediatric oncologist management of patients of any age with cancer types common in children or further research to rectify the mechanisms underlying this discrepancy between adult and pediatric oncologists could result in greater clinical trial enrollment, ultimately contributing to increased survival in the AYA population.

V128 SIOP19-1266 | Development of Quality Indicators (QI) for Evaluating Core Hospitals of Pediatric Cancer in Japan

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Background/Objectives: Fifteen hospitals have been elected as core hospitals of pediatric cancer treatment with the aim of further integration and to provide uniform accessibility in Japan. The purpose of this study was to develop quality indicators (QI) of pediatric cancer centers and to evaluate the core hospitals with the system of measurement by health information managers.

Design/Methods: Thirty-seven indicators, 24 of which were therapy-related (8 structure, 6 process and 10 outcome index) and 13 of which were QOL-related (3 structure, 7 process and 3 outcome index), were developed in 2015. Revised 36 indi-

cators (4 newly adopted, 3 deleted and 10 revised index) were adopted in 2017 by the expert panel.

Results: The system of measurement of QI differed in each core hospitals, so we formed a working group of measurement by health information managers to obtain precise and objective results. Detailed analysis of QI showed that there exist delay of allocation of pediatric surgery certified surgeons and palliative care specialists, and exist facilities disparities in consultation rate of long-term follow-up outpatients and intervention rate of palliative care teams. In university hospitals, there was tendency of higher rate to treat AYA cancer patients and to offer fertility preservation to the cancer patients than in children's hospitals. In 2017 new infection-related QI were added about the rate of catheter associated blood stream infection and surgical site infection, which 11 and 13 hospitals respectively could report by the aid of their infection control teams (ICT).

Conclusions: Establishment of universal QI for pediatric cancer care was difficult, because structure index tended to be high in university hospitals unless the definition of the index limited to pediatric values. Cooperation with ICT contributed to increased quality of care and measurement of QI by health information managers lead to adequate arrangement of such occupations in pediatric cancer core hospitals.

V129 SIOP19-0981 | Use of Fertility Drugs in Early Onset Female Cancer Survivors –A Finnish Register-Based Study on 8,929 Survivors

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Background/Objectives: Advances in multimodality cancer treatments have increased the risk of long-term complications in early onset cancer survivors. For female cancer survivors these include diminished reproductive function, often resulting in a narrowed fertile window. The aim of this study was to evaluate the use of fertility treatments in cancer survivors (aged 0-39 years at diagnosis) compared to siblings.

Design/Methods: Data from Finnish registers on cancer, birth and prescribed medication were merged to identify 8,929 survivors and 9,495 siblings without previous deliveries. Fertility drug purchases from 1993 to 2012 at the age of 16-41 years were included. A Poisson regression model was used to estimate incidence rate ratios (IRR) for the use of fertility drugs, adjusting for age and calendar time at fertility drug purchase.

Results: Fertility treatments were more common in survivors compared to siblings, as 6.1% of survivors compared to 3.8% of siblings had bought fertility drugs (IRR 1.43, 95% confidence interval [CI] 1.25-1.65). A sub-classification of fertility treatments into ovulation inductions and assisted reproductive technology (ART), showed increased use of ART (IRR 2.41, 95% CI 1.97-2.96), whereas the use of ovulation induction was similar in survivors and siblings. Analyses by calendar time periods showed the use of ART to be significantly higher in the most recent decade, from 2003 onwards.

Conclusions: Cancer survivors have an increased risk for sub-fertility, which is why fertility counselling is important. However, our results mirror a more active approach among clinicians towards fertility treatments in cancer survivors during the most recent years.

V130 SIOP19-0609 | Outcomes of Paediatric Haematology/Oncology Patients Admitted to Paediatric Intensive Care

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Background/Objectives: Cancer remains a leading cause of death in all children world-wide however with better understanding of disease, improved treatments and better supportive care, survival from childhood cancer has significantly improved. Paediatric Intensive Care (PICU) is an integral part of supportive care for children with malignancy.

Design/Methods: Patients under the care of the regional paediatric haematology and oncology team admitted to PICU between 1st of December 2010 to 31st of December 2015 were identified using hospital coding and electronic patient case notes. The primary outcome of this retrospective analysis was survival within 30 days of PICU discharge. Secondary outcomes include mortality rates for type of admissions, patients receiving ventilatory support, inotropic support, renal replacement therapy and multiple interventions.

Results: A total of 110 Childhood cancer patients were admitted to PICU on 183 occasions. During the same period the proportion of patients with leukaemia, solid tumour patients and Neuro-oncology patients were similar with 67 (37%), 56 (30%) and 60 (33%) episodes respectively for each category. Median length of stay in PICU was 3 days. Overall survival within 30 days of discharge was 94%. Respiratory failure and sepsis were the two leading causes of admissions. There were 123 Emergency admissions and 60 elective admissions. 11/123 (8.9%) patients died in the emergency admissions group while there were no deaths in the group of patients admitted electively. Survival for patients who

received ventilatory support was 92.3%, inotropic support was 93% and renal replacement therapy was 70%. 12/17 (70.5%) patients survived needing ventilation and inotropes whilst only 5/8 (62.5%) survived needing all three levels of support. At 2 year follow-up the overall survival rates decreased to 69%.

Conclusions: Survival to discharge from PICU for paediatric haematology/oncology patients have improved significantly throughout the years. This retrospective analysis confirms that full intensive care should be offered to children with malignant disease.

V131 SIOP19-1393 | Epidemiological Characteristics and Clinical Outcomes of Paediatric Cancer Cases Presenting to an Emergency Unit in Ghana

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Background/Objectives: The Paediatric Emergency Unit, PEU of the Komfo Anokye Teaching Hospital, KATH receives referrals including suspected paediatric cancers from many parts of Ghana. Here, children receive emergency and/or intensive care before been transferred to the Paediatric Cancer Unit, PCU. We aimed to describe the epidemiological characteristics and clinical outcomes of suspected paediatric cancer cases presenting to the PEU in KATH.

Design/Methods: Data was prospectively extracted from the clinical records of all children with suspected malignancies admitted through the PEU to the PCU of KATH from January to December 2017 and analysed with Microsoft EXCEL

Results: Overall, 106 children, mean age 9years and mostly males (55%) reported to PEU with suspected malignancies. Majority (66%) were from the Ashanti region with 14% and 11% coming from the Central and Eastern regions respectively. The others were referred from 4 other regions. Most, 101 (97%), caretakers were mothers and grandmothers who had basic level education 59 (54%) or no formal education 40 (37%). Many caretakers were informally employed as traders 60 (55%), farmers 21 (19%) or artisans 16 (15%). The median time from referral to reporting was 14 days (range 1 - 42days). The median length of stay on PEU ranged from 48hours (60%) to over one week (9%). Malignancy was confirmed in 70 (66%) children comprising: Lymphomas 22 (31%); Leukaemias 13 (19%); Renal cancers 12 (17%) and Retinoblastoma 8 (11%). 8 (11%) have completed treatment and survived; 5 (7%) are actively on treatment; 20 (29%) have abandoned treatment; and 37 (53%) children died by March 2019. Ten (50%) children in the treatment-abandonment group had lymphoma (Burkitt, 8); 3

(15%) retinoblastoma and 4 (20%) neuroblastoma. Among the 37 deaths, 20 (54%) were leukaemia/lymphoma-related; 5 (13%) and 4 (11%) from sarcomas and neuroblastoma respectively.

Conclusions: Majority of families were from low socio-economic backgrounds who arrived late to the PEU following referral. Treatment-abandonment and mortality rates among confirmed cancer cases, the majority of referred children, remain high.

V132 SIOP19-0949 | Factors That Take A Long Time to Diagnose of Adolescent and Young Adult Cancer Patients in Japan

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Background/Objectives: This study aimed to know the factors related to the difficulty of diagnosis of adolescent and young adult (AYA) cancer patients in Japan.

Design/Methods: We conducted a nationwide survey of AYA (15 to 39 years old) cancer patients, survivors, parents and siblings. We distributed questionnaires to AYA survivors via their doctors in 15 institutes and 31 patient advocacy groups from June to November in 2016.

Results: In total, there were 472 respondents (response rate: 32.6%) among 1446 participants who were AYA cancer patients and survivors. Thirty three percent of them were male. They were diagnosed breast cancer (23.7%), leukemia (22.9%), malignant lymphoma (7.6%), brain tumor (7.0%), testicular tumor (5.3%), osteosarcoma (5.1%) and others. The diagnostic period of AYAs who diagnosed cancer, especially between 20 and 29 years old was longer than that diagnosed under 15 years old (diagnosed within 1 month: 37.9% vs 44.2%, within 1 to 2 months: 21.4% vs 16.3%, within 2 to 3 months: 15.5% vs 7%). The 172 AYA patients who took more than a month to diagnose answered the reasons as follows. Patients aged 15 to 19 repeated changing hospitals (48.1%) because they had difficulty in diagnosing cancer, and they answered that they had no time to see a doctor (29.6%). The reason for the group from 20 to 24 years old is that they did not go to the hospital because they thought their physical condition was good (39.1%).

Conclusions: The reason why it takes a long time to diagnose adult adolescents and young adults with cancer in Japan has problems with both their health care behavior and the medical system. Early diagnosis of AYA generation cancer requires an

approach to both health care education and medical system development for AYA generation.

V133 SIOP19-0937 | Racial and Ethnic Disparities Exist in Incidence of Langerhans Cell Histiocytosis and Differ Across Age Groups

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Background/Objectives: Langerhans cell histiocytosis (LCH) is a myeloid neoplasia with median diagnosis age of 30 months. We recently reported an increased risk for LCH in children of Hispanic parents using data from the Texas Cancer Registry. However, less is known about racial/ethnic disparities among adults diagnosed with LCH. Therefore, we sought to compare the incidence of LCH by race/ethnicity in the United States among pediatric, adolescent/young adult (AYA), and adult cases using Surveillance, Epidemiology, and End Results (SEER-18) program data.

Design/Methods: LCH incidence data were obtained from the SEER-18 program, 2000-2015. Race/ethnicity was categorized as: non-Hispanic white (NHW); non-Hispanic black (NHB); non-Hispanic Asian (NHA); and Hispanic. Age-specific incidence rate ratios (IRRs) and 95% confidence intervals (CIs) were generated in SEER-STAT (v8.3.5).

Results: Data on cases with LCH ages 0-14 (nchildren=777), 15-39 (nAYAs=214), and 40+ (nadults=261) were abstracted. Compared to NHW children, Hispanic children experienced significantly elevated IRRs (IRRHispanic_children=1.30, 95% CI: 1.11-1.52). However, this trend was not observed among AYAs (IRRHispanic_AYAs=0.62, 95% CI: 0.43-0.89) or adults (IRRHispanic_adults=0.60, 95% CI: 0.37-0.95) where lower IRRs compared to NHWs were evident. While not statistically significant, this trend was also suggested among NHAs. Compared to NHW children, IRRs for NHAs were slightly elevated (IRRNHA_children=1.06; 95% CI: 0.81-1.38), whereas among AYAs a trend toward lower incidence was suggested (IRRNHA_AYAs=0.59, 95% CI: 0.32-1.01) and became stronger among NHA adults (IRRNHA_adults=0.56, 95% CI: 0.31-0.96). NHBs experienced lower IRRs compared to NHWs in all age groups: (IRRNHB_children=0.36, 95% CI: 0.25-0.51; IRRNHB_AYAs=0.47, 95% CI: 0.26-0.79; and IRRNHB_adults=0.41, 95% CI: 0.21-0.74). These estimates remained similar after adjusting for sex and SEER registry using Poisson regression.

Conclusions: These contrasts in incidence by race/ethnicity suggest differences in underlying LCH etiology across the age spectrum and particularly in children. While limitations

of registry data exist, future studies characterizing molecular components in adults compared to children is warranted.

V134 SIOP19-1282 | Innovative and More Powerful Statistical Approaches to Assess Long-Term Survival in Paediatric Oncology Using Pseudo-Values

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Background/Objectives: In paediatric oncology usually the main aim is to increase the rate of long-term survivors and hence, the probability to cure children with cancer. Note that from a statistical perspective this is intrinsically different to aiming for a prolongation of survival times in older populations. Ignoring the main interest in long-term survival probabilities by using standard approaches of survival analysis, with non-proportional hazards ambiguous results, wrong interpretations and underpowered studies may occur.

Design/Methods: Lately, the pseudo-value regression was proposed to directly model the impact of covariates on long-term survival probabilities. Using examples in Neuroblastoma, stem-cell-transplantation in childhood Acute Lymphoblastic Leukaemia (ALL) and Langerhans-cell-histiocytosis (LCH), the benefits of this innovative approach in the analysis and the design of clinical trials is demonstrated. Recently, the pseudo-value regression was generalised to deal with time-dependent interventions in order to avoid waiting-time bias when comparing survival in patients with SCT and conventional chemotherapy.

Results: The first illustrative example evaluates the prognostic value of age and MYCN-amplification in stage-4 Neuroblastoma patients of the HR-NBL1/SIOPEN trial. While an analysis based on Cox-regression and log-rank test provides severely misleading results, the estimates of the pseudo-value regression are directly linked to long-term survival probabilities with an unambiguous interpretation. Furthermore, using approaches based on pseudo-values for clinical trials comparing treatments of different intensities/durations substantial gains in statistical power can be anticipated. Design considerations of the ALL-SCT Forum, the LCH-IV trial and studies comparing patients with SCT and conventional chemotherapy in childhood ALL clearly illustrate this major benefit.

Conclusions: The pseudo-value regression is a novel statistical approach that is, although yet rarely used, particularly useful to evaluate survival in children with cancer. With non-proportional hazards, it clearly outperforms other approaches. These advantages in mind, pseudo-value regression should

become part of the standard repertoire of statisticians working in paediatric oncology.

V135 SIOP19-1340 | The French Childhood Cancer Observation Platform

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Background/Objectives: The Childhood Cancer Observation Platform (CCOP) is an infrastructure based on the French National Registry of Childhood Cancers (RNCE). It was set up under the auspices of the French pediatric oncology society, the SFCE, with the ambition of permanently following up all childhood cancer cases, and systematically integrating a large range of standardized data.

Design/Methods: The CCOP includes all primary childhood cancers diagnosed under 15 years in mainland France since 2000. The RNCE provides baseline and basic follow-up data. Besides, four additional sets of data are implemented.

Detailed treatments and responses are collected in medical records five years after diagnosis; additional information on radiotherapies for cases diagnosed since 2013 are provided by the French network of pediatric radiotherapy units in the PediaRT database. The **COHOPER cohort** ensures systematic follow-up of cases diagnosed since 2000 through an annual linkage with the National health insurance information system (SNDS) database and web-questionnaires to adult five-years-survivors (starting in October 2019). The **virtual biobank BIOCAP** includes standardized information on specimens stored in the hospital biobanks for cases diagnosed since 2009 onwards. The **GEOCAP database** includes the precise spatial coordinates of the residences at the time of diagnosis and those of contemporaneous controls.

Results: The CCOP includes 29,546 cases. The five-year systematic follow-up is completed for 51.0% of 2000-2012 cases

(11,511 cases). PediaRT provides data for 641 cases. To date, 24,130 cases are eligible for follow-up based on SNDS data and 10,054 are eligible for the web-questionnaires. BIOCAP data are collected for 19,698 specimens from 4,944 cases diagnosed over 2009-2016. GEOCAP has complete data for about 29,500 cases and 59,000 controls.

Conclusions: Even though the CCOP only started in 2013, it constitutes a powerful infrastructure to support clinical and epidemiological research, health surveillance and public health decision making in the field of childhood cancers.

V136 SIOP19-1308 | Experience Using A Score-based Need Assessment Tool (Profile) During The Initial Twinning Partnership Between Children's Hospital Colorado and Hospital Del Niño in Panama

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Background/Objectives: Twinning programs between hospitals in high-income countries and resource-strained countries can advance pediatric oncology outcomes locally. The Center for Global Health, Colorado School of Public Health, and Children's Hospital Colorado and Hospital del Niño Jose Renan Esquivel in Panama began a twinning partnership in 2018. We field-tested the face and formative validity of the St. Jude Global Pediatric Oncology Facility Integrated Local Evaluation (ProFILE) tool during their initial site visit, as the participating institutions aimed to identify gaps in health-service delivery and prioritize areas of engagement.

Design/Methods: ProFILE's question bank was used to structure the needs assessment visit. The tested version of ProFILE had 12 modules, 36 subdomains, and 354 questions. A total of 18 structured interviews were conducted during the 4-day onsite visit. Data from each module were scored and analyzed after the visit. The resulting scores and an impact-effort matrix were used to prioritize areas of engagement.

Results: Score-based results were as follows; score <50% for service integration and patients and outcomes modules, score 50-75% for national context, facility and local context, personnel, service capacity, diagnostics, surgery and radiation oncology, score >75% for service capacity, supportive care, and finances and resources. Based on quantitative and qualitative data, the twinning partners prioritized strengthening pathology services, increasing number of beds and accessibility to intensive care services for oncology patients, standardizing the use of roadmaps, order sets, and flow charts for key malignancies, supporting nurse PICU and oncology

education and mentoring, and strengthening of data systems to allow prospective and retrospective review of patient outcomes.

Conclusions: ProFILE helped illustrate health-service delivery at the facility and was a key component during dynamic prioritization at the initial stages of this pediatric oncology twinning program. It identified areas amenable to quality improvement methodologies. Repeated use of ProFILE scores will allow tracking of progress over time.

V137 SIOP19-1149 | Expansion of a Childhood Cancer Clinical Outcomes Surveillance System in Colombia: Challenges and Opportunities

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Background/Objectives: Assessing childhood cancer clinical outcomes and its determinants is essential for designing effective strategies to improve survival. In 2009, we established a childhood cancer clinical outcomes surveillance system (VIGICANCER) in Cali, Colombia. Since geographical location and local settings may affect outcomes, we expanded VIGICANCER to other Colombian regions to understand local differences. We describe the challenges and opportunities during expansion.

Design/Methods: We implemented VIGICANCER in Cali from 2009-2012 and, in 2013, we expanded it to 8 cities, supported by Cali's Population-Based Cancer Registry and pediatric oncologists (PO) locally. Our expansion was multi-step and based on standardized operational procedures but allowed flexible adaptations to local needs across regions. Our model includes: a PO leader in each pediatric oncology unit (POU), clinical monitors (CM) collecting data, centralized iterative quality controls and database management/reporting tailored to each region. We established a non-governmental organization (NGO) for management and financial sustainability.

Results: During 2013-2018, we expanded VIGICANCER to an area covering ~50% of Colombian children. As of December 2018, 4127 children were registered. A shared vision of the project's impact; collective trust among all stakeholders; and enhanced communication by a dedicated,

reliable local leader were pivotal to a successful regional implementation. Key activities/opportunities to expansion success included: engaged POs; a committed scientific team; effective project management by the NGO; and external mentoring and funding. Capacity building was essential as POU had no previous outcomes research experience. Local leaders were empowered to build each team. POs and CMs received systematic orientation and ongoing intensive training. To ensure process fidelity at all sites, a CM leader oversees all CMs, and regular, centralized database quality controls were performed.

Conclusions: Our multi-step model was successful in establishing and scaling a clinical outcomes pediatric cancer surveillance system in a middle-income country, which will inform cancer control efforts.

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V138 SIOP19-1650 | Treatment of Children with Acute Lymphoblastic Leukemia in the Palestinian Territories: Movement Restrictions and Fragmentation of Care

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Background/Objectives: The occupied Palestinian Territories (oPT), consisting of the Gaza Strip (GS), West Bank (WB), and East Jerusalem (EJ), are home to an estimated 300 new cases of childhood cancer annually, approximately 120 of whom live in the GS. The oPT are separated geographically and politically, and a lack of locally-available services for children in Gaza with acute lymphoblastic leukemia (ALL) requires their referral and travel to different regions across military checkpoints, which can result in physical and psychosocial burdens as well as significant delays in diagnosis and treatment. No studies have been published to date tracking the management of children in Gaza with ALL across regions.

Design/Methods: A retrospective review was conducted of pediatric patients with ALL referred from Gaza to HAMPCD in Bethlehem, the only public pediatric oncology department in the WB, between March 2015 and March 2019.

Results: Twenty-six patients with ALL were treated over the four-year period reviewed (57.7% female), ranging from 23 months to 11 years 7 months old (mean 5 years 7.1 months). Upon clinical suspicion of leukemia, an oncologist in GS makes a referral to HAMPCD. Patients then must request a travel permit to the WB, which can lead to a delay in diagnosis of days to weeks. Upon approval, a child travels to Bethlehem,

a bone marrow sample is obtained and sent to Jordan for flow cytometry. When ALL is confirmed, a referral is made to Hebron for central catheter placement, and back to Bethlehem for induction chemotherapy. Drug shortages lead to travel to EJ for PEG-asparaginase, and refractory/residual disease during treatment requires a permit to Israel for more intensive therapy, including bone marrow transplant.

Conclusions: Fragmentation of care for children with ALL is a burden on children and families and can lead to significant delays. Further studies are needed to create more efficient treatment pathways.

V139 SIOP19-0226 | Audit of the Initial Management of Patients Presenting to a Principle Treatment Centre with Suspected Febrile Neutropenia

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Background/Objectives: Febrile neutropenia is a major cause of treatment-related mortality in paediatric cancer. Patients with suspected febrile neutropenia should be treated as an emergency and empiric antibiotic therapy administered immediately. A previous audit in 2015 showed that time-to-antibiotic administration (TTA) from arrival for patients presenting to the accident and emergency department (A&E) at a principle treatment centre (PTC) with suspected neutropenic sepsis was not compliant with local protocol. Subsequently a new patient care pathway was introduced.

We aimed to determine whether introduction of a patient care pathway together with staff education improved compliance with the local guideline and affected patient outcome.

Design/Methods: A retrospective audit of all patients presenting to a PTC with suspected febrile neutropenia between July and December 2015 and between July and December 2017 was performed. Primary outcome measures were time from arrival to nursing and medical assessment and TTA. Secondary outcome measures were admission to PICU within 24 hours of admission, fever at 72 hours and length of hospital stay.

Results: 60 patients accounted for 74 patient episodes. There was a trend to reduction in time from arrival to nursing and medical assessment and TTA for all patients. For patients presenting to A&E there was a significant reduction in the time to medical assessment ($p=0.03$) and an increase in the percentage of patients who received antibiotics within 30 minutes of arrival ($p=0.03$). Unexpectedly there was a significant increase in the length of hospital stay for patients presenting to A&E, which may reflect an increase in the number of

high-risk patients between the two study periods. There were no other differences in secondary outcomes.

Conclusions: Introduction of a new patient care pathway together with staff education reduced the time to medical assessment and TTA for patients presenting to A&E at a PTC with suspected febrile neutropenia.

V140 SIOP19-0632 | Evaluation of Access to Timely Cancer Care in Tanzania Using A Developed Multi-Modal Transport Network Software (CANGEO)

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Background/Objectives: In 2012 there were just 102 cancer treatment facilities for 1.04 billion people in Africa. In Tanzania, a low-income country in East Africa, there are currently three referral cancer treatment centers and six total cancer treatment facilities. Previous studies estimated that only 5% of children with cancer in Tanzania reach these treatment centers. To increase patient diagnosis and treatment, decentralization is needed. Geospatial software (CanGeo) was used to determine access to cancer care in Tanzania and create an optimized decentralization strategy.

Design/Methods: CanGeo was used to construct a multi-modal transport network between hospitals and population-weighted ward centers to identify travel time. A decentralization strategy was developed using maximum coverage location problem criteria. Bugando Medical Centre (BMC), one of Tanzania's three referral cancer centers, was used as a case site to review expected versus actual patient presentation for all pediatric patients seen at BMC in 2017.

Results: Population-weighted average time to nearest cancer care facility was 5.25 hours. Up to 22.7% and 42.5% of the population have a two-hour or four-hour facility access time, respectively. Expanding basic cancer care capacity to 30 optimally selected hospitals throughout Tanzania would increase two-hour access to 71.6% and four-hour access to 95.6%. Expected incidence of pediatric cancer is 13.4/100,000 population in Tanzania and actual incidence was 1.1/100,000. Within the BMC catchment area, the overall incidence was 1.1/100,000. Attendance was 2.3/100,000 for patients who lived within one-hour but fell to 0.9/100,000 for patients with over one-hour travel time.

Conclusions: In comparison with high-income settings, access to cancer care in Tanzania remains highly limited. Travel time to cancer facility influences presentation, highlighting the importance of optimal selection of new facili-

ties for future decentralization. CanGeo can help measure and improve access to cancer care making it a useful tool for cancer policy development in low-resource settings.

V141 SIOP19-1681 | Characteristics of Presentation and Outcome of Tumours Resulting in Spinal Cord Compression. What Can We Inform the Primary Healthcare Professionals?

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Background/Objectives: Tumours presenting with spinal cord compression (SCC) are rare (<1%) and require emergency management. Parents are concerned with delayed diagnosis following a long symptom time interval (STI), delays in initiation of early investigations and treatment and subsequent impact on neurological outcome of their child. No national awareness program exists, unlike HEADSMART for brain tumours, to educate parents and primary-care professionals regarding the presentation and diagnoses of spinal tumours. We review our Regional experience to inform the initiation of a Regional campaign.

Design/Methods: Retrospective study of Regional data base of children presenting with tumours causing SCC over 10.5 year period (01/2008-06/2018) in our Tertiary Paediatric Oncology centre was conducted. Data collated on: patient demographics, presenting features including intradural versus extradural tumours, STI (time between onset of symptoms to first imaging), emergency treatment and neurological outcome at 6 months.

Results: Thirty patients (including 7 relapses) with age range of 11months-17 years, were analysed. Eleven had intramedullary tumours with low-grade glioma (LGG), ependymoma and 19 had extradural spinal tumour with Ewings Sarcoma, neuroblastoma, germ-cell tumour.

The predominant symptom was back pain (23/30); neck, abdomen and thigh/leg pain, regression of motor skills, gait disturbances was similar with intra and extradural tumours. Most patients presented with more than 1 symptom.

Thirteen months was longest STI with a LGG and shortest was 2 weeks with neuroblastoma. The emergency management included dexamethasone with neurosurgery (25) or chemotherapy (4). At 6 months 6 had full recovery.

Twelve died of their cancer at follow-up.

Conclusions: SCC presents with red flag symptom of back pain that is complex and variable depending on location,

diagnosis and age, hence parents and health professionals need awareness for early recognition. We therefore aspire to create a regional and national awareness /education program, akin to HEADSMART, in order to potentially reduce STI in this vulnerable patient population.

V142 SIOP19-0129 | A Systematic Review and Meta-Analysis of the Signs and Symptoms of Abdominal Tumours in Children and Young People

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Background/Objectives: Abdominal tumours in children are often associated with diagnostic delay. In the UK, children with Wilms tumours present with a larger volume and worse stage than those in the rest of Europe. Experience from the Headsmart campaign showed that promoting awareness of key symptoms can significantly reduce the diagnostic interval. We conducted a systematic review and meta-analysis on abdominal tumours in order to understand the key presentations.

Design/Methods: Medline, Pubmed and Embase databases were searched without language restriction from January 2005 – August 2015. Key words were “abdominal tumour (s)”, “abdominal tumor (s)”, “abdominal neoplasm (s)”, “diagnosis”, “signs (s)”, “symptom (s)”, “presentation (s)”. All references were restricted to “all child”. All papers discussing abdominal tumour presentation and time to diagnosis were included. A standard data extraction form was used. Pooled proportions (%) of children with each sign or symptom at diagnosis were estimated. Subgroup analysis of Wilms tumour and Neuroblastoma was undertaken.

Results: The search strategy identified 8532 papers. 984 papers were reviewed in full. 51 papers met the inclusion criteria, describing the symptoms and signs in 3402 children. 97 symptoms and signs were recorded but only those that occurred in 2% or more of patients are reported. These were abdominal mass (40%), abdominal pain (13%), fever (7%), hypertension (4%), haematuria (4%), abdominal distension (3%), palpable mass (2%), weight loss (2%) and incidental finding (2%). Hypertension and haematuria occurred in renal tumours (n= 2262) but not neuroblastoma (n= 487).

Conclusions: This is the first systematic review on paediatric abdominal tumours to our knowledge. This provides strong evidence of the common presentations and will form the basis for new clinical guideline on the assessment and investigation of children with a suspected abdominal tumour. This will form key messaging in our new national awareness campaign called ChildCancerSmart, raising awareness of symptoms amongst

the public and healthcare professionals for earliest possible diagnosis.

V143 SIOP19-0938 | Cohort Studies Investigating Syndrome-Cancer Associations May Suffer From Bias in Design, Analysis, and Reporting

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Background/Objectives: More genetic syndromes are becoming apparent and genetic testing is becoming widely available. With few exceptions, risk factors for childhood cancer are unknown, which also provides little chance for prevention or risk group screening. Detecting more associations between syndromes and childhood cancer offers a chance to change this. Unfortunately, studies for uncovering such associations are often subject to built in biases in design and analysis.

Design/Methods: In epidemiology, cohort studies are considered the most reliable type of study to detect risk factors for a disease: the cancer incidence rate of a (large) cohort of syndrome cases is compared to the total population incidence rate. We investigated the potential for bias in a number of scenarios considering the following factors: the undiagnosed fraction of syndrome cases in the unaffected population and in the respective cancer population, the fraction of syndrome cases among cancer cases being detected because of the cancer diagnosis, assuming a reduced life expectancy of syndrome cases. In addition, published studies were reviewed whether or not the information needed to assess their potential for bias was reported.

Results: The extent of overestimating the association depends on a) how large the undiagnosed fraction in the population is and b) what fraction of the syndromes were additionally diagnosed among the cancer cases. If for example 50% of the population syndrome cases are undiagnosed and all syndromes in the cancer cases are diagnosed, the association between syndrome and cancer will be 2-fold overestimated. So far we have been unable to find the information needed to estimate the potential size of the bias in publications using this design.

Conclusions: Reliable estimates can still be obtained from such cohort data by selecting patients whose syndrome was diagnosed independently of the cancer diagnosis. This reduces the number of observations and thus the power of the study.

V144 SIOP19-1077 | Knowledge and Awareness of Childhood Cancer Among Doctors in Ghana

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Background/Objectives: Late presentation remains a barrier to achieving improved outcomes for childhood cancer in Ghana. The objective of the study was to assess the level of knowledge of childhood cancer among doctors in Ghana.

Design/Methods: An online questionnaire was disseminated to doctors in Ghana through the Ghana Medical Association's official Google Group mailing platform and social media group pages of doctors (estimated number reached was 1800).

Results: Of the 210 respondents, 51.4% were male, 38.1% General Practitioners and 23.8% worked in Paediatrics. About 7% had never seen a child with cancer in their practice. Majority (98%) knew childhood cancer was curable. Only 28% knew the commonest childhood cancer in Ghana is lymphoma. For early warning signs of retinoblastoma, 77% chose leukocoria whereas 49% included proptosis, a late sign. Abdominal mass was identified by 82.9% as an early sign of Wilms tumour while 42.9% incorrectly included gross abdominal distension. Pallor, bone pain and bleeding gums were identified as early signs of leukaemia by over 70% while a quarter incorrectly included jaundice. Ninety-nine percent identified lymphadenopathy as an early sign of lymphoma while 13.3% chose seizures. Many thought the leading cause of poor treatment outcomes was poverty, and for 9% it was lack of adequate training of health personnel. Most (68.6%) knew childhood cancer treatment was primarily funded by parents. Only a third felt confident in picking up early warning signs of childhood cancer. Surprisingly, 4% would not recommend chemotherapy for childhood cancer. Reasons included chemotherapy being toxic and ineffective in childhood cancers.

Conclusions: There is a need for training on early warning signs of childhood cancers among various grades of doctors in Ghana. This survey will need to be repeated post-training to assess the impact.

V145 SIOP19-0874 | Improving Access to Care for Children with Cancer in Rural Cameroon

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Background/Objectives: The Cameroon Baptist Convention Health Services (CBCHS), as several health institutions in

Sub-Saharan Africa has traditionally focused on infectious disease. No dedicated service was available for children with cancer. Parents were left alone in their journey moving from one Health care provider to another one, after frustration from one traditional healers to another. Paediatric oncology services started in the CBCHS in 2003 with treatment of Burkitts lymphoma, which gradually involved the treatment of Wilms tumour, retinoblastoma, and other paediatric malignancies. Our aim is to describe the development of a comprehensive childhood cancer program in a rural African hospital setting.

Design/Methods: The authors retrospectively reviewed all services rendered to children with cancer from 2003 to 2018 in the Cameroon Baptist convention Health Services.

Results: Services began in 2003. Twinning was established with Beryl Thyer Memorial Africa Trust (BTMAT) and Stellenbosch University. World Child Cancer (WCC) joined in 2011 and Leeds children hospital in 2016. A paediatric cancer registry was started in 2008. From 2003 to 2016, 1260 patients were registered. The median age of the patients was 7 years, 58.1% were male and 41.9% female. The three most common types of cancer diagnosed in these paediatric patients were Burkitt lymphoma (n=982, 77.9%), Wilms tumor (n = 75, 6%) cases 6%, and retinoblastoma (n= 73, 6%). Outcome after a median follow up of 27 months: 628 alive (55.6%), 436 dead (38.6%), 64 (5.7%) did not complete their treatment. The general paediatric ward was renovated, providing dedicated space for paediatric oncology. A palliative care out reached component was started in 2013 with 381 home visits effected. In 2017, a parents' home was built.

Conclusions: The new paediatric oncology service has improved the care of children with cancer, giving hope to parents whom otherwise would have travelled to the capital city to the previously lone paediatric oncologic centre.

V146 SIOP19-1481 | Comparing Colonization Surveillance Results in Pediatric Patients Undergoing Hematopoietic Stem Cell Transplantation That Developed Bloodstream Infection

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Background/Objectives: Patients undergoing hematopoietic stem cell transplantation (HSCT) are at high risk for acquiring bloodstream infection, interfering with the success of the treatment and making important preventive measures. The objective of this study was to identify whether the presence of colonization through surveillance cultures to investigate

carbapenem resistant enterobacteriaceae (CRE) and vancomycin resistant *Enterococcus* (VRE) interfered in the development of infections.

Design/Methods: This is a retrospective cohort study. Bloodstream infections data were collected from May 2010 to May 2018 in patients with a diagnosis of cancer, undergoing to allogeneic HSCT with rectal swab for the search for CRE and VRE prior to admission to the transplant.

Results: Of the 80 cancer patients transplanted, 23.68% acquired bloodstream infections. There were 18 patients with median age of 10 years, 55% female. The most frequent diagnosis was Acute Myeloid Leukemia (66.6%), followed by Acute Lymphoid Leukemia (16.6%). Transplants were no-related donors represented 61.1% of the HSCT, related 33.3% and haploidentical donors 5.5%; in 22.2% of the procedures, cord blood was the source of cells. Of the reported infections, 61.1% were by Gram-positive and 33.3% Gram-negative bacteria. Regarding bloodstream isolated agents were 27.7% *Staphylococcus epidermidis*, 22.2% *Escherichia coli*, 11.1% *Enterococcus faecium* and 11.1% *Streptococcus viridans*. Rectal swab collection had been done in 77.7% of cases with 16.6% positive just for *Enterococcus faecium*. Only one patient who presented positive swab for *Enterococcus faecium* had *Enterococcus* sp isolated.

Conclusions: Although most patients with bloodstream infection had a CRE and VRE investigate, no relation was found with the bloodstream isolated agent, except in one case. This result does not minimize the importance of the collect and suggests new studies in this population, in order to identify other variables that characterize risk factors.

V147 SIOP19-0906 | Pediatric Malignancies with Primary Immunodeficiencies; A Two Years Experience at a Single Institute from Pakistan

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Background/Objectives: Primary immunodeficiencies (PIDs) are a group of inherited immune system disorders associated with increased susceptibility to infections, autoimmune disorders and malignancies. This study's objectives were to determine the frequency of PID-associated malignancies, outcome and factors associated with outcome, in pediatric patients presenting at a tertiary care hospital in Pakistan.

Design/Methods: Analytic, observational; retrospective, cohort study, conducted in the department of Pediatric Hematology-Oncology, Children's Hospital Lahore, Pakistan from Jan 2017 till Dec 2018. Patients under 16 years of age,

diagnosed with PID, presenting with malignant disorder were included.

Results: Total 1882 patients with various malignancies were registered over 2 years period while we enrolled 27 patients (1.43%) who had associated PID. The median age of presentation of patients with associated PID was 4.0 years. Male to female ratio was 1.1:1. Four different types of PIDs were encountered. Down's syndrome was found in 70.4% (n=19) patients and Griscelli syndrome in 14.8% patients (n=4). Chediak-Higashi syndrome and Ataxia-Telangiectasia, each was found in 7.4% patients (n=2). B-cell Acute Lymphoblastic Leukemia (ALL) was seen in 48% patients (n=13). Hemophagocytic Lymphohistiocytosis (HLH) and Acute Myeloid Leukemia, each was present in 22.2% of patients (n=6) while T-cell ALL and Hepatocellular carcinoma, each was found in 3.7% patients (n=1). Total 14.8% patients (n=4) completed treatment, 48.1% (n=13) were under treatment while 37.1% patients (n=10) expired during treatment. Commonest cause of death was sepsis (70%, n=7), followed by Invasive fungal infection in (30%, n=2) and Surgical site infection (10%, n=1). Underlying malignancy and type of infection were found to be statistically significant factors associated with outcome.

Conclusions: The combination of primary immunodeficiency and malignancy in pediatric population is rare and associated with poorer prognosis. Overwhelming infections are the only cause of treatment failure so vigilant supportive care in infection prevention and treatment is vital in improving the outcome of patients with PIDs.

V148 SIOP19-0263 | Oncopeds: Early Diagnosis of Childhood Cancer Using a Mobile Application: A Multicenter Pilot Study

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Background/Objectives: The diagnostic delay in children and adolescents with cancer is a public health problem in Peru leading to high rates of advanced disease and mortality. ONCOpeds® is a mobile application that provides consultations for the timely diagnosis and referral of children and adolescents with suspected cancer.

The aim of this study is to evaluate the implementation and effectiveness of ONCOpeds in reducing the time to diagnosis (TD) and referral time (RT) in children and adolescents diagnosed with cancer in Peru.

Design/Methods: A multicenter pilot study was conducted in the region of Callao between November 2017 and April 2018. Attending primary care physician were trained in the use of ONCOpeds in 5 educational sessions. Patients younger than 18 years living in Callao and diagnosed with cancer from all the pediatric cancer units were analyzed in two groups: referred by the mobile application or by the conventional referral. The TD and RT of both groups were compared using descriptive statistics and the Mann-Whitney U-test. A *p*-value < 0.05 was considered statistically significant.

Results: ONCOpeds was successfully installed in the smart-phone devices of 78 attending physicians of Callao (pediatricians and general practitioners). During this period, 23 new cases of cancer in children and adolescents from Callao were collected (median age, 11 years). Ten patients were referred through the application and 13 in a conventional manner. The TD and RT were reduced in the group referred by ONCOpeds by 53% and 61%, respectively; however, only the RT reached statistical significance (U-Mann-Whitney, *p* = 0.008).

Conclusions: The implementation of the use of ONCOpeds was feasible in this pilot study, having a potential utility in improving the diagnosis and referral in children and adolescents with suspected cancer. A larger study at the national level is required to demonstrate the effectiveness of this telemedicine tool.

V149 SIOP19-0153 | Defining Optimal Care: The Development of Paediatric Oncology Care Pathways to Deliver High-Quality Care to Children with a Cancer Diagnosis and Their Families

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Background/Objectives: The need for health services to define high-quality care is recognised internationally. In Australia, care pathways have recently been developed in adult cancer. Recognising the need in paediatrics, the Paediatric Integrated Cancer Service in Victoria, Australia, led the development of Paediatric Oncology Care Pathways (POCPs) for the three tumour streams. The objective was to document evidence-based, multidisciplinary best-practice pathways, tailored to the unique needs of children with cancer and their families. The pathways will be used to identify variations in practice and inform quality initiatives to improve service provision and ultimately patient outcomes.

Design/Methods: A literature review was undertaken and consultation with multisite key stakeholders initiated. Specialised, multidisciplinary health professionals and consumers participated directly in iterative draft revisions via statewide expert reference groups, with further external review provided by other Australian cancer services. Where there was a lack of available evidence, a consensus opinion was sought from the expert reference group.

Results: The POCPs define optimal cancer care across 7 critical timepoints, from prevention/early detection through to end-of-life care. They encompass the 3 tumour streams (leukaemia, solid and central nervous system tumours), as well as a section devoted to the fundamentals of paediatric oncology care, common to all diagnoses. They clearly describe key quality-of-care indicators, with rationale and where applicable, timeframes that enable clinical audits. Rather than a protocol with comprehensive clinical specification, the POCPs are designed to be sensitive to developments and change in clinical practice. To date, the POCPs have been used to audit and where indicated, inform quality initiatives in areas such as clinical trials, infection, fertility optimisation, multidisciplinary team meeting discussions and nutrition.

Conclusions: The POCPs guide delivery of optimal, evidence-based care for children with cancer. Aligning practice to the POCPs ensures consistency of care and articulates the expectations for high-quality care for the patient and their family.

Haematology - Acute Lymphoblastic Leukaemia

V150 SIOP19-1036 | A Room for Improvement in Central Nervous System Relapse for Children with Acute Lymphoblastic Leukemia Treated per Modified Total XV Protocol

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Background/Objectives: Optimal post remission treatment for CNS relapse is controversial. We studied the outcome of CNS relapse in children with acute lymphoblastic leukemia treated at King Hussein Cancer Center.

Design/Methods: In this retrospective analysis, treatment of any CNS relapse consisted of re-induction chemotherapy that effectively penetrates into the CSF and intrathecal chemotherapy. Patients were continued on intensive chemotherapy or underwent hematopoietic stem cell transplantation (HSCT)

based on leukemia/transplant multidisciplinary team discussion. CNS radiation was given pre transplant in the HSCT group while delayed until 12 months in the chemotherapy group.

Results: From Jun2006 to Oct2017, 600 patients with ALL aged (1-18) years were treated per modified St. Jude Total XV protocol; the cumulative incidence of CNS relapse at 5-year was 3.2%. Fifteen patients had CNS Relapse: 10 patients had isolated CNS relapse and 5 patients had a combined CNS and bone marrow relapse. The median duration of CR1 was 18 months (range, 6-47 months). All 10 patients with isolated CNS relapse and 3 of five (60%) with combined relapse achieved CR2. (N=9 continued on chemotherapy, while N=3 underwent Allo-HSCT in CR2, N=1 died of sepsis). Seven out of 9 patients (78%) who continued on chemotherapy suffered from subsequent relapse (N=2 CNS, N=1 BM, N=3 BM+CNS, N=1 BM+Testicular); 2 of these patients are alive in CCR post HSCT. 2 of 3 patients in HSCT group are alive in CR and one patient died of leukemia. The estimated 5-year-EFS and OS were 27% and 40%, respectively. In univariate-analysis the prognostic factors associated with lower EFS and OS were age at diagnosis >10 year, and very early relapse (<18 months after diagnosis).

Conclusions: Survival post CNS relapse in our patients is suboptimal. We have further intensified therapy for high risk patients and had less CNS relapses in the past 5 years. For those with relapse, optimizing CNS-directed therapy is warranted.

V151 SIOP19-1056 | Outcome of Relapsed Acute Lymphoblastic Leukemia in Children and Adolescent Treated at King Hussein Cancer Center

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Background/Objectives: The overall survival (OS) rate for children with ALL treated at our center is approximately 80%; which is in line with published results of the Total XV regimen.

Design/Methods: From Dec2003 until May2018, patients (<18-years at diagnosis) with ALL in first and subsequent relapse (s) were studied. Treatment of relapse consisted of reinduction regimens followed by intensive continuation therapy and hematopoietic stem cell transplantation (HSCT) in selected patients.

Results: We studied 93 patients (median age, 8-yrs) who were followed for a median of 71months (10-186). Sites of relapse were: bone marrow (BM) in 66% (N=61) of the

patients, combined relapse in 12% (N=11) and isolated extramedullary Relapse (IEM) relapse 23% (N=21). Complete remission (CR2) rates for all patients were 67%. The estimated 5-year-EFS and OS for the whole group were 25% and 39%, respectively. After excluding patients who failed reinduction, 5-year-EFS and OS were 39% and 60%, respectively. The 5-OS for patients with BM relapse was 32%, combined relapse 42%, and IEM 58%. The probability of 5-year-OS for patients assessable MRD post reinduction chemotherapy was favorable for those with negative MRD (-MRD, <0.01%) 69% vs. 33%(+MRD, P=0.17). Thirty five patients underwent HSCT (25 in CR2, 10 in CR3); of them 17 patients (50%) are alive at last follow up. In univariate and multivariate analysis, worse OS was observed in patients <1 or ≥10-years at diagnosis, those who had initial high risk features, T-cell-immunophenotype, and very early and early combined and BM relapse.

Conclusions: At our center, more than one-third of relapsed ALL patients were cured. However, survival rates are low in HR relapsed ALL (very early and BM relapse). Salvaging patients who relapse after upfront intensive therapies proved to be challenging even in the presence of adequate supportive care.

V152 SIOP19-1586 | Allopurinol Counteracts Inadequate Mercaptopurine Metabolism in Paediatric Acute Lymphoblastic Leukemia

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Background/Objectives: Mercaptopurine (6-MP), a cornerstone of childhood acute lymphoblastic leukemia (ALL) therapy, is metabolized to active 6-thioguanine nucleotides (6-TGN) and 6-methylmercaptopurine nucleotides (6-MMPN) potentially hepatotoxic (threshold of 5000 pmol/8x10⁸ RBC). In few cases, the equilibrium between 6-TGN and 6-MMPN is unbalanced and in favor to 6-MMPN with high risk of inefficacy and toxicities. Here, we treated patients with allopurinol which inhibits Xanthine Oxidase and Thiopurine S-methyl Transferase (TPMT) implicated in methylation of thiopurines.

Design/Methods: Therapeutic drug monitoring of ALL patients was based on the determination of metabolites concentrations in red blood cells, measured by HPLC-UV after 3 weeks of stable 6-MP dose. After parental consent, individual genotypes are determined for *TPMT* (*2, *3B, *3C), *ITPA* (c.94C>A) and *HLA*B5801* (prior to allopurinol) by TaqMan allelic discrimination.

Results: In 8 patients, 6-MMPN/6-TGN ratio was too high, superior to 50 (range: 58-248) with 6-TGN under therapeutic threshold (< 250 pmol/8x108 RBC). All patients have a wild-type *TPMT* genotype and for 3 patients, *ITPA* polymorphism could be involved to this disequilibrium. The co-administration of Allopurinol (50 mg n=5, 100mg n=2), with a reduced 6-MP dose (around -50%) dose had a positive impact on metabolic ratio, inferior to 15 (range: <1 -13) with metabolites levels inside therapeutic window and on resolving some toxicities (hypoglycemia (n=4), hepatotoxicity (n=3)). For one patient, 200mg of Allopurinol was administered without reducing 6-MP dose, the metabolic ratio decreased from 115 to 63 but metabolites levels were both at supratherapeutic levels.

Conclusions: Allopurinol was effective in redirecting 6-MP metabolism to 6-TGN. A standardized protocol for this co-administration needs to be established and DNA-TGN incorporation dosage could be helpful for this recommendation. Long-term follow-up is required to evaluate impact on safety and efficacy of ALL maintenance therapy.

V153 SIOP19-0977 | Acute Lymphoblastic Leukemia (ALL) in Infants. Children Welfare Teaching Hospital (CWTB) Experience, Baghdad, Iraq

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Background/Objectives: From January 2000 to December 2016, 1635 children with acute lymphoblastic leukemia (ALL) were registered at Children Welfare Teaching Hospital (CWTB) in Baghdad. 59 (3.6%) were infants and the outcome of these children is reported here.

Design/Methods: Children with ALL (age <1 year) were included in the study. Treatment consisted of the adapted UKALL-97, 2003 and 2011 protocols, and a specific infant protocol for 3 infants. Since October 2008, a steroid pre-phase was introduced

Results: 59 consecutive infants were registered: 31 (52.5%) males and 28 (47.5%) females; median age 6 months (range 1-12); 24 (41%) from Baghdad, 35 (59%) from outside Baghdad; 12 (20.3%) refused treatment. 47 underwent therapy and were analyzed: 45 (96%) were B-lineage ALL, 2 (4%) were T-ALL;

8 were treated according to the UKALL-97, 24 UKALL-2003, 12 UKALL-2011 and 3 with a specific infant protocol; 24 received steroid pre-phase, 14 (58%) were prednisone good responders. 24 (51%) achieved a complete remission (CR); 19 (40%) died during induction (2/3 infant protocol); 4 (8%) were resistant. 7 children relapsed at a median time of 27.5 months (range 10-43.5). OS for the entire group of patients is 38.4% at 12 months (CI 95% 24.4-52.4) and 30.2% at 24 months (CI 95% 15.8-44.6); DFS is 37.8% at 12 months (CI 95% 22.8-52.8) and 29.1% at 24 months (CI 95% 14.7-43.5); considering abandonment as an event, EFS is 27.7% at 12 months and 21.3% at 24 months. Univariate and multivariate analysis show a better OS and EFS for patients treated between 2012 and 2016 ($p=0.01$).

Conclusions: The Iraqi experience in infant ALL confirms the bad prognosis of these patients, with a high rate of initial abandonment and high incidence of induction death. However 10/47 are alive in first CR with a median follow up of 57.4 months (range 30.5-92.1).

V154 SIOP19-0987 | Acute Lymphoblastic Leukemia in a Middle Income Country – A Single Center Experience and Results

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Background/Objectives: While acute lymphoblastic leukemia (ALL) is the most common malignancy during childhood, it also has a high cure rate, with survival at 80-85%. This is a retrospective observational study on the outcome and overall survival of children diagnosed with ALL and treated at a reference center in Northeast Romania.

Design/Methods: We reviewed the ALL patients aged 0-18 who were admitted to the Pediatric Oncological Department of the "St. Mary" Children's Emergency Hospital Iasi during Jan 2010 - Dec 2014. The patients were treated with multi-agent systemic chemotherapy according to the Berlin-Frankfurt-Munich (BFM) protocol ALL-2002 and Infant06. The data collected from the medical records were processed using IBM-SPSS Statistics 20.

Results: In total, 107 pediatric patients were included in the study. The average age at admission was 6 years and 4 months, with a male to female ratio of 1.8:1. B-cell precursor ALL was diagnosed in 83.12% patients; 12.15% patients had T-cell precursor ALL and 4.67% suffered from infant leukemia. Bone marrow gene alterations were assessed in 85 cases, namely the mutational status of the BCR-ABL, MLL-AF4, ETV6-RUNX1, E2A-PBX. Thus, 12.15% of patients exhibited ETV6-RUNX1 fusion, 2.80% showed E2A-PBX fusion, another 2.80% featured BCR-ABL fusion and 1.87%

of them presented MLL-AF4 fusion. Complete remission rate was achieved in 81.3% of cases. The overall mortality rate during induction phase was 6.54%. Overall relapse was at 11.21% and at 4.67% in the high-risk group (n=27). In the latter, the survival rate was 12.15%. The overall survival rates at 1 and then 5-years were 89.72% and 76.64%, respectively.

Conclusions: The epidemiology, clinical features, immunophenotype, and molecular characteristics we identified in our patients with ALL are similar to those found in high income countries. The 5-year survival rate in our center is consistent with similar reports from other middle income countries, yet still lower than in the developed world.

V155 SIOP19-1026 | ETV6/RUNX1-Positive Childhood Acute Lymphoblastic Leukemia (ALL): Additional Aberrations, Clonal Heterogeneity and Their Impact on MRD Clearance and Relapse

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Background/Objectives: The prognostic significance of the ETV6/RUNX1 fusion in pediatric ALL has been disputable. Whether secondary aberrations and co-existing subclones are responsible for delayed MRD-clearance, moderating outcome, remains to be clarified. We tried to define the prognostic significance of the ETV6/RUNX1 fusion, as well as to study the relation between the co-existing subclones and/or secondary aberrations with minimal residual disease (MRD) and long-term outcome, in pediatric ALL.

Design/Methods: Data from 204 newly diagnosed ALL patients (median age 5.1 years), have been retrospectively recorded and analyzed. Patients were consecutively diagnosed and homogeneously treated on BFM-based-protocols (2000-2018). FISH evaluation was performed for the detection of *ETV6-RUNX1/E2A-PBX1/BCR-ABL* fusion genes, *KMT2A* gene rearrangements and *ETV6/RUNX1/CDKN2A/2B* gene duplications/deletions/amplifications.

Results: In our cohort, 41/204 patients (20.1%) were ETV6/RUNX1-positive. 31/41 ETV6/RUNX1-positive patients (75.6%) harbored additional genetic abnormalities while 18/41 (43.9%) presented with clonal heterogeneity (subclones). The most common noticed abnormalities were del12p13 (43.9%), 2-3xETV6/RUNX1 (19.5%) and del9p21 (17.1%). The presence of the ETV6/RUNX1 fusion did not have a statistically significant impact on the probability

of relapse (RFS 87.8% vs 90.8% in case of translocation absence, p=0.719). Among ETV6/RUNX1 (+) patients, children with additional aberrations presented with inferior RFS (83.9% vs 100.0% in case of sole abnormality, p=0.03). Additionally, the presence of subclones was associated with dismal prognosis (RFS 72.2% vs 100.0% in patients without subclones, p=0.002). MRD-positivity on day 15 of induction (MRDd15) was detected in 40.0% of patients with sole ETV6/RUNX1 translocation; the corresponding MRDd15 among patients carrying subclones rises to 83.3%. Within a median follow-up time of 106 months, 5/41 ETV6/RUNX1 (+) patients (12.2%) relapsed; median time of relapse occurrence was 47.8 months. Common features of all relapses were sub-clonal diversity and FCM-MRDd15 positivity at a high level (10-3/10-2).

Conclusions: ETV6/RUNX1+ childhood ALL is characterized by extreme heterogeneity; the prognostic value of the fusion itself varies, depending on coexisting clinical/biological features. Clonal heterogeneity may well be driving disparate outcomes, distinguishing a subgroup of patients with delayed MRD-clearance and heterogenous outcome.

V156 SIOP19-0875 | Health-Related Quality of Life Among Young Adult Acute Lymphoblastic Leukemia Survivors in Sweden

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Background/Objectives: Young adult (YA) survivors of acute lymphoblastic leukemia (ALL) have high risks for late effects due to the disease and treatment. In light of this, health-related quality of life (HRQL) is relevant to investigate to understand needs of support. The objective of this study was to examine HRQL among YA survivors of ALL and the distribution of a number of predisposing factors, such as depression, anxiety, self-efficacy and social support compared with a control group of siblings.

Design/Methods: An explorative design was used in a nationwide cross-sectional study. YA survivors of ALL, diagnosed during 1985-1997, registered in the Swedish Childhood Cancer Registry (n=416) and their siblings (n=103) were eligible for participation in the study. In total, 227 YA survivors of childhood ALL (112 men, 115 women, mean age 28 years) and 70 siblings (25 men, 45 women, mean age 29 years) completed the questionnaire in 2011. HRQL (SF-36), depression and anxiety (DASS-21), self-efficacy (GSES) and social support (SS-13) was assessed. Differences between groups were analyzed with Mann-Whitney u-test.

Results: YA survivors of ALL reported significantly worse general health (mean 69.6 vs. 78.4; p=0.01) and role limitations due to emotional problems (77.1 vs. 88.1; p=0.023) than their siblings. A tendency to a difference was

seen also for the mental health subscale (mean 71.3 vs. 76.1; $p=0.09$). The YA survivors of ALL scored higher on depression (mean 7.2 vs. 5.1; $p=0.10$) and anxiety (mean 4.5 vs. 3.2; $p=0.20$), but mean values of reported self-efficacy and social support were at similar levels in the groups.

Conclusions: The HRQL of YA survivors of ALL was generally lower than among their siblings. Further studies of how HRQL is distributed within this group and how this change over time will increase our understanding of how and for whom long-term follow-up and provision of HRQL interventions have the best effect.

V157 SIOP19-0343 | miRNA-Related SNPs as Predictive Markers of Outcome in Pediatric Acute Lymphoblastic Leukemia

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Background/Objectives: Although recent improvements in treatment and patient stratification in pediatric acute lymphoblastic leukemia (ALL) have led to cure rates above 85% in developed countries, it is still one of the deadliest malignancies in children. Thus, further markers are needed in order to improve ALL characterization, increasing cure rates and also allowing a better treatment management to avoid unnecessarily intensive treatments.

In this context, non-coding RNAs have emerged as a new tool for classification and prognosis. Among them, microRNAs (miRNAs) are small RNA sequences that regulate more than 50% of our genes, among which are genes involved in the pharmacokinetic (PK) and pharmacodynamic (PD) pathways of the drugs used for ALL treatment. Genetic polymorphisms in miRNAs could affect their levels or function and, as a result, affect their target genes in these pathways. Therefore, the aim of the study was to determine the association between genetic variants in miRNAs and outcome in patients with pediatric ALL.

Design/Methods: To achieve this aim, we selected all the SNPs described in pre-miRNAs with a MAF>1% (213 SNPs in 206 miRNAs) and we genotyped them, using VeraCode GoldenGate technology, in a cohort of 178 Spanish children with B-cell precursor ALL (B-ALL) homogeneously treated with LAL/SHOP protocols. Their association with event free survival (EFS) and overall survival (OS) (5 years) was analyzed.

Results: The most significant result was the association between rs28645567 A allele in pre-mir-378d-1 and poorer OS (long-rank test p -value = 6.688×10^{-9}). This SNP is predicted to change the stability of the pre-miRNA, which could impact the regulation of its target genes related to drug PK and PD.

Conclusions: Rs28645567 in pre-mir-378d-1 is associated with OS in our population. SNPs in miRNAs could be of help to predict the outcome of children with B-ALL.

V158 SIOP19-1320 | Acute Leukemia, Not Burkitt Lymphoma, is the Commonest Childhood Cancer Diagnosed at a Sub-Sahara African Paediatric Cancer Unit

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Background/Objectives: Paediatric cancer in Africa is believed to be under-reported as most children live in regions where its diagnosis and treatment are not possible and are with no cancer registries. Different reports have described Burkitt lymphoma, Kaposi sarcoma, nephroblastoma and Hodgkin lymphoma as the commonest paediatric malignancies in different regions of Africa, which is at variance with the Western world, where acute leukemia and brain tumors are commonest. We described the patterns of cancer diagnosis and treatment outcomes of children treated at a Paediatric Cancer Unit in Sub-Saharan Africa.

Design/Methods: In a 3-year retrospective analysis, from January 2016 to December 2018, data regarding age, sex, cancer diagnosis, treatment and outcomes was extracted from medical files of all children <16 years diagnosed with cancer at the Paediatric Cancer Unit of Mbarara Regional Referral Hospital in Mbarara, Uganda. Descriptive statistics and Kaplan-Meier curves were used to describe the diagnostic patterns and treatment outcomes respectively. Approval was offered by the Institutional Review Board of Mbarara University of Science and Technology.

Results: A total of 202 children were diagnosed with cancer over the three years (43, 65 and 94 in 2016, 2017 and 2018 respectively), of whom 107 (53%) were male, 95 (47%) 1-5 years, 62 (30.6%) 5-10 and 45 (22.2%) >10 years. Acute leukemia was diagnosed in 50 (24.7%) children [41 Acute Lymphoblastic Leukemia and 9 Acute Myeloid leukemia], 40 (19.8%) Wilms tumor, 26 (12.8%) rhabdomyosarcoma, 22 (10.9%) Hodgkin lymphoma, 15 (7.4%) Burkitt lymphoma and 49 (24%) had miscellaneous conditions.

Eighty-five (42%) children are alive, 68 (33.7) died and 49 (24%) abandoned therapy.

Conclusions: At variance with many other reports from Africa and similar to what is described in the Western world, acute leukemia, not Burkitt lymphoma, is the commonest cancer diagnosed at our center. More than half of the children have died or abandoned therapy.

V159 SIOP19-0908 | Inter-Relationships of Bone Mineral Density with Fat Mass and Fat-Free Mass in Long Term Survivors of Acute Lymphoblastic Leukemia in Childhood and Adolescence

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Background/Objectives: Children with ALL commonly lose bone mineral during therapy. Bone mineral density (BMD) measurements after completion of treatment have been mixed. Body size influences BMD in health. We explored the relationships of BMD with body mass index (BMI), fat mass (FM) and fat-free mass (FFM) in long term survivors.

Design/Methods: Survivors (n=75) more than 10 years from diagnosis, having completed therapy on Dana-Farber Cancer Institute protocols, underwent body composition analysis by dual energy X ray absorptiometry in a cross-sectional study. Relationships were assessed by regression analyses and Pearson Correlation Coefficients (r).

Results: The study cohort had 41 males and 34 females; 45 had had standard risk and 30 high risk disease. Mean lumbar (LS) BMD Z score was -0.31, range -2.50 to +2.10, SD 0.94. Seventeen subjects (22.7%) were osteopenic (LS BMD Z score <-1.00). There was no impact of sex, ALL risk category, type of post-induction steroid or cranial radiation on LS or whole body (WB) BMD. BMI correlated significantly with LS BMD (r=0.333, p=0.004) and WB BMD (r=0.271, p=0.033). FM index (FM/height²) Z score showed no significant correlation with LS or WB BMD. FFM index Z score was strongly correlated in males (LS BMD r=0.386, p=0.013; WB BMD r=0.642, p, 0.001) but not in females. The appendicular lean mass (ALM), a surrogate for skeletal muscle mass, correlated significantly, as ALM index, with LS/WB BMD in males (LS BMD r=0.290, p=0.070; WB BMD r=0.572, p=0.001) but not in females.

Conclusions: Over 20% of long term survivors of ALL are osteopenic. BMD correlates positively with BMI, and with skeletal muscle mass in males but not females. Interventions to enhance BMD, such as increased physical activity, are warranted.

V160 SIOP19-0248 | AMPK Binds to Chromatin-Associated Factors INT-NELFE-RNAPOLII Transcription Complex to Epigenetically Reprogram Gene Expression and Promote Adaptation/Survival in Response to Metabolic Stress in ALL

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Background/Objectives: Acute lymphoblastic leukemia (ALL) is the leading cause of cancer related death in children, and cure rates for relapsed/refractory ALL remain dismal, highlighting the need for novel targeted therapies. We previously identified AMPK as a target in ALL. Recent evidence indicates AMPK interacts with chromatin-associated proteins and alters epigenetic gene regulation in response to metabolic stress to promote cellular adaptation and survival.

Design/Methods: To identify genome-wide genes regulated by direct association of AMPK to chromatin in response to metabolic stress, we constructed RN2 (REH/Bp-ALL) and CN2 (CCRF-CEM/T-ALL) cells expressing HA-AMPK α 2, and performed ChIP-Seq using HA-tag antibody. RN2 and CN2 cells were treated with the AMPK activator A769662 [100 μ M] for 45 min in glucose-free RPMI. ChIP-Seq data were validated using ChIP-qPCR. To identify interaction between AMPK and chromatin-associated proteins, we used co-immunoprecipitation (Co-IP) assays.

Results: Using ChIP-qPCR, we found that AMPK α 2 interacted with chromatin at the p21 promoter region in NALM6/Bp-ALL cells treated with the energy stressor 2-deoxy-D-glucose. This AMPK α 2/p21-associated epigenetic effect was evidenced at both the transcriptional and translational levels. ChIP-Seq identified 212 genes in CN2 treated with No-Glucose/A769662, and 388 genes in untreated CN2 cells. ENCODE/ChEA transcription factors (TFs) analysis identified the negative-elongation-factor E (NELFE), CEBPD, TAF7, SMAD4, and ATF2 as putative TFs. Among AMPK α 2-NELFE chromatin-associated regulated genes, we selected candidates for further characterization. Using Co-IP, we uncovered that AMPK α interacted with the integrator complex (INTS12), suggesting AMPK could regulate transcription via interaction with the INT-NELFE-RNAPol2 transcription complex.

Conclusions: Our ChIP-Seq data confirm and indicate that in response to metabolic stress, AMPK binds directly to chromatin to epigenetically reprogram gene expression to promote cellular adaptation/survival. AMPK α 2 appears to epigenetically regulate transcription via interaction with INT-NELF-RNAPol2 complex. These findings may lead to unique opportunities for epigenetic-based therapeutic

interventions and combination strategies to exploit synthetic lethality in relapse/refractory ALL.

V161 SIOP19-0098 | Pharmacogenetic Study of the Central Nervous System in Pediatric Acute Lymphoblastic Leukemia

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Background/Objectives: The prognosis of pediatric acute lymphoblastic leukemia (ALL) has a favorable prognosis thanks to the combined chemotherapy used nowadays, however, relapsed disease and serious adverse effects caused by the treatment still needs to take in consideration. In this study, we focused on relapse recurring in the central nervous system (CNS) and on the adverse effect, acute toxic encephalopathy (ATE). The neurologic symptoms of ATE are diverse like depressed level of consciousness, seizures, palsies, aphasia. Interindividual differences regarding the diversity of symptoms could be explained by the genetic background.

We hypothesized genetic polymorphisms can influence these events modifying the function of enzymes and transporters in the metabolism of chemotherapeutic drugs resulting in relapse or toxicity.

Design/Methods: Our study population consisted of pediatric patients with ALL, 672 patients for ATE and 998 for CNS relapse projects, respectively. Clinical data were collected retrospectively from the patients' medical records. ATE symptoms were graded according to the Common Terminology Criteria for Adverse Events v3.0. DNA was isolated from blood collected in remission using QIAmp® Blood DNA Maxi Kit (QIAGEN). Genotyping was performed using TaqMan® OpenArray™ Genotyping System (Thermo Fisher Scientific). We studied the association between 67 single nucleotide polymorphisms (SNPs) and relapse/ ATE. Logistic regression adjusted for potential confounders was performed using SPSS 22.

Results: ATE occurred in 6,5% of the patients. *GSTP1* rs1695 G allele protected against the toxic event ($p=0.002$; $OR=0.239$; $CI95\%=0.096-0.597$). Evaluating the association between these 67 SNPs and relapse disease is still running.

Conclusions: Neuroprotective function of *GSTP1* expressed in cerebral capillary endothelium has been confirmed. In our analysis *GSTP1* variant associated with reduced incidence of ATE. Our result might contribute to personalized medicine in pediatric ALL with a possible genetic marker for risk of ATE. This study is supported by the Hungarian Paediatric Oncology Network (07/MGYH-MGYGYT/2018) and by the Semmel-

weis University, Hungary (EFOP-3.6.3-VEKOP-16-2017-00009).

V162 SIOP19-1227 | Pragmatic, Non-Interventional Study of Clofarabine in Korean Pediatric Patients with Acute Lymphoblastic Leukemia Who Failed to Respond or Relapsed After 2 More Regimen

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Background/Objectives: Clofarabine, a second-generation purine nucleoside analogue, is used in advanced leukemia patients. This study was designed to produce data to assess the efficacy of clofarabine in Korean pediatric ALL patients, in order to carry out coverage with evidence development.

Design/Methods: This multi-center prospective study enrolled patients with ALL who failed to respond or relapsed after two or more chemotherapy regimens and for whom the physician has decided to give clofarabine. The primary endpoint was overall remission rate (OR). Secondary endpoints were overall response rate (ORR), time to remission, the proportion of patients receiving hematopoietic stem cell transplantation (HSCT), overall survival rate (OS) at 6 month and safety.

Results: A total of 60 patients were enrolled between June 2014 and July 2018. The median age at enrollment was 12.0 years (range 2.0-26.0 years). Disease status at enrollment was as follows: refractory disease in 21, first relapse in 13, and second relapse in 26 patients. According to the immunophenotype, B-cell, T-cell, and mixed phenotype accounted for 39, 14, and 5 of the 60 patients, respectively. Eleven, sixteen, and one of the 60 patients achieved complete remission (CR), CR except for platelet count recovery and partial remission, respectively. The OR and ORR was 45.0% and 46.7%, respectively. The median time to response was 10.3 weeks. Sixteen patients (26.7%) had a successful HSCT. The OS at 6 months was 47%. The adverse drug reactions (ADRs)

reported in more than 10% were febrile neutropenia, vomiting, nausea, diarrhea, stomatitis, pyrexia and alanine aminotransferase elevation. The ADRs leading to fatal event were sepsis in 5, febrile neutropenia in 2, lung infection in 1, pneumonia in 1, and septic shock in 1 patient, respectively.

Conclusions: Clofarabine showed promising results and is expected to broaden treatment strategies available to refractory/relapsed Korean pediatric ALL patients. Long-term follow up are needed in this population.

V163 SIOP19-1428 | Talk my Language-Supporting the Information Needs of Teenage and Young Adult (TYA) Patients with Acute Lymphoblastic Leukaemia (ALL) Transitioning to Maintenance Therapy

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Background/Objectives: Transition from the intensive early phases of acute lymphoblastic leukaemia (ALL) treatment to the maintenance phase can be challenging for Teenage and Young Adult (TYA) patients and their supporters. This project was designed to understand their unmet information needs and to create both an age and developmentally appropriate package of resources which were clinically accurate and above all, patient led; the end format was multi-media films that could be embedded into webpages and social media.

Design/Methods: Utilising a co-design methodology, a cohort of patients with ALL (on and off treatment) took part in a workshop. The patients identified challenges relating to their transition to maintenance therapy including their reintegration back into education or work, adjusting to a 'new normal' and managing self and others expectations. They worked with a creative team to develop their ideas and how to convey their message. They were involved in writing the scripts, staging, acting and producing the films.

Results: Three short films were designed and produced so that they were appropriate for social media platforms. The films were entitled 'expectation v reality', 'why maintenance?' and '7 top tips for surviving maintenance'. The TYAs who participated in the development of the films shared very positive feedback. Evaluation by other TYAs with ALL and their supporters using an online questionnaire is ongoing. Preliminary analysis suggested that all TYAs reported finding the films helpful or very helpful.

Conclusions: This project has identified specific information needs of TYA ALL patients and their support network at the time of transition to the maintenance phase of treatment. TYA ALL patients co-created films that can be used to inform and educate future patients and their wider network including

employers and education. The pilot evaluation phase will be extended to 12 months to capture feedback regarding the utility of the films amongst their supporters.

V164 SIOP19-1594 | Safety and Efficacy of Tisagenlecleucel (CTL019) in B Acute Lymphoblastic Leukemia in Children and Young Adults: Robert Debré and Saint Louis Hospitals Experience

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Background/Objectives: Relapsed/refractory B acute lymphoblastic leukemia (B-ALL) treatment remains a major challenge. Tisagenlecleucel (CTL019) is a chimeric antigen receptor T cell- therapy that reprograms autologous T cells to target CD19+ leukemia cells. This study reports the feasibility, safety and efficacy of CTL019 in patients treated in 2 centers from the Assistance-Publique-Hôpitaux de Paris.

Design/Methods: Patients in sponsored-clinical trials (n= 16) or treated within the French compassionate program (n=18) with an apheresis performed between mars 1, 2016 and February 15, 2019 were included.

Results: Thirty-four patients referred from 20 french centers benefited from an apheresis. Twenty-nine patients were infused with CTL019 at a median age of 13.2 y (range, 4.8-29.2) after fludarabine-cyclophosphamide based lymphodepletion. Out of 34 patients, 23 (67%) had a prior history of allogeneic SCT. Median number of relapses before apheresis was 2 (range, 1-5). Among the 27 patients evaluable after one month all were in CR/Cri, 25 (92.6%) being MRD negative. Median relapse free survival (RFS) and overall survival (OS) were not reached with a median follow up of 7.2 months (range, 0.2-30.6). The 18 month-OS probability is 82.6% (95%CI, 53.2%-94.4%). Eight patients relapsed: 3 CD19+, 4 CD19-, 1 of undetermined status. Four deaths were reported: 3 due to progressive disease and 1 associated to a CRS (grade 5). Sixteen patients experienced a CRS ($\geq$ grade 3: n=12) with a median time of 4 days after CTL019 infusion (range, 0-8). ICU level care was required for 12 patients (45%). Nine

patients received tocilizumab, 4 patients siltuximab and 7 patients corticosteroids. Nine neurological events have been reported, all completely reversible except one (fatality in combination with grade 5 CRS). No patient underwent allogeneic HSCT while in remission after CAR T cells injection.

Conclusions: CTL019 confirms its efficacy in a cohort of patients heavily pretreated for refractory or relapsed B-ALL without additional therapy after remission.

V165 SIOP19-1424 | Successful Intervention Strategy for Patients with CNS2 Positive Acute Lymphoid Leukemia (ALL) at Diagnosis

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Background/Objectives: The Children's Oncology Group (COG) studies AALL0232 (high risk)/AALL0331 (standard risk) demonstrated that patients CNS2 disease at diagnosis (< 5 white cells with blasts) are at increased risk for subsequent CNS disease, regardless of risk status, negatively impacting event free survival compared with patients CNS1 at diagnosis. To address these concerns, prior to COG-wide adjustments to ALL protocols, we developed institutional therapy modifications designed to improve CNS disease control post induction for patients CNS2 at diagnosis.

Design/Methods: Between October 2014-July 2017, 34 patients with CNS2 ALL at diagnosis were treated according to institutional guidelines based on COG risk stratification: standard risk (SR)-5; high risk (HR)-10; very high risk (VHR)-19. All received weekly intrathecal (IT) therapy during induction adding IT MTX on Day 15 / 22. SR patients received high dose methotrexate (5000mg/m²) (HD MTX) x 4 as Interim Maintenance 1 (IM1) substituted for escalating dose Capizzi MTX while retaining Capizzi MTX as IM2. HR patients received HDMTX as IM1 but had a second IM block with Capizzi MTX added. VHR patients received IM1 with HDMTX and IM2 Capizzi MTX as originally designed.

Results: All SR pts remain in complete remission (CR) (median 10 months off therapy); 3/10 HR pts had events (disease - 1 marrow, 1 retinal; 1 septic death) and 7 remain in CR (median of 1 month off therapy); 7/19 VHR patients had events (disease - CNS -4; CNS/BM - 1; persistent MRD - 2) and 12 remain in CR (median 6 months off therapy). Four of 34 patients (all VHR) had isolated CNS events post induction.

Conclusions: Though numbers are small, CNS disease control was excellent among SR and HR patients. VHR patients remain a challenge and post induction therapy

should be further modified to reduce the incidence of CNS events.

V166 SIOP19-1604 | B-Cell Acute Lymphoblastic Leukemia (B-ALL) with T (5;14)(Q31;Q32);IGH-IL3 Rearrangement and Eosinophilia: A Peculiar IGH-Rearranged B-ALL

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Background/Objectives: B-cell acute lymphoblastic leukemia associated with t (5;14)(q31;q32);IGH-IL3 is an exceptional cause of eosinophilia. The IGH enhancer on 14q32 is juxtaposed to the IL3 gene on 5q31, leading to interleukin-3 overproduction and release of mature eosinophils in the blood. Clinical, biological and outcome data are extremely scarce in the literature. Except for eosinophilia, no relevant common feature has been highlighted in these patients. However, it has been classified as a distinct entity in the World Health Organization classification.

Design/Methods: Eight patients with t (5;14)(q31;q32) treated by French or Austrian protocols were retrospectively enrolled. Array comparative genomic hybridization, multiplex ligation-dependent probe amplification or genomic PCR search for IKZF1 deletion were performed in 7. Sixteen

patients found through an exhaustive search in the literature were also analyzed.

Results: For those 24 patients, median age at diagnosis is 14.3 years with a male predominance (male to female ratio = 5). Eosinophilia-related symptoms (neurologic in 26%, thromboembolic in 26% or pulmonary in 50%) are common. Median white blood cells count is high (72x10⁹/L) and linked to eosinophilia (median: 32x10⁹/L). Peripheral blasts are present at a low level or absent (median: 0x10⁹/L; range: 0-37x10⁹/L). Bone marrow morphology is marked by a low blast infiltration (median: 42%). We found an *IKZF1* deletion in 5 out of 7 analyzable patients. Younger age, male sex, low blast count and high incidence of *IKZF1* deletion are common features of t (5;14)(q31;q32) and other *IGH* locus-involving translocations. Outcome data are available for 14 patients (median follow-up: 28 months): 8 died and 6 are alive in complete remission.

Conclusions: B-cell acute lymphoblastic leukemia with t (5;14)(q31;q32) especially affects male adolescents and is characterized by a high incidence of *IKZF1* deletion. Clinical features are mainly related to eosinophilia. This disease appears to be a peculiar subset of *IGH*-rearranged B-cell acute lymphoblastic leukemia with an intermediate prognosis.

V167 SIOP19-1059 | Flow Cytometry in the Diagnosis and Detection of Residual Disease of Pediatric Hematologic Malignancies in Uganda

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Background/Objectives: Acute leukemias in low and middle income (LMIC) countries have poor survival relative to high income countries (HIC). Delayed diagnosis, inaccurate diagnosis and inability to monitor disease burden contribute to sub-optimal therapy and outcomes. We developed and tested a flow cytometry strategy to diagnose acute leukemias and detect residual disease in children with suspected leukemia in Uganda.

Design/Methods: An eight color multi-parametric flow cytometry (MFC) assay that utilizes 22 antibodies was designed for the diagnosis and detection of disease status following anti-leukemia therapy.

The Uganda leukemia lymphoma panel (ULL) employs 22 antibodies in the first three assay tubes. For complex cases, two secondary tubes comprising of additional ten antibodies is used to confirm the diagnosis.

Results: The ULL panel is efficient to diagnose leukemias that include the B- and T-cell lineage leukemias/lymphomas and most acute myeloid leukemias (AML). The panel is limited in diagnosing the rare AML cases with erythroid (AML-M6e) and megakaryoblastic (AML-M7) differentiation. The ULL panel shows robust sensitivity to detect residual B cell acute lymphoblastic leukemia (B-ALL) blasts at ~0.02%.

Conclusions: The rapid and accurate diagnosis of acute leukemias is essential for appropriate therapy and optimal outcomes. The MRD status will allow refinement of risk-stratified therapies. One limitation to the ULL panel is difficulty differentiating AML-M6e and AML-M7. However, overall a flow cytometry approach provides results with superior accuracy compared to conventional hematoxylin/eosin slides with much less time required compared to immunohistochemistry, fluorescence *in-situ* hybridization (FISH) or cytogenetics for approximately \$85 per patient.

V168 SIOP19-0333 | Clinical-Biological Characteristics and Treatment Outcomes of Pediatric PRO-B ALL Patients Enrolled in BCH-2003 and CCLG-2008 Protocol: A Study of 121 Chinese Children

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Background/Objectives: Pro-B cell acute lymphoblastic leukemia (ALL) arrested at the same stage of B cell differentiation, but it is still biological heterogeneity.

Design/Methods: In this study, the clinical features, biological characteristics, minimal residual disease (MRD) and treatment outcomes of 121 Chinese children with pro-B ALL treated on two consecutive protocols were analyzed.

Results: *KMT2A* rearrangements were the most frequently abnormalities with incidence rate of 33.06% and associated with lower frequency of CD13, CD33, CD22 and CD34 expression and higher frequency of CD7 and NG2 expression. Higher frequency of CD15 and CD133 expression was exclusive found in *KMT2A-AFF1*+ patients. Presence of CD15 and absence of CD34 was correlated with high level of MRD at early stage of treatment. Outcomes was more favorable in patients older than 1year, absence of CD20 expression and *KMT2A* rearrangements, and MRD lower than 1% at the end of induction and 0.1% before consolidation. There was no difference of 5-year EFS between two treatment protocols, with

73.9±6.5% for BCH-2003 and 76.1±5.3% for CCLG-2008, $P=0.975$. MRD $\geq 0.1\%$ before consolidation and presence of *KMT2A* gene rearrangements were independent adverse prognostic factors [odds ratios of 9.424 (95% confidence interval (CI), 3.210, 27.662), $P<0.001$; 4.142 (1.535, 11.715), $P=0.005$; respectively].

Conclusions: These findings indicate that pediatric pro-B ALL was a heterogeneous disease, and conventional chemotherapy alone could not improve the patient outcome. Prospective trials combined with monoclonal antibody are required to elucidate the treatment benefits for high-risk patients.

V169 SIOP19-1287 | Hypoxia Regulates CD9 Expression and Migration of Lymphoblasts in Childhood B Acute Lymphoblastic Leukemia

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Background/Objectives: Acute lymphoblastic leukemia (ALL) is the most frequent malignancy in children. We previously shown that the tetraspanin CD9 is involved in the migration of blast cells in extramedullary CXCL12-containing sites. We hypothesized that hypoxia could regulate CD9 expression and thereby favor blast cells into niches.

Design/Methods: To study CD9 expression regulation, we used primary cells from patients with ALL and the Reh cell line. Cells were cultured in hypoxia and gene expression analysis was performed by quantitative PCR, and cell membrane protein expression by flow cytometry. The role of the hypoxia-inducible factor 1a (HIF1a) was explored by using luciferase assays and chromatin immunoprecipitation (ChIP). The role of hypoxia in CD9-mediated cell motility was studied by in vitro migration and adhesion assays with genetically-modified and native Reh cell lines. We also performed xenograft experiments with these cells lines to study cell dissemination.

Results: We confirmed that hypoxia upregulates CD9 expression both at mRNA and protein levels. Culture at 0,2% O₂ of Reh cells, as well as lymphoblasts of patients collected at ALL diagnosis, increased CD9 mRNA levels at 24h and we confirmed that CD9 membrane expression was also increased in Reh cells at 72h. Luciferase assays and ChIP experiments showed that HIF1a was directly involved in this upregulation, through its binding on CD9 promoter. Functional in vitro tests showed that CD9 is critical for leukemic cell adhesion and migration in hypoxic conditions. Xenograft experiments with

immunocompromised mice further suggested that CD9 may be involved in leukemic cell migration in vivo through HIF1a regulation.

Conclusions: Overall, our results demonstrate that CD9 expression is regulated by oxygen levels and strongly suggest that CD9 is critical for leukemic cells migration in hypoxic conditions. Targeting CD9 and hypoxia may be an interesting therapeutic option to prevent extramedullary leukemia.

V170 SIOP19-0189 | Effect of Rituximab Added to Standard Chemotherapy on Minimal Residual Disease During Induction in CD-20 Positive Pediatric Acute Lymphoblastic Leukemia (ALL): A Randomised Controlled Pilot Trial

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Background/Objectives: Rituximab in pediatric-ALL hasn't been evaluated much. Adding Rituximab to chemotherapy has shown better outcomes in CD20-positive adult-ALL. Since CD20 positivity is common in pediatric-ALL, this study was done to establish the efficacy of Rituximab in CD20.-positive ALL.[CTRI/2017/12/010897]

Design/Methods: Twenty pediatric patients with CD20-positive ALL (CD-20 expression in >20% blasts) were randomly assigned to receive Rituximab plus standard-chemotherapy[Intervention-arm (IA)] or standard-chemotherapy alone[Standard-arm (SA)]. SA chemotherapy consisted of Prednisolone, four doses of Vincristine, Daunorubicin [0 doses for standard-risk (SR), 2doses for intermediate-risk (IR) and 4 doses for high-risk (HR)] and 8 doses of L-Asparaginase with intrathecal-Methotrexate on day-0, day-8 and end of induction (EOI). Rituximab was given at 375mg/m² on day-0/day-1 in the IA. The absolute blast count (ABC) on day-8, flowcytometry-MRD levels in the peripheral blood (PB) on day-8 and day-15 and in bone marrow (BM) at EOI were the outcome variables. Imatinib was added to Bcr-Abl positive cases (1:IA;1:SA)

Results: Baseline characteristics were comparable between IA (n=10) and SA (n=10). Mean age for all patients was 67 months. The SR:IR:HR ratio in both arms was 1:8:1. Significant difference was seen between IA vs SA for day-8 ABC (x10³/cumm)[0.46 (0.00-11.4):SA vs 0.00 (0.00-0.00):IA;p=0.005]. The day-8 PB-MRD[7.12 (0.00-36.6):SA vs 0.20 (0.00-39.9):IA;p=0.22] showed higher values for SA but the difference wasn't significant. There was no

difference for day-15 PB-MRD and EOI-BM MRD. There was no difference in occurrence of adverse effects between both arms. Two patients in the SA had day-8 poor prednisolone response (PB-ABC>1000/cumm). Two (1:IA;1:SA) had induction failures and one patient in IA (defaulter for 15 days during induction) had a positive EOI-MRD. There were two deaths in each group.

Conclusions: Rituximab added to standard-chemotherapy was effective in achieving lower day-8 ABC and lower day-8 PB-MRD in CD-20 positive pediatric-ALL patients. Addition of Rituximab didn't lead a significant increase in adverse effects. Studies with larger sample-size are needed to further test its efficacy.

V171 SIOP19-1218 | Frequency, Risk Factors, Severity and Clinical Manifestations of Vincristine Induced Peripheral Neuropathy in Children Undergoing Chemotherapy for Acute Lymphoblastic Leukemia During Induction

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Background/Objectives: As cure rates of childhood Acute Lymphoblastic Leukemia (ALL) is exceeding 80%, there is compelling need to alleviate treatment related toxicities that can compromise quality of life. Vincristine is an anticancer agent which is given to every child with ALL and peripheral neuropathy is the major dose-limiting toxicity of this microtubule inhibitor. But there is limited data documenting true incidence, risk factors, severity and clinical manifestations of vincristine induced peripheral neuropathy from Bangladeshi population.

Design/Methods: It was a prospective observational study which was conducted from September 2017 to August 2018 in the Department of Paediatric Haematology and Oncology, BSMMU, Dhaka. All newly diagnosed cases of ALL and AML between the age of 5- 17.9 years with no pre-existing neurological abnormality were included. Relevant data regarding assessments of peripheral neuropathy using pediatric modified -Total neuropathy score (pm-TNS) and NCI-CTCAE grade were collected prospectively and analyzed.

Results: Among seventy two diagnosed ALL patients, 29.2% (21) developed peripheral neuropathy (PN) (p-value 0.038) compared to thirty AML patients only 10% (3) developed PN which was taken as control group. Higher frequency of peripheral neuropathy 57.1% was found in age below 10 yrs patients (p-value <0.001). Higher frequency of peripheral

neuropathy was found in female patients (57.1%). Highest frequency of peripheral neuropathy was observed in week 4 of induction chemotherapy (66.7%). In this study, NCI-CTCAE grade 1 peripheral neuropathy was observed during induction period. Major clinical manifestations observed were decreased distal muscle strength (58.3%), difficulty in walking (58.3%) and constipation (54.2%). There was no association of peripheral neuropathy with demographic characteristics (sex, weight, height, BMI of patients), initial WBC count.

Conclusions: In this study, the frequency of vincristine induced peripheral neuropathy (VIPN) was found to be 29.2% during induction period. VIPN was found significantly higher in age below 10 years which was milder in severity.

V172 SIOP19-0471 | The Association of Gut Microbiome with Asparaginase Levels in Pediatric Patients with Acute Lymphoblastic Leukemia: A Pilot Study

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Background/Objectives: Asparaginase levels are being increasingly measured to monitor and optimize treatment in patients with acute lymphoblastic leukemia. However, the predictors of serum asparaginase levels are unclear indicating the need to explore host-environment relationships. The present pilot study was designed to explore the relationship of the gut microbiome with serum asparaginase levels in pediatric patients with ALL

Design/Methods: In this ethics approved prospective study, after informed consent, patients with ALL treated at the IWK Health Center in Halifax, Nova Scotia Canada provided both stool and blood samples throughout ALL therapy. Blood samples were taken 7-9 days after each dose of PEG-asparaginase to measure asparaginase levels. Stool samples were taken at diagnosis and subsequently (approximately monthly) for assessing gut microbiome composition.

After appropriate processing, V4-V5 16S rRNA gene sequencing was performed by the Integrated Microbiome Resource at Dalhousie University. Sequencing data was quality filtered to remove low precision reads. Deblur was used to identify amplicon sequence variants (ASV). Weighted UniFrac distances for each sample was calculated using QIIME2. Sample bias adjusted beta dispersion values were determined using the Vegan R package.

Results: 43 stool and 33 blood samples from 8 patients were assessed. The mean age of patients was 5.06 years with 4 males and 4 females enrolled. The mean measurement of asparaginase within blood samples was 1.152 IU/ml. The coefficient of variation of asparaginase levels (standard deviation/mean) was correlated with gut microbiome median beta dispersion distances. We found a significant positive correlation ($p=0.019$, $r=0.79$ (95% CI, 0.20 – 0.96) indicating that variation within microbiome structure may be related to variable levels of asparaginase.

Conclusions: The preliminary study shows a novel observation that variability in the gut microbiome may be associated with serum asparaginase levels. Further confirmatory work is necessary to validate characteristics, if any, of microbiome in relation to asparaginase levels.

V173 SIOP19-1135 | NT5C2 Mutations in Chinese Patients with Relapsed Pediatric Acute Lymphoblastic Leukemia

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Background/Objectives: Relapsed acute lymphoblastic leukemia (ALL) is resistant to chemotherapy and associated with dismal outcomes. Gain-of-function mutations in the 5'-nucleotidase II gene (NT5C2) drive resistance to 6-mercaptopurine and are prevalent in early relapse leukemia, which make it the most common therapeutic target in relapsed ALL. However, there are now few data on NT5C2 mutations in pediatric relapsed ALL with Asian ancestry. The aim of the present study was to investigate the frequency and prognostic role of NT5C2 mutations in pediatric relapsed ALL in Chinese population.

Design/Methods: This study enrolled 58 children with relapsed ALL. The DNA of exon 9, 13, 15, and 16 of NT5C2 were amplified by PCR method and detected by Sanger sequencing, and the molecular characteristics and clinical features of patients with mutant NT5C2 were analyzed. The NUDT15 gene, which is associated with thiopurine intolerance, was also sequenced for 45 patients.

Results: Two kinds of NT5C2 somatic mutations were identified in 3 cases. The NT5C2 R367Q mutation was detected in 2/15 (7.5%) relapse T cell ALLs and H352D mutation which was not reported before was detected in 1/43 (2.3%) relapse B-precursor ALLs. All the mutations were heterozygous and located in exon 13. Clinically, all patients carrying NT5C2 mutations relapsed early, although the difference was not significant ($P=0.150$). In addition, all the patients with NT5C2 carried wide type of NUDT15 alleles.

Conclusions: These findings suggest that NT5C2 mutation is a recurrent event in relapsed ALL in Chinese population. The novel H352D mutation expands the mutation spectrum of NT5C2.

V174 SIOP19-0656 | Changes of Body Composition as Measured by Quantitative Computed Tomography in Patients with Acute Lymphoblastic Leukemia

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Background/Objectives: Children with acute lymphoblastic leukemia (ALL) are at risk of obesity. Quantitative computed tomography (QCT) can provide compartment-specific information for lean tissue (LT), subcutaneous adipose tissue (SAT), and visceral adipose tissue (VAT).

Design/Methods: Body mass index (BMI) and QCT data at diagnosis and the end of therapy were obtained in 367 children with ALL who were enrolled in Total XV protocol. Body composition ratios were calculated for LT, SAT, and VAT at the level of the first and second lumbar vertebrae (L1 and L2, respectively). The ratios' associations with BMI were evaluated by calculating Pearson's correlation coefficient. The effects of age at diagnosis (2-10 years vs. ≥ 10 years), race (white vs. black or other), sex (female vs. male), risk (low vs. standard/high), cell lineage (B cell vs. T cell), and time point (at diagnosis vs. off therapy) on BMI were evaluated by mixed model analysis.

Results: BMI was positively correlated with SAT and VAT and negatively correlated with LT (all $P<0.001$). The only factor significantly correlated with higher BMI was end of therapy evaluation ($P<0.001$). Because all ratios at L1 and L2 were correlated ($P<0.001$) and L2 had more visceral tissue involvement, L2 data were evaluated. SAT ratio was higher at the end of therapy and in patients who were female, had standard/high-risk leukemia, or aged ≥ 10 years (all $P\leq 0.029$). VAT ratio was higher at the end of therapy and in patients who were white (vs. black) or aged ≥ 10 years (all $P\leq 0.001$). LT ratio was lower at the end of therapy, and in female patients, at standard/high-risk, white (vs. black), or aged ≥ 10 years (all $P\leq 0.035$).

Conclusions: QCT analysis showed increases in adipose tissue and decreases in LT in association with increased BMI during ALL therapy. QCT can be used for body

compartment analysis in patients who have significant changes in BMI.

V175 SIOP19-0578 | Mineral Homeostasis and Bone Mass at Diagnosis in Children with Acute Lymphoblastic Leukemia

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Background/Objectives: To evaluate the skeletal profile of children and adolescents with newly diagnosed acute lymphoblastic leukemia (ALL).

Design/Methods: Children diagnosed with ALL in our Oncology Department were recruited during a two-year period and underwent skeletal metabolism evaluation and dual-energy X-ray absorptiometry (DXA) at the time of diagnosis. They were divided in two subgroups, according to the presence or absence of osteonecrosis (ON).

Results: 28 patients (15 boys), aged 7.1 ± 3.5 years, with ALL were treated according to the ALL IC BFM 2009 protocol. Seven out of 28 patients had MRI-diagnosed ON, (6 girls, aged 10.8 ± 2.22 years), with median time interval from diagnosis of 12 months. ON affected 15 joints in total, with hips and knees being the most commonly involved.

At diagnosis, 53,6% of the patients were vitamin D insufficient (25-OH-D:12-20 ng/ml) and 3,6% were deficient (<12 ng/ml). 5/7 children with ON were vitamin D insufficient. Bone turnover was also affected.

The patients had lower levels of osteocalcin (OC, $p < 0.001$) and procollagen type I propeptide (PICP, $p < 0.001$) and higher level of urine deoxypyridinoline/urine creatinine ($p = 0.002$) compared to controls. The subgroup analysis revealed that patients with ON had lower osteocalcin levels ($p = 0.05$).

A DXA scan was performed in 17 patients; two had low-normal bone mineral density of the lumbar spine (LS-BMD)(z-score: -1 and -2) and only one patient had low LS-BMD (z-score <-2). One patient had low-normal BMD of total body less head scans (TBLH-BMD). Patients with ON had lower LS-BMD ($p = 0.03$), compared to those with no ON.

Conclusions: Vitamin D, bone turnover markers and BMD are already affected at the time of diagnosis in ALL pediatric

patients. Patients with ON have more severely affected skeletal metabolism markers and lower lumbar BMD at diagnosis and this observation could have some predictive value for prompt ON detection. These findings support the early bone health surveillance and intervention.

V176 SIOP19-1072 | Very High Risk Acute Lymphoblastic Leukemia: Comparison Between Chemotherapy and Hematopoietic Stem Cell Transplantation in First Remission

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Background/Objectives: High-risk acute lymphoblastic leukemia (HR-ALL) in childhood has a dismal prognosis and requires additional therapeutic approaches to improve survival, such as stem cell transplantation (HSCT) and intensified chemotherapy. Within this group, there is a very high risk (VHR-ALL) group of patients with significantly worse prognosis.

OBJECTIVES: To compare the outcome of children with diagnosis of VHR-ALL who received consolidation of treatment with HSCT versus high-dose chemotherapy only during first complete remission (CR).

Design/Methods: From December-2002 to December-2018, 261 patients were diagnosed with HR-ALL, and 194 were defined as VHR-ALL according to ALLIC criteria. Eleven died during induction and 2 presented resistant disease, thus remaining 181 patients as candidates for receiving HSCT. Fifty-six (32%) patients underwent HSCT and 123 received only chemotherapy. We retrospectively analyzed adverse events, causes of deaths and Disease-free-survival probability (DFS_p) of both groups with Kaplan-Meier calculation and comparisons with long-Rank-test.

Results: From the 56 patients who underwent HSCT, 37 were MFD, 17 MUD and 2 haplo-HSCT. From the 123 who received chemotherapy, 34 relapsed, 1 developed a therapy-related cancer and 19 died in CR and from the 56 patients who received HSCT, 1 relapsed, 2 presented second malignancies and 24 died in CR (9 MFD/13 MUD/2 haplo-HSCT)(p-value of relapse and deaths in CR=0.0001). Severe infection was the cause of death in 86% of cases. DFS_p (SE) was 51 (7)% for the group of HSCT and 48 (5)% for patients who received only chemotherapy.

Conclusions: 1-There was no advantage in survival for VHR-ALL who received HSCT. However, the pattern of events was different, with significantly higher rate of deaths in CR in the HSCT group and significantly higher relapse rate in the

group of patients who received chemotherapy. 2-Death rate was higher in patients who received HSCT from alternatives donors. 3-Severe infections were the main cause of mortality in both groups.

V177 SIOP19-1020 | Use of Blinatumomab for Relapse Therapy of B-Cell Precursor Acute Lymphoblastic Leukemia

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Background/Objectives: Despite tremendous progress that has been made in the therapy of acute lymphoblastic leukemia (ALL) 15-20% of children experience treatment failure. Relapsed/refractory ALL is associated with a poor prognosis, since options for salvage therapy, mostly conventional chemotherapy, are limited. Blinatumomab, a bispecific CD19 directed CD3 T-cell engager, has shown to be effective in both minimal residual disease (MRD) and relapsed/refractory B-cell ALL.

We report on relapsed pediatric patients with B-cell ALL who were treated with blinatumomab on a compassionate use basis.

Design/Methods: In our Department between December 2017 and March 2019, 7 children with relapse ALL, age 1 to 18 years, were treated with blinatumomab. Total of 9 cycles were given. Three patients were administered blinatumomab for first refractory relapse (M3 bone marrow), two out of three in second remission with positive MRD, and one in third remission with positive MRD. None of the patients had received previous hematopoietic stem cell transplantation (HSCT). All patients were given blinatumomab in monotherapy as a 4-week continuous intravenous infusion, with a 2-week treatment-free interval after each cycle. After one week escalation of dose 5 mcg/m² to 15 mcg/m²/day was carried out.

Results: Six out of seven patients completed at least one cycle of blinatumomab, two patients received 2 cycles. Major toxicities were grade 3 seizures in one patient and grade 4 cytokine release syndrome in 1 child. The most common toxicities were elevation of transaminases (Grade 3/4). Four patients achieved negative MRD after the first cycle of treatment; one after the second cycle. Two patients did not respond. Four patients were successfully transplanted, another is being prepared to HSCT.

Conclusions: Blinatumomab is well tolerated agent that can induce MRD remission in pediatric patients with relapsed B-

precursor acute lymphoblastic leukemia and facilitate subsequent HSCT.

V178 SIOP19-0306 | A Practical And Cost Effective (PACE) Approach to Detect pH-Like ALL in Resource Constraint Settings

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Background/Objectives: Ph-like ALL comprises a wide spectrum of genetic lesions, including translocations, fusions, point mutations and deletions. The sizeable range of genetic lesions make the diagnosis challenging and expensive. We used a practical and cost effective (PACE) approach to detect ph like ALL.

Design/Methods: Patients testing positive for ETV6-RUNX1, high hyperdiploidy, TCF3-PBX1, BCR-ABL1 and KMT2A (MLL) rearrangements were excluded. An algorithmic approach was followed. CRLF2 over-expression was evaluated by RT PCR. CRLF2 over-expressed cases were further characterized by RT-PCR for CRLF2-P2RY8 fusion, and FISH for CRLF2-IGH fusion. Hot-spot mutation analysis was done by Sanger sequencing for JAK R683G & IL-7R (S185C in exon5 and microdeletion in exon6. Multiplex RT-PCR detected common tyrosine kinase fusion mutations like ETV6-ABL1, NUP214-ABL1, RCSD1- ABL1, RCSD1-ABL2, PAG1-ABL2, SSBP2-CSF1R and SSBP2-PDGFRB. MLPA assay was performed for B-cell developmental gene copy number abnormalities (BDG-CNA's)

Results: Fifty nine children were analyzed for Ph like ALL. Definite Ph-like signature mutations identified in 8/59 (13.5%) cases. Six had CRLF2 over-expression: CRLF2-IGH:4/6, CRLF2-P2RY8:2/6, no JAK/IL7R mutations identified. Two patients had RCSD1-ABL1 kinase gene fusion. BDG-CNA's: 29/59 cases, IKZF1 deletions in 14, 9/14 associated with other B-cell gene deletions. Fifteen cases had deletions in other genes. Overall cost: around 100 USD/sample

Conclusions: A combination of molecular diagnostic techniques: RT PCR, RT quantitative PCR, FISH and Sanger sequencing, identified eight definite Ph-like mutations and 29 possible Ph-like mutations based on enriched BDG-CNA's. Our approach offered low cost detection of Ph-like ALL cases compared to array and RNA sequencing (100 USD vs. 350 USD). Addition of FISH probes for JAK2, EPOR and ABL1/2 to enable comprehensive possible kinase fusion rearrangements at an additional cost of 50-80 USD/sample will make this approach an excellent option in resource constraint situa-

tions as array and RNA sequencing is beyond reach for most laboratories in LMIC's.

V179 SIOP19-0324 | Philadelphia-Like Mutations in Childhood ALL: A Report from North India

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Background/Objectives: Philadelphia-like ALL (Ph-like ALL), an independent predictor of poor outcome, accounts for 10-15% of pediatric ALL. This study was performed to evaluate the frequency and clinical characteristics of Ph-like ALL in our population.

Design/Methods: One ninety four children ≤ 12 years diagnosed with ALL from July 2017-Sept 2018. Fifty nine evaluated for Ph-like ALL (Group 1). [135 excluded: ETV6-RUNX1+ve: 25, E2A-PBX1+ve: 11, KMT2A-AFF1+ve: 3, BCR-ABL1+ve: 12, inadequate samples/hyperdiploidy: 70 (Group 2)]. Diagnostics: CRLF2 over-expression by RT-PCR, CRLF2-P2RY8 fusion by RT-PCR, CRLF2-IGH fusion by FISH, kinase gene fusions by multiplex RT-PCR, JAK & IL-7R hot-spot mutation analysis by Sanger sequencing and MLPA assay for B-cell developmental gene copy number abnormalities (BDG-CNA's). RNA sequencing/whole exome sequencing was not performed. Clinical features were compared between the groups.

Results: Mean age was 4.5 ± 2.6 years; six children were > 10 years. Definite Ph-like signature mutations identified in 8/59 (13.5%) cases. Six had CRLF2 over-expression: CRLF2-IGH:4/6, CRLF2-P2RY8:2/6, no JAK/IL7R mutations identified. Two patients had RCSD1-ABL1 kinase gene fusion. BDG-CNA's: 29/59 cases, IKZF1 deletions in 14, 9/14 being associated with other B-cell gene deletions. Fifteen cases had deletions in other genes. A significantly high-initial total leucocyte count ($> 50,000/\text{mm}^3$) seen in 44% cases in group 1 vs. 15% in group 2 ($p=0.001$). Prophase prednisolone response: Group 1: 81%; Group 2: 91% ($p=0.054$). MRD negative ($< 0.01\%$) end induction: 72% (group1) and 70% (group 2) ($p=0.77$).

Conclusions: We identified eight definite Ph-like mutations and 29 cases of possible Ph-like mutations based on enriched BDG-CNA's. These 29 cases have been termed possible, as extensive FISH or RNA sequencing was not performed. A high percentage of Ph-like B-ALL children present with hyperleukocytosis. A long term follow up is required to better define the prognostic significance in our cohort.

V180 SIOP19-0524 | Toxicity of Intensive Chemotherapy in Association With Imatinib in Pediatric Philadelphia Positive Acute Lymphoblastic Leukemia: French Experience of the Esphall Trial

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Background/Objectives: Prognosis of pediatric acute lymphoblastic leukemia with t (9;22) (Ph+ ALL) has significantly improved over the last decades, thanks to the use of a BCR-ABL specific tyrosine kinase inhibitor (TKI), imatinib. The results of the EsPhALL trial, combining intensive chemotherapy and imatinib, were promising with 70% 5-year survival, at cost of important toxicity which was not found in the pre imatinib era. The aim of this study was to better understand this toxicity by evaluating the most toxic phases of the EsPhALL trial, describing the most frequent toxicities and identifying predisposing factors.

Design/Methods: Our study analyzed toxicity data of the 46 French patients with Ph+ ALL, enrolled in the EsPhALL studies and who received imatinib. Among them, 22 patients received hematopoietic stem cell transplantation (HSCT) in first complete remission (CR1). We considered non hematological grade 3 or 4 toxicities, serious adverse events, 14 days delay or more per patient and per phase. Univariate analysis was performed to identify predisposing factors among age, nutritional status, sex and treatment risk group.

Results: Among the 24 non allografted patients, three died during the chemotherapy protocol (12.5%). The most toxic phases were induction and Ib phase, and the two reinductions. The most concerning toxicities in all phases were severe infections and gastro intestinal toxicity. Patients who died of toxicity presented in average 2.42 grade 3 or 4 non hematological toxicities per phase, versus 0.59 for patients who survived ($p < .001$).

Conclusions: Patients receiving chemotherapy and imatinib must require careful supportive care especially when they present grade 3-4 toxicity in the early phases of treatment. The future EsPhALL/COG trial will be based on a less intensive chemotherapy backbone for patients with a good early response to chemotherapy, in association with imatinib, to decrease the toxicity related mortality, while the actual survival rates.

V181 SIOP19-1376 | Nutritional Status of Patients with Acute Lymphocytic Leukemia (ALL), in Children's Cancer Hospital Egypt (CCHE-57357)

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Background/Objectives: Nutritional status plays a crucial role in the morbidities and mortality of patients with Acute Lymphocytic Leukemia (ALL), as well in the quality of life of the patient. In pediatric oncology, rapid rate of growth and high nutritional needs represent another challenges during the course of treatment to avoid malnutrition and retarded growth. The aim of the study was to assess the nutritional status at time of diagnosis and throughout the treatment journey in children with ALL to identify those patients who may require special nutritional intervention and appropriate referral to qualified nutritionist.

Design/Methods: Design/methods: It was observational descriptive, retrospective study, included patients aged ≤ 18 years who were newly diagnosed ALL and admitted to the Children's Cancer Hospital Egypt (CCHE/57357) in the year 2012 and followed to the end of treatment. Available patients weight (in kg) and height (in cm) measures: at diagnosis, end of induction, end of consolidation, week 48 maintenance, week 100 maintenance and end of treatment. Age and sex specific weight, height and BMI standard deviation scores were

calculated based on growth reference values from the World Health Organization.

Results: In spite the long journey of treatment, and the catabolic effect of the diseases and the chemotherapy 91% of patients gained weight (more than 10% of the initial weight), Weight for age (Z score) was increased progressively, the percentage of obese patients was nearly doubled at the end of treatment (9% obese). On the other hand, height velocity was affected in all age groups, the percentage of stunted children was increased 3 folds comparing the initial height/age Z score (4%) to that at end of treatment (11%), resulting in increased BMI in all age groups

Conclusions: Corticosteroids therapy predisposes children to weight gain and overweight, on the other hand the height for age is decreased, regular nutrition assessment is needed

V182 SIOP19-1023 | Comparison of Asparaginase Activity in Serum of Children With Acute Lymphoblastic Leukemia (ALL) Treated by L-Asparaginase of Two Manufacturers

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Background/Objectives: L-asparaginase (ASNase) is a universal component of various chemotherapeutic regimens for children with ALL. Since 2016 in Russia generic ASNase manufactured by Veropharm Ltd (Russia) (Vero-ASNase) have being used. Different ASNase preparations might have different pharmacokinetics. The aim of our study was to compare serum ASNase activity in children with ALL administered either Asparaginase MedacTM (Medac GmbH, Hamburg) or Vero-ASNase.

Design/Methods: We measured ASNase activity in 271 serum samples from 55 children with ALL who received intramuscular injection of ASNase once a week at dose 10,000 U/m². Due to the logistical reasons in the majority of case (230 of 271) ASNase activity was evaluated at day 6 after the single dose of L-asparaginase (in 105 cases patients received Asparaginase Medac, in 125 Vero-ASNase). In the rest 41 samples (17 cases after Asparaginase Medac and 24 after Vero-ASNase) ASNase activity was measured at day 7. Serum was stored at -80°C until performing the assay. ASNase activity was measured on a Beckman AU 480 analyzer using a coupled enzymatic assay and the rate of absorption reduction was detected at 340 nm. Low limit quantitation (LoQ) of the applied method was 12.5 U/l.

Results: After the administration of Asparaginase Medac at day 6 in 75% of samples the activity of the drug exceeded LoQ (median – 75.2 U/l, min- 30.6 U/l, - max – 213 U/l), at day 7 – in 71% of cases (median – 36.1 U/l, min- 14.0 U/l, - max – 54.7 U/l). While after the 6th days after the administration Vero-ASNase only 4 of 125 (3%) samples revealed measurable activity exceeded LoQ and at day 7 in all samples ASNase activity was lower than LoQ ($p < 0.001$).

Conclusions: Despite similar schedule and dosage a significant difference in serum ASNase activity was noted in two various trade-name L-asparaginase.

V183 SIOP19-0515 | Germline DNA Methylation Changes in Children with Acute Lymphoblastic Leukemia

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Background/Objectives: Studies performed using newborn blood spots, together with the high rate of concordance between identical twins, suggest an in utero origin of acute lymphoblastic leukemia (ALL). However, the birth prevalence of pre-leukemic genetic lesions far exceeds the incidence of ALL and suggests that additional cooperating events are necessary in most instances. Given the strong evidence for a fetal origin of ALL, and because DNA methylation is critical for cell differentiation during fetal development, we sought to determine whether we could identify differentially methylated positions (DMPs) and differentially methylated regions (DMRs) in germline DNA samples from children with ALL and matched, healthy controls.

Design/Methods: Buccal brushings were collected from N=26 ALL patients at Texas Children's Hospital and N=26 controls. DNA methylation was assayed using the Illumina Human MethylationEPIC array. We performed quality control and analysis of DMPs and DMRs using the minfi and cpgasoc packages in the R statistical environment.

Results: We confirmed that cells from buccal brushings were predominantly of epithelial rather than immune lineage. We identified 514 DMPs and 34 DMRs at genome-wide significance at a false discovery rate of 5% for which the absolute mean difference in normalized beta value comparing cases to controls was > 0.05 . Top DMRs mapped to regions with high biologic plausibility, including the transcription start sites of ARID5B, a well-established ALL risk gene, TP53AIP1, and multiple HOXA family genes.

Conclusions: These data provide important preliminary evidence of germline DNA methylation changes in children with ALL, which may be an important cooperating mechanism in leukemogenesis. The identification of additional molecular events mediating the development of clinical leukemia in children with pre-leukemic genetic lesions has the potential to significantly improve our ability to identify those at greatest risk of ALL.

V184 SIOP19-0510 | Clinical Efficacy and Long Term Survival of T-Cell Lymphoblastic Lymphoma/Leukemia in Children

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Background/Objectives: To analysis the clinical characteristics, efficiency and prognosis of T-cell lymphoblastic lymphoma/leukemia in children.

Design/Methods: Retrospective analysis of children diagnosed as T-cell lymphoblastic lymphoma (T-LBL) and T-cell acute lymphoblastic leukemia (T-ALL) were assessed in the period between January 2008 to June 2018 in Shanghai Children's Hospital between the long-term efficacy of treatment and prognostic factors. The Kaplan-Meier method was used to assess the survival rates and the prognostic factors were analyzed.

Results: In total, 49 patients with T-LBL/ALL that were diagnosed at Shanghai Children's Hospital were enrolled in the present study including 22 cases of T-LBL and 27 cases of T-ALL with average age was 7.59 ± 3.23 years. The number of peripheral blood leukocytes, the proportion of immature cells in peripheral blood, the level of LDH in blood and the proportion of immature cells in bone marrow of T-ALL patients were significantly higher than those of T-LBL patients ($P=0.0032, 0.0002, 0.0067, 0.0001$), and the patients rate with mediastinal infiltration of T-ALL was significantly lower than that of T-LBL ($P=0.022$). 39 patients (79.59%) achieved survival and 10 patients (20.41%) died. The 10-year overall survival (OS) and event-free survival (EFS) rate of patients were $70.78 \pm 8.55\%$ and $65.89 \pm 8.65\%$ respectively. The 10-year OS rates of T-LBL and T-ALL patients were $68.56 \pm 11.98\%$ and $73.39 \pm 11.21\%$ ($P=0.62$) while the 10-year EFS rates of T-LBL and T-ALL patients were $63.98 \pm 12.02\%$ and $68.49 \pm 11.48\%$ ($P=0.57$). The recurrence rate of patients with T-LBL treated with Pegaspargase (7.7%) was lower than that of patients treated with L-asparaginase (42.9%) ($P=0.1$). The immunophenotype of 4 patients was early precursor T-lymphocytic leukemia (ETP-ALL), whose long-term survival was significantly lower than that of non-ETP patients ($P=0.007$).

Conclusions: Childhood T-LBL/ALL can achieve better efficacy by using the chemotherapy schemes for childhood

leukemia. ETP-ALL has a poor prognosis and may require further adjustment of treatment strategies.

V185 SIOP19-0472 | Efficacy and Safety of Dual Sofosbuvir/Daclatasvir Therapy in Chronic Hepatitis C Infected Survivors of Childhood Cancer

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Background/Objectives: Childhood cancer survivors are potentially at a higher risk of infection with hepatitis C virus (HCV) and little data is published on their treatment by the recently introduced direct acting antiviral (DAA) drugs. We aimed to evaluate the efficacy, safety and tolerability of dual sofosbuvir/daclatasvir (SOF/DCV) DAA therapy in childhood cancer survivors infected with chronic HCV.

Design/Methods: this prospective, open-label multicenter study was conducted on 20 chronic HCV, genotype 4, survivor of acute leukemia/lymphoma. Their age ranged from 8 to 16 years (with a mean of 13.12 ± 4.22) and 50% were males. All children were treated with a regimen of dual DAA drug therapy in the form of a single daily weight-adjusted dose of both sofosbuvir and daclatasvir for 12 weeks. Patients were monitored throughout the treatment and follow-up period for safety and efficacy outcome measures including liver, kidney functions and hematological indices in addition to careful clinical evaluation. Viremia was monitored at enrollment, 2 weeks (rapid virologic response RVR) and 12 weeks (end of treatment response EOTR) and the 12 weeks after end of treatment (sustained virologic response SVR 12

Results: No fatalities or treatment-emergent serious or severe adverse events were reported throughout the study. All patients showed normalized liver enzymes with normal other hematological, liver and renal function tests at the end of the study. The RVR and EOTR were 100% and we project an intent-to-treat (ITT) SVR 12 rate to be 20 of 20 (100%; 95% confidence interval [CI] 84% -100%).

Conclusions: SOF/DCV combined therapy might be used safely and effectively in the treatment of chronic HCV genotype 4 infection in survivors of acute leukemia/lymphoma

V186 SIOP19-1374 | Role of Fluconazole as Antifungal Prophylaxis During Induction Phase of Chemotherapy in Paediatric Acute Leukemia

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Background/Objectives:

Patients with malignancies often develop febrile neutropenia (FN) as a complication of chemotherapy. Fungal infections (FI), are often observed during the neutropenic phase. Anti-fungal prophylaxis is recommended for patients with haematological malignancies to reduce the risk of IFI. The aim was to evaluate the role of fluconazole as antifungal prophylaxis in leukemic children during induction chemotherapy.

Design/Methods: This was a randomized, double-blinded, placebo-controlled prospective study carried out from September 2016 to August 2017. There were 60 patients (30 in fluconazole and 30 in placebo group), with age ranging from 1 to 18 years old. Computer-generated randomisation tables were used to select the cases and controls. Fluconazole prophylaxis was given at 6 mg/kg PO daily, from 1 day prior to chemotherapy initiation till completion of induction therapy. Evaluation of the patient was done at baseline, and twice weekly until after one week of completion of antifungal prophylaxis. Data regarding evidence of fungal infection, side effects of fluconazole and requirement of empirical antifungal agent were recorded by using semi-structured questionnaires. At the end of study, drugs were uncoded. Written informed consent was taken from each patient's guardian.

Results: Mean age of the patients was 7.08 ± 3.33 years in the fluconazole group. Male:female ratio was 1.14:1. Out of the 60 patients, 44 had ALL and 16 had AML. Mean duration of neutropenia in fluconazole and placebo groups were 13.40 ± 5.75 days and 16.83 ± 5.77 days respectively. Duration of empirical antifungal therapy in fluconazole and placebo groups differed significantly ($p=0.008$). The difference in neutrophil recovery in the two groups was also significant ($p=0.015$). Success rate of fluconazole prophylaxis in preventing IFI was 83.3% ($n=2$). Hypokalaemia was observed 36.66% of cases in the fluconazole group.

Conclusions: Prophylactic fluconazole can be used to decrease fungal infection as well as the duration of febrile neutropenia during induction chemotherapy in children with leukemia.

V187 SIOP19-0443 | NUDT15 Mutation: A New Prognostic Factor in Childhood Acute Lymphoblastic Leukemia?

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Background/Objectives: The nudix hydrolase 15 (*NUDT15*) polymorphism recently emerges as a biomarker of severe hematological toxicity during 6-mercaptopurine (6-MP) therapy of children with acute lymphoblastic leukemia (ALL). Initially described restricted to Asian population, recent publications highlighted its presence in patients with European ancestry. In November 2018, the Clinical Pharmacogenetics Implementation Consortium (CPIC) updated the guideline for thiopurines dosing based on Thiopurine S-methyl transferase (*TPMT*) and *NUDT15* genotypes. Here, we presented a feedback from a French monocentric experience in ALL patients

Design/Methods: We retrospectively genotyped 238 children for *NUDT15* c.94C>A treated for ALL at Trousseau hospital, Paris, between 2014 and 2018. Parents have given their consent for thiopurines' therapeutic drug monitoring including performing *TPMT* genotype (*2, *3B, *3C). We focused, for patients with a mutated *NUDT15* genotype, on treatment response in terms of morbi-mortality.

Results: This *NUDT15* polymorphism was found for 8 patients (3.3%): two patients with a European ancestry and the others with an Asian ancestry. Seven children had a *NUDT15* mutated heterozygous genotype without *TPMT* alterations and one patient with a mutated homozygous *NUDT15* genotype associated with *TPMT* *1/*3C. Hematological and/or infectious complications were reported for all patients with this variant with hospitalization in intensive care unit for the one with a mutated *NUDT15* genotype and *TPMT* *1/*3C. Reduced 6-MP dose (between 30% to 50% of the standard dose for heterozygous patients and 3% of the standard dose for mutated homozygous patient) was required for maintenance therapy. Three patients had a relapse.

Conclusions: This report supports CPIC guidelines for screening *NUDT15* polymorphism before 6-MP treatment regardless patients' origins. The impact of this polymorphism on relapse occurrence is worrying and prospective results with dose adjustments at 6-MP initiation will be crucial to understand if treatment interruptions and/or reduced dose were at risk of relapse.

V188

SIOP19-0566 | Hypogammaglobulinemia in Indian Children with Acute Lymphoblastic Leukemia During Maintenance Chemotherapy

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Background/Objectives: Children with acute lymphoblastic leukemia (ALL) have B and T cell immune dysfunction. Indian children have different ranges of serum Immunoglobulin (Ig) reference values as compared to western counterparts. This study was done to find out proportion of Indian

children with ALL having hypogammaglobulinemia during maintenance chemotherapy.

Design/Methods: Total 163 children with ALL, 1 to 14 years of age, undergoing maintenance chemotherapy were recruited between July 2018 to March 2019 and their serum IgG, IgM and IgA values were measured by turbidimetric method (Vitros® kit). Their Ig values were compared to age related normal ranges to find out proportion of children having hypogammaglobulinemia.

Results: Abnormally low levels of serum IgG and IgM were found in 55.2% (n=90) and 84.7% (n=138) of children, respectively. Out of 61 children in the 5-10 year age group, 15 (9.2% of total) had serum IgA level <40 mg/dL. Among rest of the study group, 50% (n=83) children had serum IgA level in hypogammaglobulinemia range. Younger children (≤5 years) had significantly low levels of IgA and IgM values as compared to older age group (>5years) (P<0.001, P=0.003, respectively). There was no significant difference of Ig levels between high risk and low risk children with ALL. Lower levels of kit for serum IgG, IgA and IgM values were 270 mg/dL, 40 mg/dL and 25 mg/dL, respectively; hence absolute values of serum immunoglobulin below this level could not be obtained.

Conclusions: Children with ALL on maintenance chemotherapy have B cell immune dysfunction manifested as hypogammaglobulinemia, especially involving IgM; which is involved in major immune response during acute infection. Younger children are at more risk of developing hypogammaglobulinemia. These findings suggest that immunoglobulin supplementation can be considered in children with ALL during maintenance chemotherapy during periods of severe infection.

V189 SIOP19-0273 | Analysis of Genetic Prognostic Markers of Pediatric B-Acute Lymphoblastic Leukemia in Slovak Population

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Background/Objectives: Acute lymphoblastic leukemia (ALL) is a genetically heterogeneous disease. The genetic profile of the leukemic blasts has significant impact on prognosis and stratification of therapy. In a part of patients with B-ALL (B-other) lack cytogenetic abnormalities with

clinical relevance for prognosis. The aim of our study was to determine the number of pediatric B-other cases in Slovak population and retrospectively implement SNP-array method for further characterization of their genetic profile.

Design/Methods: In total, 133 children and adolescents were diagnosed with B-ALL between 2013 and 2017. Bone marrow samples were analyzed at a central laboratory using conventional cytogenetics, fluorescence in situ hybridization (FISH) and molecular genetic methods (RT-PCR, MLPA). Retrospective review was based on our laboratory and clinical data from the Slovak clinical cancer registry of children and adolescent. Genome-wide SNP array analysis was performed using the CytoScan HD microarray assay (Affymetrix/Thermo Fisher Scientific) according to the manufacturer's recommended procedure. Data were analysed by the Affymetrix ChAS software.

Results: Patients without cytogenetic marker accounted for 39% ($n = 52/133$) of the total population. We obtained 20 samples from 18 patients and were analysed using CytoScan array. In 17/18 (94.44%) of investigated cases genomic changes were identified, only in one patient we did not identify any aberration. Overall, we identified 126 copy number alteration and 11 copy neutral loss of heterozygosity (CN-LOH). Clinically relevant aberrations with prognostic and therapeutic implications were found in 4/18 (22.22%) cases: masked hypodiploidy (1/4), intrachromosomal amplification of chromosome 21 (iAMP21) (1/4) and IKZF1PLUS (2/4).

Conclusions: The use of SNP-array contributes to the identification of prognostic markers. Integrating identified genomic changes in clinical practice can bring improvement of prognosis for children with ALL in Slovakia.

V190 SIOP19-1572 | Identification and Quantification of the Novel Alternative mRNA Splice Variants of Proliferating Cell Nuclear Antigen (PCNA) in Acute Lymphoblastic Leukemia Using Droplet Digital PCR

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Background/Objectives: Acute Lymphoblastic Leukemia (ALL) is the most common childhood malignancy as well as México. However, approximately 30% of patients relapse with poor prognosis. The gene expression profiles contribute to molecular classification and play an important role in the cancer biology. The human transcriptome is incompletely eluci-

dated since only more that 80% of transcripts can be processes via alternative splicing (AS) which increase transcripts and protein diversity. AS has been associated with diverse cancer-associated processes. The contribution of the expression of aberrant proteins is unclear and the diversity of AS expressed is unknown. Proliferation cell nuclear antigen (PCNA) is a gene that plays several roles in cell biology, two transcripts have been reported and both coding for same protein.

Objective. Identification and absolute quantification of expression level four RNA transcripts of PCNA in ALL

Design/Methods: We performed microarray analysis bone marrow of patients with ALL, the significant transcripts were validated and include to PCNA. We design primers to amplify the potential alternative splice variants. The PCR products were purified and sequence. After, we quantified four PCNA transcript variants by ddPCR in 80 bone marrow of patients with ALL. We designed specific RNA interference (PCNA3i, 4i) and evaluated their functions in HTR8 cell line.

Results: Our microarray analysis showed potential site of AS, by PCR and sequencing identify two additional PCNA transcripts PCNA3 and PCNA4. We evaluated the canonical PCNA transcripts (PCNA1,2). We observed that PCNA2, 4 are top expressed in ALL. The PCNA3i reduce the proliferative capacity, while PCNA4i reduce the migration in HTR8.

Conclusions: We identify and validate expression of two additional PCNA transcripts in ALL. The PCNA3, 4 play roles in cell proliferation and migration.

Haematology - Lymphomas

V191 SIOP19-0494 | Deaths in Pediatric Burkitt Lymphoma Patients. What Could Be Improved?

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Background/Objectives: The aim of this work is to analyze causes of death among pediatric Burkitt lymphoma (BL), to identify adverse prognostic factors at different phases of treatment. To set a series of recommendation to avoid unexpected treatment related mortality (TRM).

Design/Methods: A retrospective analysis that included all BL patients who were diagnosed and treated at the Children Cancer Hospital (CCHE) during the period from 06/2012 till

end of 12/2018 and died. All patients were treated according to LMB96 protocol, and were stratified as low (LR), intermediate (IR) or high risk (HR) group. Analysis included epidemiologic data, initial presentation, tumor stage, risk stratification, direct cause of death, and phase of treatment where death occurred.

Results: Out of 570 patients, 84 (14.7%) died. Majority (69%) were males with mean age 7.6 years. Most of them (94%) had advanced stage (III and IV) disease. Forty eight LR (12.2%), and 36 HR (28.3%) patient died. Majority (78.6%) were in active disease, while 21.4% in CR/PR. Main causes of death were septic shock (34.5%), disease progression in (31%), tumor lysis syndrome (TLS) (11.9%). Three patients (3.6%) died upon arrival to the hospital without receiving any kind of chemotherapy, 17 (20.4%) during prephase, 24 (28.5%) during induction 8 (9.5%) during consolidation, 2 (6.1%) during maintenance phase. For relapsing patients, 18 (21.4%) died from chemotherapy toxicity of second line, while 6 (7.1%) were on palliative care.

Conclusions: Despite being a well-equipped tertiary care hospital, we report a very high mortality rate. Late presentation, TLS and sever sepsis are main causes of death throughout different phases of treatment. For relapsed patient, toxicity of 2nd line chemotherapy and tumor progression are the main causes of death. We need intensify supportive care measures, and to better identify patients at high risk for mortality to avoid unnecessary patients' death.

V192 SIOP19-1272 | R-CHOP versus LMB-96 for the Treatment of Low Risk Pediatric Diffuse Large B Cell Non Hodgkin Lymphoma- A Single Center Experience

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Background/Objectives: The aim of this work is to report treatment outcome of low risk [stage I & II] pediatric diffuse large B cell lymphoma (DLBCL) treated with R-CHOP versus those treated on LMB 96 protocol. Also to study the pharmaco-economics of both types of chemotherapy.

Design/Methods: A retrospective analysis that included all patients treated during the period from July 2007 till end of July 2018. Patients were randomly assigned to each line of therapy after combined clinic discussion. Data collected

included epidemiology, prognostic factors, and response criteria. Pharmaco-economics was studied by calculating patients' average total expenses/costs throughout their treatment duration. Costs of medications, outpatient visits (OP), hospital stays was also calculated.

Results: Fifteen patients were included in each arm, males and stage II disease were predominant in both groups. Most of the patients (93.3%) received 4 or more cycles of R-CHOP, while the majority (66.7%) were treated as group B LMB 96 protocol and received 4 courses of chemotherapy. Median follow up period was 39 months (range 6-100). Final analysis showed all 15 patients alive in LMB-96 group with 2 (13.3%) disease progression (DP), compared to 13/15 alive in R-CHOP group, with 1 DP (6.6%), 1 late relapse and 1 treatment related mortality.

The 3 years OS for LMB versus R-CHOP group was 100% and 92.9% (95% CI 68.4%-100%) respectively (p=0.301), while 3 years EFS was 86.2% for both groups (95% CI 68.4%-100%) (p=0.499). Average total expenses/costs of patients treated with LMB protocol was 20.000 US \$, compared to 7.700 US\$ for R-CHOP.

Conclusions: R-CHOP is as effective as LMB-96 for the treatment of low risk DLBCL. It has the advantage of being of lower cost, and given on OP basis. On the other hand, further studies needs to be conducted to evaluate the toxicity of Rituximab given for low risk patients.

V193 SIOP19-0207 | The Role of the Pre-Therapy Inflammatory Plasma Proteome in Predicting Clinical Outcomes in Children and Adolescents with Hodgkin Lymphoma

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Background/Objectives: The immune microenvironment that characterizes Hodgkin lymphoma (HL) contributes to prognosis of adult HL, but its role is largely undefined in pediatric HL. We hypothesize that inflammatory mediators in plasma of children and adolescents with HL could identify biomarkers associated with disease (risk) and outcomes (therapy response and relapse).

Design/Methods: Pre-therapy plasma samples were obtained from subjects with pediatric HL and healthy pediatric controls. Plasma concentrations of 144 cytokines/chemokines were measured with the Luminex platform (Milliplex MAP kits, EMD Millipore). Associations between protein concentration and disease characteristics were determined by class comparison analysis using a multivariate permutation test, correcting for false discovery.

Results: Fifty-six subjects with HL (mean age: 13 years, range 3-18) and 56 age-matched controls were included. The cytokine/chemokine profile of subjects with HL was distinct from controls: subjects with HL had a significantly higher concentration of 34 cytokines, including TARC (18.7-fold, $p < 1e-07$), MDC (5.3-fold, $p < 1e-07$), IL-6 (3.7-fold, $p < 1e-07$), and IL-10 (3.7-fold, $p = 7e-06$). Compared to subjects with low/intermediate-risk HL ($n = 43$), subjects with high-risk HL ($n = 13$) had a significantly higher concentration of 12 cytokines, including sTNFR1 (1.8-fold, $p = 1e-06$), IL-10 (7.9-fold, $p = 2e-05$), and TNF- α (2.0-fold, $p = 3e-04$). Evaluating differences in pre-therapy plasma and response to therapy, slow early responders ($n = 10$) had a significantly higher concentration of IL-28a (5.9-fold, $p = 5e-04$) and IL-1RA (6.0-fold, $p = 8e-04$) than rapid early responders ($n = 46$). Relapsed subjects ($n = 7$) had a significantly higher concentration of IL-6 than non-relapsed subjects ($n = 49$) (7.3-fold, $p = 2e-04$).

Conclusions: This pilot series demonstrates that pre-therapy plasma proteome of pediatric subjects with HL is distinct compared to healthy controls and may correlate with disease characteristics and outcomes. Once validated in a larger cohort, these biological predictors could be incorporated into biologically based risk stratification and individualized treatment strategies, ultimately optimizing outcomes and minimizing toxicities for children and adolescents with HL.

V194 SIOP19-1333 | Hematologic Malignancies in Children and Adolescents with Ataxia Telangiectasia: 20 Years of Nationwide Experience in France

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Background/Objectives: About 25% of patients with ataxia telangiectasia (AT) develop malignancies before the age of 20. Guidelines for treatments are lacking. Our aim was to describe the management of hematologic malignancies in children and adolescents with AT.

Design/Methods: For this national retrospective study, all patients with AT who had leukemia or lymphoma before the age of 18 were included. Characteristics of AT, malignancies and treatments were described.

Results: Thirty children (21 males) with AT treated between 1996 and 2016 in 16 French pediatric centers were reviewed. Malignancies were: 10 large B-cell diffuse lymphoma; 7 Hodgkin lymphoma (HL), 4 Burkitt lymphoma, 2 T-NHL; 4 T-ALL, 2 BCP-ALL, 1 AML). Patients had biallelic null mutations in ATM gene in 64% of cases. Median age at diagnosis was 8.1 years. 5/6 HL and 4/13 NHL were EBV+. A younger age and a diagnosis after 2010 were associated with a curative choice. Ten patients were managed with non-curative intent and died. Twenty patients received chemotherapy including rituximab in 8 cases; main drugs doses were reduced in 16 cases. Immunoglobulin replacement, prophylactic antibiotics and nutritional support tended to improve tolerance. Complete remission (CR) was achieved for 17 patients but 3 relapsed (reduced treatment). One patient developed B-NHL 3 years after HL and is currently on CR2. Eleven patients died of progression or relapse ($n = 4$), AT-related complications in CR1 at 5.4 and 11.2 years ($n = 2$), toxicity ($n = 5$ including 3 with reduced treatment): 3 sepsis, 1 pneumocystis and 1 late renal failure in CR at 8.1 years. Nine patients were alive in CR, with a median follow-up of 4.2 years (2.3-9.4).

Conclusions: A curative strategy may be offered in children with AT whose neurological condition is still preserved allowing a prolonged remission in half of them. Modalities of chemotherapies and supportive care were significantly adapted and this deserves precise guidelines.

V195 SIOP19-1427 | Disease Patterns of Pediatric Non-Hodgkin Lymphoma: A Study from the North Area in Algeria

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Background/Objectives: Non-Hodgkin lymphoma (NHL) is the fourth most common malignancy in children and is primarily represented by only a few histological subtypes. Great advances have been made in the treatment of pediatric NHL. In high-income countries, cure rates now exceed 85%. However, in low- and middle-income countries, cure rates remain less than 50%.

Design/Methods: Data were collected by a retrospective review of the charts of all 115 patients admitted to 7 units of pediatric oncology during the period from 2012 until 2016. Data concerning the diagnosis, treatment and outcome were collected.

Results: A total of 115 NHL cases were diagnosed: The average age was 7.4 years. The male/female ratio was 3.2. Abdominal involvement was the most common presentation (48%). Burkitt's lymphoma (BL) was the most common NHL subtype (68.5%), followed by lymphoblastic lymphoma, diffuse large B-cell lymphoma and anaplastic large-cell lymphoma. The diagnosis was confirmed by a cytological study in 45 cases (39%) and/or histological study in 83 cases (72%), the immunostaining was made in 72 patients (64%). Almost 92% of patients were classified in a high grade stage (III–IV) at the diagnosis. Serious bacterial and fungal infections, severe myelosuppression and mucositis were the most frequent toxicities. A total of 31 patients (27%) succumbed to the disease and only 2 patients (1.2%) were lost to follow-up. The 5-year overall survival rates was 68±5%. Only high-grade stages of the disease have a significant relation with the probability of survival ($p=0.033$).

Conclusions: The results of this study show a better survival rate than the results of the study from 1989 to 1999 with less toxic deaths (14% versus 30%) and patients lost to follow-up (3% versus 26%). However, efforts should be made in order to improve the survival rates and approach the 90% described in the literature.

V196 SIOP19-0063 | Clinical Presentations, Diagnostic Patterns and Treatment Outcomes of Children with Lymphoma in Uganda

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Background/Objectives: Lymphomas are some of the commonest cancers in children worldwide. Their clinical behavior, treatments and outcomes are diverse, and have not been described in Uganda before. We described the clinical presentations, diagnostic patterns and treatment outcomes of Ugandan children diagnosed with lymphoma at Uganda Cancer Institute (UCI) in Kampala, Uganda.

Design/Methods: In a retrospective review, data regarding the clinical presentations, diagnosis and treatment outcomes from the case files of children <16 years diagnosed with lymphoma at Uganda Cancer Institute from March 2016 to March 2018 was extracted and analysed. Descriptive statistics and Kaplan-Meier curves were used to describe the clinical presentations, diagnostic patterns and treatment outcomes respectively. Approval was offered by the Institutional Review Board (IRB) of UCI.

Results: Of the 816 children admitted into the service over the 2 year period, 172 (21%) were diagnosed with lymphoma, 102 (59.3%) were males, 137 (82%) had Non-Hodgkin lymphoma, [93 (67.9% Mature B cell lymphoma and 44 (32.1%) lymphoblastic lymphoma]. Almost all the children (170/172) presented with swellings and the median duration of the symptoms were 52 and 8 weeks respectively for Hodgkin and Non-Hodgkin lymphoma. The overall 2-year survival was 90%, 87% and 40% for Hodgkin, Mature B cell and lymphoblastic lymphomas, respectively.

Conclusions: Swellings are the universal presentations of children with lymphoma in Uganda. Children with Hodgkin lymphoma have excellent outcomes. This is the first study in Sub-Saharan Africa to describe excellent Mature B-cell lymphoma outcomes and are attributed to better diagnostic methods (immunohistochemistry and flow cytometry) and more intense chemotherapy (high-dose methotrexate with supportive care) that were introduced during the study period, and will be studied further.

V197 SIOP19-0885 | LMB Chemotherapy is Effective for Burkitt Lymphoma Occurring After Solid Organ Transplantation in Children: A Report from the Societe Francaise des Cancers de L'Enfant (SFCE)

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Background/Objectives: Guidelines on optimal treatment for Burkitt lymphoma after solid organ transplantation (PSOT-BL) are lacking, as well as coherent case series. PSOT-BL is said to have a worse outcome than the other post transplantation lymphoproliferative disorders.

Design/Methods: For this national retrospective study, 3 data sources were solicited, to include patients < 18 years with PSOT-BL: the French pediatric organ transplant registry, the Registre National des Hémopathies de L'Enfant and French hemato-oncology centres.

Results: From 1997 to 2018, 17 cases (12 boys) were reported, aged 2.6 to 15.6 years (median 6.9 years) at diagnosis of PSOT-BL. Eleven patients had received liver, five kidney, and one liver-kidney transplantation. Median time of PSOT-BL onset was 3.4 years post-transplantation (R, 1.3-13.0). There were 10 stages III, 2 stage IV (1 CNS+), 5 L3 ALL (1 CNS+). EBV blood viral load was high in 14/16 evaluable patients. *MYC* was rearranged in 11/12 evaluable cases. Immunosuppressive treatment was reduced (RIS) in 16/17 patients without acute graft rejection. One patient received low-dose cyclophosphamide, steroids and rituximab for late (11.6 y) EBV-negative PSOT-BL, but progressed and ultimately died despite second-line intensive chemotherapy. All other 16 patients were treated according to LMB regimen (3 after failure of RIS and rituximab) with reduced high-dose methotrexate intensity (n=7) and rituximab (n=8). Two early deaths occurred in liver-transplanted patients presenting with L3 ALL, massive liver infiltration/acute failure and tumour lysis syndrome (n=1). Four patients underwent dialysis/hemofiltration at diagnosis. One kidney-transplant patient presented severe neurological toxicity due to high-dose aracytine. Other graft toxicities or infectious events were manageable. The 14 patients treated with intensive LMB chemotherapy are alive in first complete remission with a median follow-up of 9 years.

Conclusions: Pediatric patients with PSOT-BL can be cured by intensive LMB-based chemotherapy, rituximab and adapted supportive care, without specific graft rejection or unacceptable toxicity.

V198 SIOP19-0883 | Major Response to Venetoclax and Decitabine in a Patient with Refractory T-Cell Lymphoblastic Lymphoma

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Background/Objectives: Overall survival of children and adolescents with relapsed T-cell lymphoblastic lymphoma remains poor due to the limited salvage therapeutic options and few available clinical trials for these patients. Novel agents with improved efficacy is essential to improving survival in young patients with refractory lymphoid neoplasms. The BCL-2 inhibitor venetoclax has been found to be active pre-clinically and in adult patients with hematological malignancies however, has not been assessed in younger patients with T-cell lymphomas. Venetoclax combined with hypomethylating agents such as decitabine or azacitidine has shown favorable responses in elderly patients with acute myeloid leukemia.

Design/Methods: We report the case of a 19-year-old boy with stage III T-cell lymphoblastic lymphoma of the chest who failed upfront conventional chemotherapy as per COG AALL1231 and was subsequently refractory to 4 lines of salvage therapy at MD Anderson Cancer Center.

Results: The patient had a 10cm anterior mediastinal mass with heterogenous attenuation, as well as enlarged nodes in the neck, mediastinum, hilar regions and upper abdomen and a large left pleural effusion leading to a mediastinal shift to the right. The patient was treated with a ten-day course of 20 mg/m² of decitabine in combination with 100mg of venetoclax and achieved a dramatic clinical and radiological tumor response in the setting of extensive disease that was visualized after only 1 treatment cycle. Despite growth factor administration, the patient developed severe prolonged cytopenias which prevented him from receiving a second cycle of therapy. Seven weeks after this salvage treatment was given, the patient presented with new progressive disease in his chest and ultimately succumbed to his T-cell lymphoblastic lymphoma.

Conclusions: This case highlights the potential clinical activity of this drug combination and suggests combination therapy with venetoclax/decitabine be considered in future pediatric clinical trials.

V199 SIOP19-0296 | Treatment of Childhood Hodgkin Lymphoma in Sub-Saharan Africa: A Report from French-African Pediatric Oncology Group (GFAOP)

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Background/Objectives: The treatment strategy of childhood Hodgkin lymphoma (HL) includes chemotherapy and radiation therapy, according to the stage of the disease. Studies reported on the treatment of HL by chemotherapy alone have shown encouraging results.

Design/Methods: We present the result of the prospective multicenter study on the management of HL in GFAOP pediatric oncology centers of sub-Saharan Africa, from 01/10/2006 to 30/11/2012. This study aimed to evaluate the feasibility, epidemiologic and therapeutic aspects of children diagnosed with HL treated with COPP/ABV hybrid chemotherapy alone. Patients had to be less than 18 years of age at diagnosis with histologically proven HL.

Results: One hundred and six patients were included. The median age was 10 years. The sex ratio was 3:1 (F=26; M=80). The distribution of patients according to disease stage was as follows: stage IA (n=2); IB (n=7; 7%); IIA (n=6; 6%); IIB (n=18; 17%); IIIA (n=8; 8%); IIIB (n=47; 44%); IVA (n=3; 3%) and IVB (n=13). The unfavorable group (G2) accounted for 80% of patients. The nodular sclerosis subtype represents 36% of patients (n=38), followed by mixed cellularity (n=; 21 20%) and lymphocyte rich (n=17; 16%). Eighteen patients relapsed. The overall survival rate of treated patients was 82% with the median follow up of 30 months.

Conclusions: Treatment of HL with chemotherapy alone is feasible in subsaharan Africa. Teams must focus on initial risk stratification and early evaluation of the therapeutic response of patients, to improve overall survival.

V200 SIOP19-0182 | Clinical Features and Outcome of Children with Non-Hodgkin Lymphoma in a Tertiary Government Hospital from 2010 to 2017

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Background/Objectives: In developing countries, where 90% of Non Hodgkin Lymphoma (NHL) worldwide occur, cure rates remain to be less than 50%. Studies have mentioned that the reasons underlying poor cancer survival in resource constrained settings include delays in health-seeking behavior, poor nutritional status, scarcity of health facilities, healthcare system delays, lack of supportive care and foremost treatment abandonment. Hence, this study aims to describe the demographic and clinical characteristics of children with NHL and correlate it with their outcome as well as to determine the 5-year survival.

Design/Methods: Medical charts of newly diagnosed NHL ages 1 to 18 years old from January 2010 to December 2016 were reviewed. Data collected were age, sex, nutritional status, location of tumor, initial lab, stage, delay in treatment, histopathologic type, site and time of recurrence and presentation as oncologic emergency.

Results: A total of 53 patients were included. Eighty percent were diagnosed at advanced stage. The most common histopathologic subtype is a mature B cell neoplasm, specifically Burkitt Lymphoma. Half of the patients presented as oncologic emergency. Sixty-four percent of patients were started chemotherapy after more than 60 days from onset of symptoms. Longest interval was from the time before patient was referred to an oncologist followed by the release of histopathologic results. Twenty percent of patients abandoned treatment. The 5 year overall survival and event free survival were 38% and 32.7%, respectively. Cardiothoracic and neurologic emergencies, and intrathoracic location of tumor showed significant prognostic impact for mortality. Most patients died of septic shock (41.7%).

Conclusions: The 5-year overall and event-free survival rates were lower than those reported for developed countries but is comparable with reports of other developing countries. Early detection not only for parents but for physicians' as well and availability of resources should be achieved. Infection is the most frequent and a serious problem in cancer patients.

V201 SIOP19-1313 | R-CHOP for Non-Hodgkins Lymphoma in Botswana

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Background/Objectives: Between 2008 and 2015, two-year overall survival for children diagnosed with Non-Hodgkin's Lymphoma (NHL) in Botswana was 50% (N=8). Starting in 2016, children with NHL were treated using rituximab with

cyclophosphamide, vincristine, doxorubicin and prednisone (R-CHOP).

Design/Methods: A retrospective review was performed via the Botswana Paediatric Oncology Database (BPOD) evaluating six consecutive patients diagnosed with NHL (one follicular lymphoma, two Burkitt lymphoma and three diffuse large B-cell lymphoma confirmed by immunohistochemistry) from 2016 to 2018. The regimen included intravenous (IV) rituximab 375mg/m² and intra-theal methotrexate (age-based dosing) on day 1; IV cyclophosphamide 750mg/m², vincristine 1.4mg/m², and doxorubicin 30mg/m² on day 2; and oral prednisolone 40mg/m² daily on days 1-5. Six to eight cycles were given depending on risk group.

Results: Six consecutive patients, median age of 15.3 years (range 1.5-16.7), 50% male and one HIV positive, were treated with R-CHOP. With all patients followed for a median of 0.9 years (range 0.3 to 1.6), four patients (66.7%) remain alive in complete remission. Both patients that died had extensive disease at presentation and were given a COP (cyclophosphamide, vincristine and prednisolone) pre-phase. One patient died following cycle one of R-CHOP; the second patient initially had a dramatic response following one cycle of R-CHOP, then relapsed after cycle three and transitioned to palliative care. Half of the patients experienced delays in therapy due to cytopenias and one patient, also HIV positive, required 25% dose reduction due to myelotoxicity.

Conclusions: The experience in Botswana demonstrates feasibility of incorporating rituximab into an NHL regimen in a resource-limited setting. The short follow-up time and small cohort prevent assessment of the benefit of R-CHOP over other NHL adapted regimens for LMICs. Further efforts are needed to improve diagnostic and treatment capabilities in LMICs, allowing the implementation of NHL protocols proven to be effective in high income countries.

V202 SIOP19-0503 | Primary Gastric Lymphoma: A Report of 16 Pediatric Cases Treated at a Single Institute

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Background/Objectives: Gastrointestinal tract is the most common extranodal site for childhood non-Hodgkin lymphomas (NHL). Most arise from intestine. Primary gastric lymphoma is very rare. We report our institutional experience with gastric lymphoma over a 46-year period.

Design/Methods: From 1972 to 2019, 1696 children with NHL were admitted to our department. Of these, sixteen children with primary gastric lymphoma were evaluated retro-

spectively. Patient and tumor features, treatments and survival rates were recorded.

Results: There were 11 males, 5 females with a median age of 10 months. Median duration of symptoms was 2 months. Most common complaints were abdominal pain, distention and vomiting. Two patients presented with hematemesis and melena. Severe weight loss was present in seven cases. Histopathological subtypes were Burkitt lymphoma in four patients, diffuse large B-cell lymphoma in two, lymphoblastic lymphoma NOS in three, precursor B-lymphoblastic lymphoma in one, anaplastic large cell lymphoma in one, H.pylori related MZL in one and undefined in three. The most common site was antrum. Diffuse wall thickening was observed in two patients. Gross total and subtotal gastrectomy with gastroduodenostomy or jejunostomy were performed in four patients. Four patients received radiotherapy. All patients except one, who was lost to follow-up just after diagnosis, received chemotherapy. Malign lymphoid proliferation in patients with MZL was resolved after H.pylori eradication. Nine patients lived without disease median 59 (12-252) months. One patient was lost to follow-up after relapse. Two patients died without disease due to neutropenic infection, two with gastrointestinal bleeding and two with progressive disease. Five-year EFS and OS were 69.6 and 64.3%, respectively.

Conclusions: Primary gastric lymphoma constitutes 0.94% of our NHL cases. Unlike adults in whom majority of cases were MALT lymphoma, most of our cases had high grade histopathology. Although surgical procedures were applied in four early cases, most were treated with chemotherapy.

V203 SIOP19-0676 | Clinical Course and Prognosis of Children with Hodgkin Lymphoma in Central and Southern Mexico Areas. Results of the Mexican Association of Pediatric Hematology and Oncology

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Background/Objectives: In developed countries, the survival of children with Hodgkin Lymphoma is very high, the treatment according to risk groups has been able to reduce toxicity and long-term sequelae.

Objective: To know the clinical course and prognosis of pediatric patients with Hodgkin Lymphoma at the central and southern areas from Mexico.

Design/Methods: Material and methods

We Included in a cohort, clinical records of pediatric patients with Hodgkin Lymphoma. Diagnosed and treated in 14 hospitals of the south and center zone. We analyzed clinical variables, demographics, histological variety, primary site, treatment scheme used, survival and the related factors.

Results: 359 patients were assessed, 242 Male and 117 females, aged from 2 to 17 years average of 10 ± 2 years old, primary site 78% cervical, followed by mediastinum, 60% with histological variety nodular sclerosis. 67% presented Symptoms B. The risk allocation was 15% low, mean 37% and high 57%. 90% treated with national protocol based on ABVD/CVPD, more radiotherapy to compromised fields. Presented Relapse 8%. The survival reported was 93% to 5 years for all patients. The variables that influenced the prognosis were the presence of symptoms B and stage of the disease, was performed TPH in 7 patients. Deaths were attributed in 50% to toxicity related to treatment. There were significant differences in the survival of patients in the south and center area, for stages III and IV with 50% vs. 75% to 5 years respectively.

Conclusions: In Mexico, multiple factors influence the results of treatment of children with cancer, in this series most of our patients are of high and intermediate risk, the presence of B symptoms and advanced stage to the diagnosis, involve a late diagnosis which are determinants in the survival. Multiple social and cultural circumstances can explain the discrepancy in the results of treatment in the different regions of our country.

V204 SIOP19-0914 | Demographic Profile and Treatment Outcomes of Children with Diffuse Large B-Cell Lymphomas (DLBCL) - Experience from a Single Tertiary Cancer Center in India

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Background/Objectives: Diffuse large B-cell lymphoma (DLBCL) constitute 10-20% of pediatric Non-Hodgkin Lymphomas (NHL), with better prognosis than when occurring in adults. We report the clinico-demographic profile and outcomes of pediatric DLBCL treated with a uniform protocol at our center- a large tertiary cancer institute in India.

Design/Methods: Children ≤ 15 -years age diagnosed with DLBCL on morphology and immuno-histochemistry from January 2013 through December 2018 were included. All children were uniformly treated on MCP-842 chemotherapy protocol, a Non-High Dose Methotrexate based (non-HDMTX) regimen and received 8-cycles of chemotherapy irrespective of stage. Children with advanced disease received pre-phase COP (Cyclophosphamide, Oncovin, Prednisolone) therapy. Interim assessment was done at the end of 2-cycles with 18-FDG Positron-Emission and Computerized Tomography (PET-CT) scans. The data was descriptively analyzed, and 3- year event-free and overall-survival (EFS & OS) were estimated by Kaplan- Meier analysis on SPSSv.24®.

Results: Of 446 children with NHL registered in the study period, 16 (3.5%) had DLBCL on biopsy. Two patients with only intracranial disease were excluded. The male/female ratio was 6:1, and median-age, 12-years (range: 9-15years). Twelve (85%) had stage-III disease, and Stage-II and IV were 1 each (7%). Post 2-cycles MCP-842, complete metabolic and morphologic response (CMMR) was seen in 9 (64%) patients, while 5 (35%) had partial response (PR). However all 5 patients with PR achieved CMMR by end-of treatment on PET-CT. There were 3 (21.4%) deaths (1 each due to CNS relapse, secondary AML and viral encephalitis). At a median follow-up of 23 months (range: 6- 67 months), the 3-year EFS and OS was $70 \pm 15\%$ and $82 \pm 11\%$ respectively.

Conclusions: Most of our DLBCL patients had advanced disease at presentation, but had excellent outcomes on MCP-842, a non-HDMTX-based protocol which was easily administered on out-patient basis and well-tolerated.

V205 SIOP19-0467 | Outcome of Gemcitabine and Vinorelbine as a Second Line in Relapsing/Refractory Pediatric Hodgkin Lymphoma

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Background/Objectives: Although Hodgkin lymphoma (HL) is largely curable with first-line therapy, one-third of patients will refractory to frontline treatment or will relapse later. the aim of the study is to evaluate the response & outcome of Gemcitabine and Vinorelbine as a second line treatment for Relapsing/Refractory Pediatric Hodgkin Lymphoma.

Design/Methods: A retrospective study including all pediatric classic Hodgkin Lymphoma patients receiving first line ABVD $\pm$ radiotherapy & who were refractory or relapsed, in the period from August 2017 till December 2018 at CCHE, and received, gemcitabine, vinorelbine as 2nd line therapy.

Results: Twenty eight patients were included in the study out of 1370 patients with classic Hodgkin Disease, 17 patients (60.7%) were males, and 11 patients (39.3%) were females with mean age 11.6 ± 3.6 . Nodular sclerosis had the upper hand as initial diagnosis which was in 19 patients (67.9%), followed by mixed cellularity which was in 21.4% patients. Initial stage IIIB, and IVB were account in 50% of the study patients. About 67.9% were received involved field radiotherapy in the first line of treatment. Median time of relapse was 16.32 months (0-105 months). In the current study, all patients received gemcitabine, vinorelbine as 2nd line therapy, Interim FDG PET was positive in 35.7% of study patients, post 2nd cycle. Nine patients (32%) continue on the same line and Auto BMT was done for them, 19 patients (67.8%) failed the current treatment and shifted to 3rd line salvage chemotherapy line in the form of ICE, and Auto BMT was done for 8 patients, and the rest are still under treatment. No toxicity or morbidity were reported in the study patients.

Conclusions: gemcitabine/ venorlbine as 2nd line treatment in relapsed or refractory pediatric classic Hodgkin Disease is an outpatient therapy with low toxicity profile, but regarding to our patients response, it was inferior to literature.

V206 SIOP19-1034 | Outcome of Childhood ALK Positive Anaplastic Large Cell Lymphoma Relapses: A Report of 75 French Children

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Background/Objectives: To analyse treatment and outcome of French children treated for relapsed/resistant ALK positive anaplastic large cell lymphoma recurrences.

Design/Methods: Among 245 French patients included in the ALCL 99 protocol for an ALK+ ALCL between 1999 and 2017, 75 were treated for a progression or a relapse.

Results: The median time to relapse was 8.1 months (2.9m after end of treatment) with 10 relapses during front-line chemotherapy or within one month of the last chemotherapy course. 26 patients were included in the European ALCL-relapse trial (NCT00317408) between 2004 and 2013. Treatment of the first relapse varied according the period and risk factors: 42 received a second line multi-agent chemotherapy followed by a consolidation in 36/42 patients who achieved CR (autologous SCT in 18, allogeneic SCT in 16), 17 patients received weekly vinblastine and 5 ALK inhibitors. Overall, 68 (90%) achieved a second complete remission (CR2). All 7 patients who did not achieve CR2 died with a median time of 4.8 months (0.5-9.6). With a median follow-up of 4.5 years, 42 patients were alive in CR 2, 16 in CR3, 2 in CR 4, and 15 patients died, 4 from toxicity, 9 from progressive disease, and 2 for another reason. The 5 y EFS and OS after relapse were 60% (95% CI 47-71%), 3% and 80% (95%CI 69-87%) respectively. The last treatment given to patients who survive without further relapse, were weekly vinblastine (27 patients), CC and CVA chemotherapy with allogeneic (12) or autologous (7) SCT, ALK inhibitors (8), multi chemotherapy without consolidation (4) or not (2).

Conclusions: In relapsed ALK+ ALCL, high survival rate can be reached with various therapeutic approaches. Given the high rescue rate in patients experiencing multiple relapses, preference should be given to treatment associated with low morbidities.

V207 SIOP19-0877 | Application of a New Score at Diagnosis to Identify Risk Categories in Pediatric Patients with Hodgkin's Lymphoma

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Background/Objectives: Hodgkin's lymphoma is a neoplasm with high curability rate in pediatric patients. A Children's Oncology Group study proposed the CHIPS (Childhood Hodgkin International Prognostic Score) to identify patients with worse prognosis that may be benefited with treatment intensification. Our aim was to validate the CHIPS score retrospectively in a cohort of patients admitted at our Hospital from 2000 to 2015.

Design/Methods: A retrospective, analytical study of patients with Hodgkin's lymphoma treated at our Institution according to LH-HPG 2000 protocol between September 2000 and December 2015. Risk factors that defines the CHIPS score are: stage IV disease, large mediastinal mass (Bulky), albumin dosage <3.5 and fever. The score is 0 when there is no risk factor and 1-4 when there are 1-4 risk factors.

Results: The cohort included 127 patients. Median age at diagnosis was 10.7 (3-17) years. Sex distribution was 1/2.5 (female/male). CHIPS 0 group represented 26.8%; CHIPS 1, 33.8%; CHIPS 2, 19.7%; CHIPS 3, 15% and CHIPS 4, 4.7%. The overall survival and event free survival probabilities (EFSp) were 94% and 87.5% respectively. The 5 years-EFSp according to CHIPS score was 85.3%; 86.8%; 87.8%; 86.3% y 67% for CHIPS 0, 1, 2, 3 and 4 groups respectively. There were not any statistically significant differences in EFSp among the CHIPS score groups.

Conclusions: There were not any statistically significant disease free survival differences among groups with CHIPS score stratification in our setting. This showed that therapy risk stratification was good enough in terms of EFSp in the retrospective evaluation of our cohort.

V208 SIOP19-0438 | Impact of Multidisciplinary Tumor Board on Treatment Plan and Outcome in Children and Adolescent with Classical Hodgkin Lymphoma

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Background/Objectives: All classical Hodgkin Lymphoma (cHL) children/adolescents cases are presented in a multidisciplinary multicentric pediatric tumor board (RCPD) to define

treatment plan. Between January 2013 and December 2016, no trial was open for recruitment in France. Treatment recommendations were based on the preliminary results of the Euronet PHL-C1 protocol. This work aims to describe RCPD decisions, delivered treatment and outcome of cHL patients during this period.

Design/Methods: Medical report, histology, biology of all consecutive cHL presented in RCPD Lymphoma "Ile-de-France" (6 centers) with CT/MRI/abdominal ultrasound/PET-FDG-CT available.

Results: Between January 2013 and December 2016, 148 patients were recorded, 77 girls, with median age 13 years. Patients were treated according to adapted Euronet PHL-C1 in 114 cases (77%); 34 had a different treatment plan with number of chemotherapy courses adapted to metabolic response after 2 cycles of Vincristine, Etoposide, Doxorubicine, Prednisone (OEPA) or use of another chemotherapy. Radiotherapy (RT) was defined by the response after 2 OEPA: in case of adequate response (AR), no RT was planned except for 3 patients with residual disease. Response was inadequate for 55 patients (37%), 16 /55 were treated without RT because of: young age n= 2, extensive disease n=7, progression n=2, doubtful response after 2 OEPA n=3, medical condition n=2, parental refusal n=2. The use of RT was limited to 39 patients (26%). With a median follow up of 32 months, 146 patients are alive, 2 patients died (cHL relapse n=1). Seventeen patients (11%) relapsed. Median time to relapse was 9 months.

Conclusions: With this approach, survival is excellent, and the relapse cumulative rate is in the range of expected result. Although limited by the short follow up, this retrospective study confirms that a large proportion of cHL can be cured without RT.

V209 SIOP19-0526 | Clinical Course and Outcome of B Cell Non-Hodgkin Lymphoma in Children-Single Institution Study from Low Income Country

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Background/Objectives: Pediatric non-Hodgkin lymphoma (NHL) represents 50 percent of childhood lymphomas. Over the years there has been improvement in the outcome of NHL, and this is mostly due to the understanding of the histological subtypes, cytogenetics and staging along with the introduction of the highly intensive treatment regimens and good supportive care. This study was conducted to determine the clinical presentation, course and outcome of B cell NHL in resource limited country.

Design/Methods: Retrospective study was carried out from January 2012 till December 2016. Children diagnosed with

B cell NHL at Shaukat khanum Memorial Cancer Hospital (SKMCH), were included in the study after IRB approval.

Results: Total 286 patients presented to the SKMCH with the median age 6 years (range 1-16 years). Mean time of presentation from the onset of symptoms to the oncologist was 50.1 days. Burkitt lymphoma was diagnosed in 195 patients (68.2%), followed by diffuse large B cell in 84 patients (29.4%). Majority of our patients had extensive disease on presentation, stage III was present in 162 patients (56.6%), stage IV in 77 patients (26.9%). Complete remission was achieved in 171 patients (59.8%) whereas 89 patients (31.1%) died during treatment. Common cause of death was neutropenic colitis in 49 (52.1%) patients. Eleven patients (3.8%) had progressive disease, where as disease relapse was present in 7 patients (2.4%). The 2-year overall survival (OS) was 66.4%, whereas event free survival (EFS) was 59.9%. Patients having extensive disease (stage III/Stage IV) had poor outcomes with P value less than 0.005. Chemotherapy related toxicity was seen in 18 patients (6.3%).

Conclusions: Majority of children presented to our institute had extensive disease, so measures are needed for early recognition, identification and prompt referral to pediatric cancer institute. Better supportive care strategies can decrease risk of neutropenic infections.

Key words: B cell NHL, outcome, low income country

V210 SIOP19-0185 | Should Treatment of ALK Positive Anaplastic Large Cell Lymphoma be Stratified According to Minimal Residual Disease?

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Background/Objectives: Minimal residual disease (MRD) is a biomarker for directing treatment and predicts outcomes in patients with leukemia. In ALK+ALCL, the detection of ALK fusion transcript product by RT-PCR on blood and/or bone marrow can be used to qualitatively monitor MRD. In 2014, Damm-Welk and colleagues showed that the small group of patients in whom MRD was detectable after the first 4 weeks

of treatment had a very high risk of relapse with 5-y EFS of 19%. We aimed to validate these results among the French ALCL99 patients.

Design/Methods: This study was performed on data prospectively collected in French patients registered in the ALCL99 database and uniformly treated with the ALCL99 protocol.

Results: Data on MDD at diagnosis are available in 136/227 French ALK+ALCL patients. Among them, 86 (63.2%) had a detectable minimal disease at diagnosis (MDD+) and 50 (36.8%) had no detectable MDD (MDD-). Among the 86 patients with MDD+, 32 (39%) had an MRD measurement performed after first course AM1, with 17 detectable MRD (MRD+) and 15 no detectable MRD (MRD-). EFS was significantly correlated with the MDD/MRD status (log-rank p-value<0.001) as 3-y EFS was 80.6% (IC95% [66.1-89.9]) in MDD- patients, 69.6% (IC95% [42.5-87.7]) in MDD+/MRD- patients and 15.2% (IC95% [3.2-49.0]) in MDD+/MRD+ patients. Patients with MDD+/MRD+ had a significant poorer 3-years OS of 76.0% (IC95% [48.1-91.5]) vs 93.5% (IC95% [89.2-96.2]) in the whole cohort (log-rank p-value=0.01).

Conclusions: The prognostic value of MDD/MRD status in ALK+ALCL advocates for its use as a stratification biomarker in future clinical trials to propose early treatment intensification of ALK+ALCL patients with the highest risk of relapse to improve their outcome and decrease the total burden of treatment for cure.

V211 SIOP19-0909 | Profound and Sustained Response with ALK Inhibitors in Patients with CNS Relapse or Progressive ALK- Positive Anaplastic Lymphoma

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Background/Objectives: Pediatric ALK-positive anaplastic large cell lymphoma (ALK+ALCL) is a rare disease. Outcome is good in most patients with a 5 year-survival reaching 90% in recent reports, even though 30-35% patients suffer from one or sometimes multiple relapses. Patients presenting with CNS relapse/progression have a poorer prognosis. Next generation ALK inhibitors (ALKi), developed for brain metastases in lung cancer, have a good CNS penetration and could be used to improve outcome in these patients.

Design/Methods: We reviewed retrospectively the French experience of ALKi in pediatric patients with relapsed/progressive ALK+ALCL and CNS involvement.

Results: Five patients with ALK+ALCL with 6 CNS relapses (n=3) or progression (n=3) treated with ALKi were identified. Age at diagnosis ranged from 3.2 to 15.7 years. Age at introduction of ALKi ranged from 4 to 20.2 years. CNS involvement was present at diagnosis in one patient and at relapse/progression in 4, including 2 isolated CNS relapse. There were 3/6 intracranial masses, 2/6 LCR positive CNS and 1/6 combined CNS involvement. ALKi was given after failure of previous chemotherapy in 5 patients and as maintenance after a few courses of HDMTX in one. ALKi was ceritinib (2/6), lorlatinib (2/6) and alectinib (2/6). Best response was CR or CRu in 4/6, VGPR in 1/6 and PD in 1/6. Interestingly, after having experienced PD while on ceritinib, one patient achieved durable CR with alectinib. Best response on ALKi was obtained with a delay ranging from 0.5 to 5.9 months. After CR/CRu/VGPR, patients were treated with ALKi for a median of 6.3 months (3 to 18.1). All the patients were still in CR and 3 are still on therapy with TKI at the date of last follow-up.

Conclusions: These observations suggests that complete and durable response can be safely obtained by using next generation ALK inhibitors in high risk patients ALK+ALCL with CNS relapse or progression.

V212 SIOP19-1709 | Clinical Application of Multiparameter Flow Cytometry on Diagnosis and Follow Up of Pediatric Lymphoma

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Background/Objectives: Pediatric lymphomas are the third most common cancer in childhood. Although, multiparameter flow cytometry (MFC) is a highly specific and sensitive method for diagnosis and follow up of hematologic malignancies with bone marrow involvement, studies on nonleukemic lymphomas on clinical practice need standardization. Here we report a standardized protocol for diagnosis and follow up of suspicious pediatric lymphoma.

Design/Methods: A total of 186 samples were consecutively obtained from 130 patients with suspicion of pediatric lymphoma, collected at diagnosis or during follow-up since November 2009 till January 2019. For research purpose, all samples were analyzed by 8-color multiparameter flow cytometry in parallel with histopathology /immunohistochemistry (HP plus IMH). During the

study period, we had optimized the panel design on a 3-round orientation/classification panel to diagnosis of reactive/inflammatory vs hematopoietic solid tumors.

Results: Seventy-eight (60%) patients had cancer and the other 52 (40%) had inflammatory/reactive diseases. The overall concordance rate between both approaches (HP plus IMH vs MFC) were 92.3% (156/169) when considered the identification of non-infiltrated samples (disease free, reactive or inflammatory) vs infiltrated samples (hematopoietic solid tumor) with a kappa= 0.888 confidence interval: 0.831 – 0.944, excluding 15 PB. All reactive/inflammatory were correctly diagnosed with 100% agreement with only 11 false negative cases diagnosed as: Hodgkin lymphoma (8/14), anaplastic lymphoma (1/6) and diffuse large B cell lymphoma (1/6). Accordingly to WHO classification we could correctly identify 6 disease groups of hematopoietic solid tumors: anaplastic large cell lymphoma (CD45+/CD56-/CD2+/CD30+/CD7-/CD3-/CD5-/CD4-/CD8-); T lymphoblastic lymphoma (CD45+/CD2+/CD7-/CD3+/CD5-/CD4-/CD8-); B lymphoblastic lymphoma (CD45-/CD19+/CD34-/CD10-/CD81+/CD38+); Burkitt lymphoma (CD45+/CD19+/CD20+/CD38+/CD10-/CD12-/CD24+); diffuse large B cell lymphoma (CD45+/CD19+/CD20+/CD38+/CD10-/CD12-/CD24+); and Hodgkin disease (CD45-/CD56-/CD15-/CD30+/CD19-/CD20-).

Conclusions: In summary, this study establishes a standardized protocol for MFC on routine clinical practice of pediatric non-Hodgkin lymphoma and open new research approaches for a better diagnosis of Hodgkin disease by MFC.

V213 SIOP19-0809 | Limited Chemotherapy for Early-Stage Non-Hodgkin's Lymphoma (NHL) in Children: The Experience of Istituto Nazionale Tumori Milano

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Background/Objectives: Early-stage NHLs are associated with high survival rates. To minimize the risk of long-term sequelae the duration/intensity of chemotherapy have been progressively reduced.

Design/Methods: Between 1988-2018, 46 children with early stage NHL (27 Murphy stage I, 19 stage II) were treated at a single Institution with two subsequent protocols (named I & II, respectively). Median age was 10 years (range 2-19), 25/46 males, 25 had Burkitt lymphoma, 7 DLBCL, 5 precursor B-cell lymphoblastic lymphoma, 4 MALT and 4 other subtypes. Protocol I (21 patients) consisted of a 7-week induction phase

with vincristine, doxorubicin, cyclophosphamide, methotrexate, and prednisone, followed by a maintenance for a total duration of 8 months. Protocol II (25 patients) was modified by adding etoposide and a further dose of methotrexate during induction (for a total of 9 weeks), yet abolishing maintenance. Neither protocols included CNS-directed prophylaxis.

Results: At a median follow-up of 152 months (range 1-244) 37 patients are alive in first continuous complete remission, 2 relapsed (1 died after second-line treatment, the other achieved cure with the institutional regimen for advanced-stage disease), 3 patients with partial response obtained remission by intensifying treatment with advanced-stage regimen (2 patients) or radiotherapy (1 patient). Three patients died for other causes: 1 cardiac arrest after doxorubicin, 1 Ewing's sarcoma 10 years after, 1 pulmonary tuberculosis 3 years after in an HIV+ patient. None of the patients experienced CNS disease relapse. Acute toxicity was manageable, except for the patient with presumed acute cardiac toxic death; no chronic sequelae were evident. The 5-year EFS were 80.2% and 96% for protocol I and II, respectively, and the 5-years OS were 90% and 96%.

Conclusions: Nine weeks of low-intensity chemotherapy without CNS prophylaxis seem adequate treatment to treat children with early-stage NHL without jeopardizing the excellent survival rate of this disease.

V214 SIOP19-0053 | Effect of Second Cycle Pre-Induction Chemotherapy in Critically Ill Burkitt's Lymphoma Children

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Background/Objectives: Background: Advanced stage Burkitt's lymphoma (BL) is associated with tumor burden. Toxicities from intensive therapies are significant. Our aim was to analyze the outcome of patients who could not receive induction chemotherapy on time, and were given a 2nd pre-phase (CVP), and to measure the impact of delay on disease outcome.

Design/Methods: A retrospective, non-randomized study. Patients less than 18 years, with BL included in 8 years period in Children Cancer Hospital Egypt (CCHE).

Results: Four hundred and eight patients were diagnosed as BL from July 2007 till October 2015, 286 patients (70.1%) received induction on time as per protocol, while 122 patients (29.9%) were not fit to receive their induction chemotherapy on due time. The delay ranged from 6-45 days. Forty five patients (36.88%) out of the delayed patients received 2nd CVP, 16 patients (13.1%) showed relapse/progression. OS among the delayed group then received 2nd CVP versus who were delayed then received induction chemotherapy was (76.1%), (88.7%) respectively. OS in patients who were delayed versus who were not delayed was (84%), (85.9%) respectively.

Conclusions: In critically ill patients delay of chemotherapy in induction phase is important to reduce morbidity and mortality. The Delay of chemotherapy has no impact on OS in BL patients. A second pre-phase therapy in our opinion should not be adopted for all critical ill patients who will not tolerate intensive therapy during early phases of treatment, but instead we recommend a recovery from organ toxicity and starting intensive therapy (COPADM) rather than giving a 2nd CVP with careful surveillance of disease progression.

V215 SIOP19-0054 | Prognostic Factors and Treatment Outcome of Pediatric Anaplastic Large Cell Lymphoma Treated at the Children Cancer Hospital Egypt

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Background/Objectives: Anaplastic Large Cell Lymphoma (ALCL) is accounts for 10–15% of all childhood lymphomas [2,3]. The aim of the study is to report a single center epidemiologic data, treatment outcome, and survival of ALCL patients during 8 years period.

Design/Methods: This retrospective study included ALCL patients from July 2007 till end of 2015 at CCHE.

Results: A total of 48 ALCL patients, with a male to female ratio were 2:1. The mean age was 11.7 years, and range was 3.3 to 17.2 years. According to Murphy's staging systems, 21 patients (43.7%) were low stage, while 27 (56.2%) had advanced stage. Seventeen patients (35.4%) had extranodal

disease. ALK status was positive in 42 (87.5%) patients. The 5 years overall survival (OS) was 81.2%, the 5 years event free survival [EFS] 68.6%. Median FU period was 58.7 months, range 0.6 -105.8 months. OS by stage was 85.7% for low, and 77.8% for advanced stage with no statistical significance. Multivariate analysis including age, sex, clinical stage, ALK status, extranodal disease, response to induction chemotherapy showed statically no significance.

Conclusions: A single center experience in the treatment of a rare type of NHL in a low income country. All patients were uniformly treated on protocol with maintenance weekly vinblastine. Chemotherapy on this protocol is non-intensive, given on outpatient basis and well tolerated. We couldn't identify any prognostic factor, and patients had good therapeutic outcome compared to other treatment protocols. ALCL could be salvaged after relapse with intensive chemotherapy and HSCT.

V216 SIOP19-0614 | Prognostic Factors and Treatment Outcome of Relapsing and Refractory Mature B Cell Non Hodgkin Lymphoma CCHE Experience

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Background/Objectives: Relapsed non-Hodgkin lymphoma (NHL) treated by highly toxic chemotherapy followed by HSCT with dismal prognosis. The aim of the current study was to analyze prognostic factors and outcome of relapsing/refractory pediatric mature B cell NHL.

Design/Methods: A retrospective study including all pediatric patients initially diagnosed as mature B cell NHL who were primary refractory to chemotherapy or relapsed over 6 years period at CCHE.

Results: Thirty four patients (7%) out of 494 patients were included. Twenty-three patients (67.6%) had Burkitt lymphoma, while 5 (14.7%) had diffuse large B cell lymphoma. The majority were males (79.4%) with a median age 6.2 years. According to Modified Murphy Staging, 23 (67.6%) stage III,

and 5 (14.7%) stage IV. At initial presentation, bone marrow (BM) involvement was detected in 2 patients (5.9%), and 3 (8.8%) had CNS involvement. Thirty patients (88.2%) received LMB 96 protocol, and 4 (11.8%) received R-CHOP as primary chemotherapy. Median delay in 1st line treatment was 22 days (range 0 to 162). Twenty two patients (64.7%) relapsed, while 12 (35.3%) had tumor progression. Fifteen patients (68.2%) were relapsed early, and late relapse was in 7 (31.8%). CNS relapse was in 6 patients (23.5%), BM relapse was in 6 (20.5%), and both were in 2 (5.9%). R-ICE was the 2nd line of treatment in 29 patients (85.3%), and complete 2nd remission was achieved only in 7 patients (20.6%). Allogeneic HSCT was done for 2 patients (5.9%), and auto HSCT for 3 patients (8.8%). The 3 years OS was 35.3%, with no statistical difference between relapsing and progressive disease. The 3 years OS for patient who underwent HSCT was 80% compared 20% for no HSCT (p value 0.034).

Conclusions: Relapse rate is similar to or higher than the literature because of delay of chemotherapy. HSCT in patients with second remission improve the outcome.

V217 SIOP19-0058 | Changes of Clinical, Laboratory Features of Children with B-Cell Non-Hodgkin's Lymphoma, Correlations with EBV Status; is Burkitt' Lymphoma Changing from Endemic to Sporadic in Turkey?

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Background/Objectives: As second frequent childhood malignancy in Turkey we aimed to evaluate the clinical features and outcomes of patients with B-NHL including Burkitt' lymphoma, beside to see correlation with EBV status by the time in Burkitt's lymphoma.

Design/Methods: We retrospectively evaluated 67 patients with B-NHL who were treated by pediatric oncology department of Ankara University School of Medicine between January 1992 and November 2018. The patients were divided into three groups in order to evaluate altered data over time (Group 1: 1992-2002; Group 2: 2003-2013 and Group 3: 2014-2018).

Results: The mean age at initial diagnosis was highest in group 3 (5.3 ± 2 , 8.9 ± 4.3 , 10.1 ± 3.5 , respectively), ($p < 0.05$). Burkitt lymphoma frequency was the lowest in group 1 (11.5%, 51.9% and 42.9% respectively), ($p < 0.05$). The most common primary site to be involved in group 1 and 2 was abdomen, however, peripheral lymph nodes were found higher rate in group 3 (92.3%, 66.6% and 64.2%, respectively), ($p < 0.05$). Serum LDH level was found the highest in group 1 and the lowest in group 3 (42.3%, 25.9% and 14.3%), ($p < 0.05$). EBV positivity was found 76.9% in group 1, 33.3% in

group 2 and 7.1% in group 3, respectively, ($p < 0.05$). Overall survival rates were 69.2%, 81.5% and 100%, respectively in groups 1, 2 and 3 ($p < 0.05$).

Conclusions: According to the epidemiological and laboratory findings epidemic form of Burkitt's lymphoma has been shifted from sporadic form in Turkish children over time. Early diagnosis treatment opportunities increase every year, this condition is supported by a progressive decrease in LDH. Additionally, in recent years, targeted drugs such as rituximab have been added to the treatment. As a result of these factors, the present study shows that the overall survival rates increase gradually over the years.

V218 SIOP19-0105 | Different Programmed Death-1/Programmed Death-Ligand 1 Expression Patterns for Each Pediatric Lymphoma Subtype

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Background/Objectives: Anti-programmed death-1 (PD-1) monoclonal antibodies have recently been recognized as promising therapy for adult patients with lymphoma, particularly in classical Hodgkin lymphoma. However, majority of data on PD-1 and programmed death-ligand 1 (PD-L1) expressions in lymphoma are generated from adult patients. Therefore, this study investigated those expression patterns in pediatric lymphoma.

Design/Methods: Immunohistochemical analyses were performed on formalin-fixed paraffin-embedded tumor biopsies from 40 newly diagnosed pediatric patients with lymphoma or lymphoproliferative disorders treated at Kobe Children's Hospital from 2003 to 2019.

Results: Forty samples comprised of 12 Burkitt lymphoma (BL), 8 anaplastic large-cell lymphoma (ALCL), 7 T-lymphoblastic lymphoma (T-LBL), 5 diffuse large B-cell lymphoma (DLBCL), 2 Nodular sclerosis classical Hodgkin lymphoma (NSCL), 2 Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL), 2 chronic active EBV-associated lymphoproliferative disorders (CAEBV-LPD), 1 T cell/histiocyte rich B-cell lymphoma (T/HRBCL), and 1 subcutaneous panniculitis-like T-cell lymphoma (SPTCL) were evaluated. PD-1 was expressed in tumor cells in some BL (2/12) and T-LBL (1/7) samples, but not in ALCL, DLBCL, NSCL, NLPHL, CAEBV-LPD, T/HRBCL, or SPTCL samples. PD-1+ tumor infiltrating lymphocytes were observed in some BL (5/12), ALCL (2/8), T-LBL (3/7), DLBCL (4/5), NSCL (1/2), NLPHL (2/2), CAEBV-LPD (1/2) samples, but

not in T/HRBCL or SPTCL samples. Remarkably, PD-L1 was robustly expressed in tumor cells in ALCL (6/8), NSCL (2/2), CAEBV-LPD (2/2), T/HRBCL (1/1), and SPTCL (1/1) samples, but not in BL, T-LBL, DLBCL, and NLPHL samples. PD-L1+ tumor infiltrating macrophages were observed in the BL (10/12), ALCL (1/8), T-LBL (3/7), DLBCL (3/5), NLPHL (1/2), and CAEBV-LPD (2/2) samples, but not in NSCL, T/HRBCL, and SPTCL samples.

Conclusions: In this pediatric cohort, PD-L1 was overexpressed in tumor cells in ALCL, NSCL, CAEBV-LPD, T/HRBCL, and SPTCL. Besides NSCL, PD-1 blockade might be a promising treatment strategy for ALCL, CAEBV-LPD, T/HRBCL, and SPTCL in children.

V219 SIOP19-0464 | Lack of Response to Romidepsin in Children with Relapsed / Refractory Peripheral T -Cell Lymphoma (PTCL): A Single Centre Experience

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Background/Objectives: Peripheral T-cell lymphoma (PTCL) - not otherwise specified (NOS), is a rare subtype of pediatric non-Hodgkin lymphoma with very poor prognosis. Romidepsin, a Histone deacetylase inhibitor (HDACi) has shown promising activity in adults with relapsed PTCL; however, there is no data on its use in children with relapsed or refractory PTCL. Recently discovered PTEN mutation, could be a potential target if found as a recurrent aberration in PTCL.

Design/Methods: We conducted a single centre retrospective chart review of patients with relapsed PTCL-NOS treated at the Hospital for Sick Children, Toronto between January 2009 and December 2016. Romidepsin was administered monthly at a dose of 14 mg/m² as a 4-hour infusion on days 1, 8, and 15 until disease progression. Tumor-normal sequencing by a large cancer panel was performed through the institutional SickKids Cancer Sequencing (KiCS) program with informed consent.

Results: Four Patients with relapsed/refractory PTCL-NOS were treated with romidepsin (single agent in 2, combined with alemtuzumab in 2) after having failed at least 2 prior lines of chemotherapy. Romidepsin was tolerated well, however all patients died of disease progression within 1-3 years from initial diagnosis. Sequencing performed in one patient revealed

a somatic fully clonal frameshift insertion in PTEN, with loss of heterozygosity.

Conclusions: Unlike adult PTCL, romidepsin failed to demonstrate any meaningful response in pediatric PTCL. It remains to be determined whether combination therapy between HDACi and immune checkpoint inhibitors, proteasome inhibitors or other chemotherapy drugs may help in overcoming HDACi resistance in relapsed/refractory pediatric PTCL.

V220 SIOP19-1136 | Improvement in Diagnosis in Children with Burkitt Lymphoma in Kenya: Implementation of Fluorescence In Situ Hybridization Testing for MYC and the MYC/IGH Translocation

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Background/Objectives: Background/Objectives: Burkitt lymphoma (BL) is a common pediatric cancer in sub-Saharan Africa. Delay of diagnosis of the disease results in delay of treatment. We initiated fluorescence *in situ* hybridization (FISH) for BL to advance the accuracy and speed of diagnosis in the AMPATH Reference Laboratory at Moi Teaching and Referral Hospital (MTRH) in Eldoret, Kenya. Diagnostic testing for BL at MTRH includes morphology of biopsy specimens by hematoxylin & eosin staining only.

Design/Methods: FISH is a molecular cytogenetic tool for identifying recurring translocations in leukemia. In BL, the t(8;14)(q24;q32) is the characteristic cytogenetic translocation involving the juxtaposition of *IGH* to *MYC* on chromosome 14 resulting in *MYC* dysregulation. Probes flanking the *IGH* and *MYC* breakpoints, create a dual color, dual fusion signal pattern in BL cells containing the translocation. Disruption of the *MYC* gene locus is identified/confirmed with a breakapart probe strategy; 5' segment of *MYC* (red) and 3' segment (green) split to yield red, green, and fusion signal patterns in cells with a rearrangement of the gene. We report on a subset of 96 children, 0-13 years, enrolled in a prospective trial to improve the diagnosis and staging of children with suspected BL. Touch prep or smears were stained with Giemsa and reviewed by pathologists. Unstained tissue slides were

processed for FISH. Flow cytometry research results were available on fresh tissue for some subjects.

Results: Nineteen of 20 (95%) specimens yielded FISH results. Of these, 18/19 had both a histological diagnosis and flow results. One specimen had neither. Fifteen of 18 (83%) of FISH results correlated either path or flow; 14/18 (78%) with both and three with neither.

Conclusions: This study supports the feasibility of performing FISH for BL to improve the diagnosis in BL.

V221 SIOP19-0293 | High Dose Methotrexate and Survival Outcomes for Pediatric Mature B-Cell Non-Hodgkin Lymphoma (NHL) in Malawi: A Single Institution Study

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Background/Objectives: Dose-intensive regimens incorporating high dose (HD) methotrexate (Mtx) have been associated with excellent survival for pediatric mature B-cell NHL in high income countries. This contrasts with low-income countries (LICs) where less intensive regimens have been used to treat pediatric NHL with poorer outcomes. The impact of adopting regimens containing *HD-Mtx* (1-3 g/m²) on the survival of pediatric NHL in LICs is not well studied, and there has not been any head to head comparison with *non HD-Mtx* regimens.

Design/Methods: Following IRB approval, we retrospectively reviewed the medical records children (age <16 years) diagnosed with NHL and treated at Kamuzu Central Hospital, Malawi between 2014- 2018. Treatments received were grouped into *HD-Mtx* and *non HD-Mtx* regimens. Patients who received *HD-Mtx* were treated in more recent years. Using Kaplan-Meier curves, Progression-free survival (PFS) was estimated, and a Cox-proportional-logistic-regression model used to test the association between treatment groups and survival.

Results: One hundred and seventy seven children were included in the analysis, with a mean age at diagnosis of 8 years (SD=3.4) and 70% were male. At diagnosis, 63% had advanced disease (Stage III/IV), 33% were Stage I/II, and 4% was unknown. Eighty-four patients (46%) received *HD-Mtx* and 93 (54%) had *non HD-Mtx* regimen. The proportion of patients with advanced disease in each of the groups was not different (p=0.86). Fifty-two patients died (29%) (33% in *HD-Mtx* and 22% in *non HD-Mtx*). Treatment-related mortality (TRM) was higher in the *HD-Mtx* group (20.2% versus 5.3%, p= 0.01). The PFS at 1 year in the *HD-Mtx* group was 55% versus 73% in *non HD-Mtx* (p=0.098).

Conclusions: The survival benefit of *HD-Mtx* regimens for pediatric NHL in LICs may be offset by higher TRM. Adequate support services and monitoring should be established before these intensive regimens are incorporated into therapy in LICs.

V222 SIOP19-0552 | Improved Outcomes for High-Risk Pediatric Burkitt Lymphoma in Malawi with High-Dose Methotrexate: A Prospective Single Center Study

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Background/Objectives: Burkitt lymphoma (BL) is the commonest pediatric cancer in sub-Saharan Africa (SSA), with poor outcomes compared to resource-rich settings. High-dose methotrexate (HD-MTX) is a pillar of effective BL treatment, but reports of HD-MTX based regimens in SSA show marked variability in safety and efficacy.

Design/Methods: We prospectively enrolled children <18 years with pathologically confirmed high-risk BL diagnosed from 2013-2018 at Kamuzu Central Hospital. Before 2016, children were treated with moderate-intensity CHOP. After 2016, children were increasingly treated with high-intensity regimens incorporating HD-MTX at doses 1-3 g/m² as institutional practice shifted. Similar to most SSA centers, real-time monitoring of MTX levels was unavailable. We examined the outcomes of high-risk BL cases, defined as stage III/IV or lactate dehydrogenase (LDH) >2x normal.

Results: Of 170 high-risk cases, 103 (61%) received CHOP, 56 (33%) received HD-MTX, and 11 (6%) died before intensive treatment. Median age was 9 years (IQR 6-12), 104 (61%) were male, 108 (64%) had moderate-severe malnutrition, 157 (92%) had stage III/IV, and median LDH was 900 (IQR 572-1,958). Children received a median of 5 (IQR 2-7) chemotherapy cycles [CHOP 5 (IQR 2-7), HD-MTX 4 (IQR 3-6)]. In February 2019, vital status was known for all but 8 (5%) children. HD-MTX significantly improved 12-month OS (53%, CI 38-66%) compared to CHOP (34%, CI 25-44%, *p*=0.02). Mortality was associated with poor performance (Hazard Ratio (HR) 0.42 CI 0.2-0.7%), age >9 years (HR 1.7, CI 1.1-2.7%), and LDH >900 (HR 2.1, CI 1.3-3.1%),

but not gender or malnutrition. Treatment-related mortality appeared comparable for CHOP 25/103 (24%) and HD-MTX 9/56 (16%), especially given supportive-care improvements over-time.

Conclusions: Chemotherapy regimens incorporating HD-MTX may improve 12-month OS compared to CHOP among children with high-risk BL in Malawi. There is a continued need for controlled, multicenter trials to define best practices in SSA, including optimization of MTX application, to improve outcomes.

Haematology - Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes

V223 SIOP19-1514 | Age-Dependent Differences in Cytogenetic Findings in Pediatric Acute Myeloid Leukemia

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Background/Objectives: BACKGROUND: Acute Myeloid Leukemia (AML) is a heterogeneous disease. Cytogenetic findings at diagnosis provide important information and may be used for classification in 3 distinct prognostic groups (low, intermediate and high risk). The distribution of cytogenetic changes may vary with age.

Design/Methods: METHODS Bone marrow cytogenetic evaluation at diagnosis of all patients with AML treated in a single institution between September 2012 and February 2019 were analyzed. Data were stratified according to age groups: infants and toddlers (under 24 months), children (2-<12 years) and adolescents (12-16 years). The cytogenetic anomalies RUNX1, inv (16), t (16,16), NPM1, and t (15, 17), were classified as favorable, normal karyotype and (9;11), (p22;q23) as intermediate and 11q23/*MLL* aberrations, complex karyotype and FLT3-ITD mutation as unfavorable.

Results: Thirty pediatric patients with AML (24/30 de novo AML, 4/30 Mixed Phenotype Acute Leukemia and 2/30 with secondary AML) were included in the study. Frequencies of cytogenetic subgroups were age-dependent. Favorable cytogenetics were identified in 10/30 (33,3%) in the whole group, but it was significantly lower in the infant/toddler age group [10.0%] compared to older patients [children:50% and

adolescents:40%]. Unfavorable cytogenetics were identified in 14/30 (46.7%) and they were more frequent in infants/toddlers [57.2%] than in children [28.5%] or adolescents [14.3%]. Intermediate cytogenetic anomalies were observed in 6/30 (20%), with no statistically significant differences in between age groups. Five patients with intermediate and four patients with unfavorable prognosis cytogenetic findings died. Overall survival was 70.0%, for a median time 2.6 years (0.04-6.2).

Conclusions: A significant decrease in the proportion of unfavorable cytogenetic subtypes and an increase of favorable cytogenetics was observed with increasing age. The difference in the incidence of specific cytogenetic lesions according to age group implies heterogeneity in the pathogenesis of AML, which needs to be taken into account in designing genetically-driven appropriate personalized therapeutic protocols.

V224 SIOP19-0090 | Treatment and Outcome of Chronic Myeloid Leukemia in Children and Adolescents: The Indian Pediatric Oncology Group (INPOG) CML-16-01 Multicentric Study

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Background/Objectives: The Indian Pediatric Oncology Group was established in 2015 for improving outcomes in childhood cancer through collaborative research. The aim of the study was to describe characteristics of pediatric CML and long-term outcome with imatinib in a multicentric, retrospective study.

Design/Methods: Invitation to participate was mailed to the members of the Hematology-Oncology Chapter of the Indian Academy of Pediatrics. Patients with CML, ≤ 18 years at diagnosis and diagnosed during 2003-2018 were included.

Results: Nine centers across India participated; 171 children/adolescents with CML were reported; 161 were included for analysis. The mean age at diagnosis was 9.7 ± 3.5 years (range: 2.0-18.0); 68% were males. The mean size of the spleen (splenomegaly noted in 96%) was 12.1 ± 5.1 cms below the costal margin. The median haemoglobin, total leukocyte count and the platelet count were 8.8 g/dL (range: 3.7-16.9),

$215.5 \times 10^3/\mu\text{L}$ (range: 14.6-1049) and $365 \times 10^3/\mu\text{L}$ (range: 28-1570). The baseline disease phase was chronic (CP), accelerated (AP) and blast crisis (BC) in 148 (92%), 6 (3.7%) and 7 (4.3%) patients, respectively. The mean dose of imatinib was 311.2 ± 47.8 mg/m²/day (range: 200-500). The source of funding was self-financed (42%), GIPAP (25%) or others (33%). Twenty-two (14%) patients abandoned therapy. CHR (3-months), CCyR (12-months) and MMR (18-months) were attained in 125/140 (89%), 51/55 (93%) and 65/84 (77%) patients, respectively. Two (1.4%) and 14 (9.5%) progressed to AP and BC, respectively.

The OS for the entire cohort was $84.4 \pm 4.3\%$. The progression-free survival (PFS) for patients in CP was $81.1 \pm 4.8\%$ at a median duration of 28-months (range: 1-171). Fifteen patients died (14: BC; 1: pulmonary embolism). One patient underwent HSCT for BC. No major adverse events were reported that necessitated permanent cessation of imatinib.

Conclusions: The PFS of 161 children/adolescents with CML receiving imatinib from 9 centers across India was $81.1 \pm 4.8\%$. Highlights included, male preponderance (68%), treatment abandonment (14%) and scarcity of patients undergoing HSCT.

V225 SIOP19-0325 | Imatinib Induced Hypogammaglobulinemia in Children with Chronic Myeloid Leukemia

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Background/Objectives: Imatinib-induced tyrosine kinase inhibition extends beyond the BCR-ABL mutation, resulting in adverse effects. We evaluated hypogammaglobulinemia as a potential 'off-target' action of imatinib in children with CML.

Design/Methods: A cross-sectional, observational study was performed during 2015-2017. Patients with CML in chronic phase, age < 18 -years at diagnosis, receiving imatinib for a duration exceeding 6-months were enrolled. Serum immunoglobulin G, A, and M were measured by end-point nephelometry (MININEPH, The Binding Site, Birmingham, UK) and compared with age-appropriate references.

Results: Thirty-two patients were screened for eligibility. Two were excluded, one each for poor compliance and evolution to blast crisis. Thirty patients with CML in the chronic phase were enrolled. The mean age at diagnosis was 10.6 ± 3.1 years (range: 5-18). The mean age at enrolment was 16.4 ± 4.1 years (range: 9-23). The median dose of imatinib was 287.5

mg/m² (IQR: 267.3, 345.0). The median duration of imatinib-therapy was 6-years (IQR: 3.0, 10.3). A major molecular remission was recorded in 24/28 (85.7%) patients.

The median level of IgG, IgA, and IgM were 929 mg/dl (IQR: 420, 1184), 45 mg/dl (IQR: 45.2, 260.2) and 71.50 mg/dl (IQR: 37, 105.8), respectively. The IgG level was normal, reduced and elevated in 20 (66.7%), 9 (30%) and 1 (3.3%) patient (s), respectively. The IgA level was normal, reduced and elevated in 20 (66.7%), 8 (26.7%) and 2 (6.7%) patients, respectively. The IgM level was normal, reduced and elevated in 19 (63.3%), 9 (30%) and 2 (6.7%) patients, respectively. Seven (23.3%) patients had pan-hypogammaglobulinemia. Two patients had isolated low IgG; one had isolated low IgM. One had low IgA and IgM. No patient had a major episode of infection.

Conclusions: In a cross-sectional study of thirty children with CML receiving imatinib for a median duration of 6-years, nearly one-fourth had pan-hypogammaglobulinemia. We suggest checking immunoglobulin levels in patients with CML receiving imatinib with recurrent/unusual infections.

V226 SIOP19-0599 | SIOP-PODC Adapted Risk Stratification and Treatment Guidelines: Recommendations for Acute Myeloid Leukemia in Resource-Limited Settings

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Background/Objectives: In low-and-middle-income countries (LMIC), mortality associated with disease and treatment in patients with AML can be upto 50%. Toxic deaths (due to intensive chemotherapy), relapse (due to less intensive protocols) and abandonment are barriers to cure in LMIC. In high-income-countries (HIC), survival rates >70% are being reported, even without the use of allogeneic-SCT in first complete remission (CR).

Design/Methods: Recommendations were developed for adapted management of AML in children/adolescents <18-years. A writing group was established under the auspices of SIOP-PODC committee's Adapted Treatment Regimen Working Group, consisting of hemato-oncologists with experience

in treating AML in LMIC as well as HIC. Recommendations were circulated for peer review and discussed at SIOP-PODC meetings. The guidelines are applicable mainly for level-2 setting. APML and AML in Down syndrome are excluded.

Results: A strategy of low-dose chemotherapy as a bridge to standard protocol is recommended. The pre-phase chemotherapy includes two alternatives. Option 1: PrET: Etoposide, 6-thioguanine (alternative: 6-MP), and prednisolone. Option 2: Single-agent etoposide. Diagnostic CSF is performed following the pre-phase. The standard induction includes two courses: Mitoxantrone or daunorubicin plus cytarabine. An alternative low-dose induction protocol is suggested, being MAG: Mitoxantrone 5 mg/m², once a day on days 1, 3 and 5; Cytarabine 10 mg/m² q12h and G-CSF for 10 days. Alternative to mitoxantrone is daunorubicin/doxorubicin. Consolidation: Course 3 and 4, consists of high-dose cytarabine: 3 g/m² q12h on days 1, 2 and 3; a lower dose (1.5 g/m²) is an alternative. If CR is not attained after course 2 and allo-SCT is unavailable, the patient is considered for palliative care, as cure is not anticipated with chemotherapy alone.

Conclusions: Pediatric AML is potentially curable in the majority of patients with conventional chemotherapy. The aim is that these adapted treatment guidelines will contribute to an improved outcome for children and adolescents with AML in resource-limited settings.

V227 SIOP19-0028 | Is Acute Myeloblastic Leukemia in Children Under Two Years of Age a Specific Entity? A Report from the French ELAM02 Study Group

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Background/Objectives: The clinical and biological characteristics of children under two years (infants) with acute myeloid leukemia (AML) are different from those of older children. We aimed to describe the specific characteristics

of this population and the potential factors that influence the prognosis.

Design/Methods: We analyzed data concerning 438 children with newly-diagnosed AML treated in the ELAM02 protocol between March 2005 and December 2011, of which 103 were under two years old at diagnosis. The evaluation criteria were overall survival (OS) and event-free survival (EFS) of infants *versus* older children. The clinical and biological features were secondary criteria.

Results: Infants presented more frequent extra-medullary presentation than older children. They had a significantly higher proportion of skin lesions and central nervous system involvement (15% *vs* 3%, $P < 0.0001$ and 26% *vs* 12%, $P = 0.0005$, respectively). The global incidence of *KMT2A* rearrangements was nearly 55% for infants *versus* 11% for older children ($P < 0.0001$). Median five-year OS was 70.4% for infants *versus* 71.4% for older children ($P = 0.83$). Five-year EFS was 67% for infants *versus* 58% for older children ($P = 0.27$).

Conclusions: Infants with AML represent a cohort of patients with specific clinical and biological features. These remarkable differences had no significant impact on their outcome in the ELAM02 protocol.

V228 SIOP19-0843 | Early and Severe Central Nervous System (CNS) Complications at Diagnosis in Pediatric Patients with Acute Leukemia

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Background/Objectives: Children diagnosed with acute leukemia have an increased risk of severe neurological complications, mortality and sequelae. Identified risk factors include hyperleukocytosis, thrombocytopenia and coagulopathy. Aim of the study is to analyze the frequency and patterns of early CNS complications in pediatric acute lymphoblastic and myeloblastic leukemia (ALL and AML).

Design/Methods: Descriptive retrospective review of medical records of patients with ALL and AML diagnosed between January-2013 and December-2018. We analyzed clinical, laboratory and radiological data performed at admission and during the first week.

Results: Among 64 patients with ALL, 8 presented with hyperleukocytosis (WBC > 100 x 10⁹/L). Median WBC was 306 x 10⁹/L (110-781 x 10⁹/L). The patient with the highest

WBC level suffered left hemiparesia, anisocoria and somnolence within the first three hours of PICU admission. Neuroimaging confirmed brainstem hemorrhage. Neurological sequelae persisted until his death due to hematological relapse after 7 months in treatment. Thirteen children were diagnosed with AML. One newborn with megakaryoblastic leukemia had severe hypotony, retinal hemorrhages and CNS involvement in neuroimaging (bilateral and diffuse hemorrhagic supra and infratentorial leukoencephalopathy). Necropsy confirmed massive leukemic infiltration in brain. Two patients had promyelocytic leukemia (APL), one with hyperleucocytosis (WBC 121 x 10⁹/L) and coagulopathy (IDC) who suffered acute brain hemorrhage prior to admission and died within hours. Among the other 10 patients with AML, only one 8-month infant had hyperleucocytosis (WBC 288 x 10⁹/L) and coagulopathy (IDC), and presented seizures due to an hemorrhage. Clinical recovery was observed, but he died after BMT.

Conclusions: CNS complications were more frequent in patients with hyperleucocytosis and AML than ALL (2/2 *vs* 1/8). CNS hemorrhages might be the initial presentation of some high risk acute leukemias. Although risk factors are identified, the prophylactic measures available nowadays are insufficient. Early CNS complications impact on the initial clinical approach in severe cases and increase early mortality worsening the prognosis.

V229 SIOP19-1199 | Outcome of Hematopoietic Stem Cell Transplant in Pediatric Acute Myeloid Leukemia in a Middle-Income Country

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Background/Objectives: Acute myeloid leukemia (AML) is an hematological disease with poor outcome in developing countries, depending of the classification patients will need a hematopoietic stem cell transplant (HSCT). Identify Overall Survival (OS) and their correlation with risk factors as well as description of the common causes of mortality.

Design/Methods: Retrospective descriptive study that included 103 patients <18 years old with AML diagnosis of which 43 patients received a stem cell transplant in the National Institute of Pediatrics in Mexico in the period from January 2008 till December 2016. Risk factors included age at diagnosis, gender, FAB classification, type of stem cell transplant, graft failure and complications.

Results: Forty-three transplants (22 females and 21 males). 62% source of stem cells was peripheral blood (n=27) and

13.9% umbilical cord (N = 6). 33% of the patients present Graft failure (n=14). Forty-three transplants were performed of which 12 were haploidentical, 7 umbilical cord and 24 related donor. OS in patients with chronic Graft-Versus-Host-Disease (cGVHD) was 78.6% compared to those who did not 82.8% (p=0.827). In patients with GVHD the OS was 85.7% compared to those who did not 79.3% (p=0.382). Fourteen patients (32.5%) presented aGVHD with skin involvement in the majority of cases. OS was determined according to the type of transplant being allogeneic transplant of unrelated donor 57.1%, allogeneic donor related 91.7% and haploidentical donor related 75% (p=0.86). OS in transplant patients was 81% and not transplanted 61.7% (p=0.162). Causes of death were respiratory distress syndrome 37.5%, bacterial infection 25%, viral 12.5% and active disease 12.5%.

Conclusions: OS reported in our study is higher than reported in the international literature, however there is not a sufficient factor to mark this difference. OS according to the type of transplant were found to have a tendency to significance (p=0.086), possibly due to the small number of patients.

V230 SIOP19-0649 | Menin Regulates Long-Term Maintenance of MN1 High Leukemia

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Background/Objectives: Meningioma-1 (MN1) is rearranged in a subset of acute myeloid leukemias (AML) and high expression levels are associated with poor prognosis. In the mouse, MN1 AML harbors a distinctive transcription program characterized by high HoxA cluster and Meis1 expression, reminiscent of KMT2A-rearranged (KMT2Ar) leukemia. However, exactly how MN1 exerts its oncogenic functions remains unclear, limiting the development of targeted therapies. We have previously shown that deletion of *Kmt2a* delayed onset and decreased penetrance of MN1 driven leukemia. Since the interaction of KMT2A with Menin has been found to be critical for KMT2A-r leukemias, we investigated the role of Menin in MN1 high leukemia.

Design/Methods: Using a conditional knock-out mice, we established MN1 leukemia on a *Menin* f/f background. *Menin* was deleted using Cre recombinase and cells were injected into irradiated C57B/6 recipients. To investigate the consequences of *Menin* deletion on gene expression, we performed RNA sequencing.

Results: In primary transplants, we observed selective pressure against full loss of *Menin*, as half of the animals in the

Menin f/f group had failed to properly rearrange both alleles. However, this did not translate into a survival advantage. The effect of *Menin* deletion became dramatic in secondary transplants. Secondary recipients of *Menin* -/- leukemias completely failed to develop leukemia while control animals showed a mean survival of 29 days (p<0.0001). *In vitro*, replating efficiency was severely impaired with increased apoptosis and cell cycle arrest. RNA-seq analysis revealed specific downregulation of the MN1 gene expression program. Additionally, we found downregulation of immature markers (CD34, c-kit) associated with upregulation of differentiation markers.

Conclusions: Our data suggest that Menin is necessary for the long-term maintenance of MN1 leukemia. As pharmacologic inhibitors of the Menin-KMT2A interaction are currently in pre-clinical development, combination with cytotoxic therapies could constitute a promising therapeutic approach in this high-risk AML.

V231 SIOP19-0573 | Hemophagocytic Lymphohistiocytosis Secondary to Visceral Leishmaniasis in Children: Report of Two Cases in One Center in Beirut and Review of Literature

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Background/Objectives: Hemophagocytic Lymphohistiocytosis (HLH) is a potentially fatal disorder due to cytokine dysfunction, resulting in uncontrolled accumulation of activated histiocytes/macrophages and T-lymphocytes in many organs. Visceral leishmaniasis (VL) is a neglected parasitic disease that can, in rare cases, be complicated by HLH. However, because many clinical and laboratory features of VL and HLH overlap, diagnosing leishmaniasis as the inciting etiology of this syndrome can be quite challenging.

Design/Methods: Lebanon is considered to be Leishmania-free. However, it is endemic in Syria, and since the start of the Syrian crisis in 2011, many cases of Syrian refugees were diagnosed with leishmania in Lebanon. We report two cases of children (1 Lebanese and 1 Syrian) affected by hemophagocytic lymphohistiocytosis secondary to visceral leishmaniasis.

Results: The Syrian child was diagnosed with VL using PCR for Leishmania on bone marrow blood. The patient had seven

of the eight criteria of HLH, Unfortunately he died later on during the 3rd week of induction chemotherapy (Protocol HLH 2004).

The Lebanese child is originating from a village close to the Syrian border where there are many Syrian refugee camps. He was diagnosed with HLH (seven of eight criteria were positive on him to diagnose HLH), PCR for Leishmania was positive on Bone Marrow, he responded to chemotherapy according to the HLH 2004 protocol, but had many relapses/flair ups. He is now alive on symptomatic treatment because no donor for bone marrow transplantation could be found. To note that both children were on Liposomal Amphotericin B treatment during all the induction course of chemotherapy upon the protocol for Leishmania treatment.

Conclusions: VL should be considered in patients with HLH and coming from endemic areas for Leishmania to minimize potentially harmful investigations and immunosuppressive treatments. Liposomal Amphotericin B should be started rapidly with the HLH protocol when VL is suspected

V232 SIOP19-1568 | Effects of Arsenic Trioxide and ALL-Trans Retinoic Acid on the Resistance of Sorafenib in FLT3-ITD Leukemia

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Background/Objectives: Previous studies have shown that sorafenib, an tyrosinase inhibitor which has a prominent but shortlived remission in FLT3-ITD leukemia patients, synergizes with all-trans retinoic acid (ATRA) or arsenic trioxide (ATO) to eliminate FLT3-ITD leukemia cells. However, it is unclear whether ATO or ATRA can delay the resistance of sorafenib in FLT3-ITD leukemia cells. In this study, high-dose ATO, ATRA or sorafenib were used to induce drug resistant cell lines, and the effects of combination drugs on cell resistance were investigated.

Design/Methods: The FLT3-ITD leukemia cell line MV4;11 was treated by high-dose chemotherapeutic drugs. The treatment groups was divided into group A (sorafenib alone), group B (sorafenib combined with ATO), group C (sorafenib combined with ATRA), group D (sorafenib combined with ATO and ATRA), the therapeutic concentrations of sorafenib, ATO, and ATRA were 10 nmol, 1.5 μ mol, and 2 μ mol, respectively. After 34 days of induction, the resistance index was analyzed by MTS assay. The apoptosis and cell cycle after treatment of sorafenib (10nmol) were detected by flow cytometry.

Results: After induction of MV4;11 cells by high-dose drugs, the resistance index of group A to sorafenib was 7.16, group B, C and D was 5.96, 274.13, 188.19, respectively. Quantitative assessment of apoptosis by Annexin V/PI staining showed

that after treatment with 10 nmol of sorafenib, 40% apoptosis occurred in control group cells. The apoptosis rates of group A and B cells are 25-28%, and almost no apoptosis occurred in group C and D cells. PI staining-based cell cycle analysis showed that the cell cycle of group A and B cells were arrested at G1 Phase, which had little effect on cell cycle in group C and D cells.

Conclusions: Treatment of FLT3-ITD leukemia cells with sorafenib in combination with ATRA will accelerate resistance to sorafenib, and ATO has no effect on the development of sorafenib resistance.

V233 SIOP19-1281 | CONECT-AML (Collaborative Network on Research for Children and Teenagers with Acute Myeloid Leukemia) "Together, We Are Stronger": Evaluation After One Year

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Background/Objectives: Pediatric AML still remains a challenging disease, requiring progress to reduce the risk of relapse, improve survival and reduce long-term sequelae. To accelerate this process, clinicians, researchers, associations and parents need to work together.

Design/Methods: CONECT-AML was funded through a grant from the French Institute for Cancer and two charities (INCa-ARC-Ligue_11905). It coordinates 10 research teams, questioning both biological issues, follow-up of sequelae, ethics or information to parents and patients. This project is ancillary to the international prospective MyeChild01 Phase III trial (NCT02724163), opened in 21 French clinical departments. Clinical and biological data are reviewed centrally during a bi-monthly meeting, leading to a report sent to the investigator. A public health information website (www.conect-aml.eu) was opened in December 2018. An ethics think tank was created to question ethical challenges associated with this research.

Results: After one year, 55 leukemic samples were collected. Among them, 27 came from French patients enrolled (n=30) in MyeChild01. Twenty-five were used for PDX modeling in NSG-W41 or NSG mice, allowing engraftment of 5 samples out of the 14 evaluable ≥ 4 months post-transplantation. Drug testing from primary leukemic cells was done for 23 patients. Targeted NGS profiling was done for all patients. Since November, teleconference meetings allowed to discuss 26 patients. Each patient case was discussed on average 2.85 times. The information website on pediatric AML, opened in December 1st, received 10 000 visits (average of 3 pages per visit). Regarding ethics, a survey for clinicians is planned for June 2019.

Conclusions: CONECT AML is an original project, combining clinical research, basic research, ethics, popularization of science for patients and families with the support and involvement of charities. Attached to MyeChild01 protocol, it facilitates multiparametric study of leukemic samples and has led to an effective return to clinicians. Integration at the European level would definitively strengthen the network.

V234 SIOP19-1691 | LSC17 Genes Score Versus Leukemic Stem Cell (LSC) Quantification by Multiparameter Flow Cytometry (MFC) to Design Stemness Signature in Pediatric AML from ELAM02

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Background/Objectives: AML is a clonal disorder of hematopoietic stem cells characterized by arrest of differentiation and subsequent accumulation of blast cells. Here we present how to combine FLOWSom and KALUZA software to obtain robust identification among tumoral and normal progenitors. We compared the flowLSC Profile with stemness 17 genes score to identify patients with adverse outcome.

Design/Methods: 54 pediatric AML patients were treated in Lyon clinical center (IHOP) between 2008 and 2016 according to the ELAM02 clinical trial. Among them 40 children (aged 0,3-19 years) undergoing HSCT based on the following criteria: high-risk AML in CR1 (29/40) and 11/40 in CR2. The Kaplan-Meier methods was used for survival or probability estimates. The log-Rank test was used for comparison between groups. The quantification of CD34+CD38- fraction at diagnosis from total bulk leukemia was made as previously described.

Results: Between 44 AML patients we observed a strong correlation identifying patients with adverse prognostic using previously published threshold by Flow ($> 1\%$ CD34+CD38- from bulk leukemia cells). 25 from 44 patients showed a concordance between GES 17 LSC and Flow CD34+CD38-. Two kind of discrepancies were observed: first, 8 patients was classified as "high" by Flow and "low" by GES LSC 17 and secondly, 11 patients were classified inversely as "low" by Flow and "high" by GES LSC 17 scoring. From the first case, was mainly cbf-AML and the secondly case were mainly CD34-AML patients.

Conclusions: In summary, our preliminary data tend to show the relevance to establish a scoring system including the level of FlowLSC at diagnosis and GES LSC 17 to distinguish patients with high risk in patients with high CD34+ expression. The previous analysis of the ELAM02 trial data demonstrates the utility of the LSC17 score as a tool for patient selection. These results should be confirmed in a prospectively larger cohort of patients.

V235 SIOP19-0693 | Clinical Profile and Outcome of Acute Promyelocytic Leukemia in Children: A Single Centre Experience

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Background/Objectives: Acute promyelocytic leukemia (APML), is a distinct subtype of acute myeloid leukemia (AML) characterized by a tendency to bleed and respond very well to differentiating agents. We studied the baseline characteristics, toxicities and outcome of children with APML at a tertiary cancer Institute in India.

Design/Methods: Patients diagnosed with APML from January-2013 through December-2017 were included. All were treated uniformly on an institutional-APML protocol consisting of Arsenic Trioxide (ATO) and PrET (prednisolone, oral 6-Thioguanine and Etoposide) during induction, All-trans Retinoic Acid (ATRA) and Daunomycin (cumulative dose:405mg/m²) during consolidation, and 8-cycles of maintenance therapy-4 with ATO+ET, and 4 with ATRA alone. Total duration of therapy was 22 months. Data was subjected to descriptive and survival analysis.

Results: Of 71 evaluable patients, 36 (50.7%) had low/Intermediate risk and 35 (49.3%) had high-risk (HR) disease. The rate of morphological, cytogenetic and molecular complete remission (CR) at the end of induction (Day-60) was 95.1%, 83.9% and 27.9% respectively and at the end of consolidation (Day-120) was 100%, 99% and

97% respectively. Mean time to remission amongst HR and non-HR patients was not significantly different (111 ± 5 vs 98 ± 8 days, $p=0.16$). Differentiation syndrome (DS), and life-threatening bleed and mortality were seen in 12 (16.9%), and 10 (14%). Deaths occurred in 5 (7%) patients, of which 4 were within 7 of presentation. All patients with mortality had life threatening bleed, while 1 had additional DS. The 3-year EFS and OS were $83.7 \pm 4.8\%$ and $88.4 \pm 4.3\%$ respectively. 3-year OS for HR patients was not significantly different from non-HR ($82.6 \pm 7.4\%$ vs $87.8 \pm 7.1\%$, $p=0.41$). Only life-threatening bleeding (HR:21.9; $p<0.01$) but not WBC $>10 \times 10^3/\mu\text{L}$ ($p=0.43$), platelets $<40 \times 10^3/\mu\text{L}$ ($p=0.62$) or fibrinogen $<200\text{g/L}$ ($p=0.29$) was associated with increased risk of mortality.

Conclusions: Children with APML at our center had excellent outcomes, though early mortality due to bleeding remains a challenge. The difference in outcome between HR and non-HR patients was negated probably due to a uniform treatment strategy in both groups.

V236 SIOP19-0364 | Outcome of FLT3 Gene Mutation in Children with Acute Myeloid Leukemia in CCHE Hospital

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Background/Objectives: The presence of FLT 3 –ITD mutation in pediatric AML is associated with high rates of induction failure, worse survival and consider as high risk group. The aim of the work is to evaluate pediatric AML patients with mutant FLT3 treated at Children Cancer Hospital Egypt (CCHE) during 10 years period.

Design/Methods: It is a retrospective study to evaluate pediatric AML with mutant FLT3 from July 2007 till July 2017 at CCHE.

Results: The result showed that, 71 patients (10.33%) had FLT3 gene mutation out of 687 patients with AML. Sixty five patients (91.6%) had FLT3 gene mutation with allelic ratio >0.4 , 43 patients (66.1%) achieved CR, and 22 patients (33.8%) were refractory and/or died in induction I. BMT was done for 9 patients (13.8%) in 1st CR, 8 of them are alive in CR, and 1 patient (1.5%) relapsed and died. seven patients (10.7%) are alive in CR without BMT. Eight patients (12.3%) died, and 1 patient (1.5%) lost FU, 18 patients (27.6%)

relapsed soon after 1stCR, 1 patient (1.5%) is in 2nd CR and alive. The rest of relapsed patients (23%) received salvage chemotherapy and died. Three years OS and EFS for the patients with FLT3 gene mutation with allelic ratio >0.4 are 26.9%-22.8% respectively. Three years OS and EFS for patient treated with BMT were 77.8%-78.8% respectively versus patients were treated and achieve CR without BMT which were 16.3%-12.8% respectively.

Conclusions: In conclusion, FLT 3 –ITD mutation in pediatric AML is associated higher rates of induction failure, survival of relapsing patients is extremely poor, and BMT in first remission if possible is the best option, otherwise significantly worse OS and EFS. Trial of the FLT3 inhibitor sorafenib is mandatory to improve outcomes for this subset of patients.

V237 SIOP19-0549 | The Poor Prognosis of Pediatric AML-MDS Related Change and its Genetic Background – A JPLSG AML05 Study

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Background/Objectives: The definition between advanced myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML) has been changed from French-American-British (FAB) to World Health Organization (WHO) classification. The correlation of advanced MDS/AML remains obscure in pediatric populations. AML with multilineage dysplasia (MLD) and AML with MDS related change (AML-MRC) was defined by WHO classification, it included AML-MRC with morphological features (AML-MRC^{Mo}) or cytogenetic abnormalities (AML-MRC^{Cy}). Our previous report suggested the poorer prognosis of pediatric AML-MRC, however, its genetic background still remains obscure.

Design/Methods: Total 369 patients in AML05 study of Japanese Pediatric Leukemia & Lymphoma Study Group (JPLSG) were genetically analyzed included *NRAS*, *KRAS*, *FLT3*, *KIT*, *WT1*, *CEBPA*, *ASXL1*, *ASXL2*, *RUNX1*, *MLL*, *NPM1*, *MEL* and *EVII*. All patient's morphological features and karyotype were confirmed by central laboratory and defined by FAB and WHO classification.

Results: We found 34 (9.2%) RAEBT, 31 (8.4%) AML-MLD and 74 (20.1%) AML-MRC patients [27 AML-MRC^{Mo} and 47 AML-MRC^{Cy}]. Majority of AML-MLD were categorized into AML-MRC^{Mo}. AML-MRC showed the lower complete remission rate (67.6%) and high relapse rate (43.2%).

Although, 67.2% of AML-MRC patients received hematopoietic stem cell transplantation (HSCT) [12 at 1stCR, 17 at 2ndCR], the survival rate was quite different (58.3% vs. 17.6%). By karyotypic analysis, more than half (51.4%) of the AML-MRC had the complex karyotype. By genetic analysis, *CEBPA* (14.9%), *FLT3*-ITD (13.5%), and *NRAS* (13.5%) genes were highly mutated in AML-MRC. Interestingly, high expression of *MEL* or *EVII* were observed in AML-MRC. To compare AML-MRCMo and AML-MRCCy, *FLT3*-ITD, *MLL*-PTD, *NRAS*, *RUNX1*, and *NPM1* were highly mutated in AML-MRCMo. AML-MRCCy contained 19 M7, and the survival rate of AML-MRCCy without FAB-M7 was poor (42.9%).

Conclusions: Our result suggested that AML-MRC showed the poorer prognosis, therefore HSCT at 1st CR will be recommended in future study. Furthermore, we should pay attention to the FAB-M7 in AML-MRCCy, especially in pediatric population.

V238 SIOP19-1092 | Assessing Longitudinal Changes in Body Mass Index, Height, and Weight During and After Therapy in Children with Acute Myeloid Leukemia

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Background/Objectives: It is unclear how treatment of acute myeloid leukemia (AML) affects height, weight, and body mass index (BMI).

Design/Methods: Longitudinal changes in Z-scores for height, weight, and BMI from the time of diagnosis to 5 years off-therapy were evaluated in 227 children and adolescents (0 to 21 years at diagnosis) with AML who were enrolled on the St. Jude Children's Research Hospital AML02 and AML08 protocols from 2002 through 2017. Patients who experienced relapse, transplant, or death were censored.

Results: The median BMI Z-score at diagnosis (0.170) did not change significantly during therapy (0.064 at the end of consolidation II, $P=0.652$) but increased significantly during the off-therapy period (0.804 at 2 years off therapy, $P<0.001$). The median weight Z-score decreased after the first course of induction (-0.102 , $P=0.085$) and differed significantly from that at diagnosis (0.193) by the end of consolidation II (-0.195 , $P=0.035$). After completion of therapy, median weight Z-scores increased (0.584 at 2 years off therapy, $P=0.009$). Median height Z-scores declined during therapy (from 0.209 at diagnosis to -0.110 at the end of consolidation II, $P=0.022$) and did not recover to the level at diagnosis during off-therapy period (-0.032 at 2 years off-therapy, $P=0.060$). Being ≥ 10 years of age at diagnosis was associated with having signifi-

cantly higher median BMI and weight Z-scores than those of patients <10 years.

Conclusions: During AML treatment, both weight and height Z-scores decrease without significant changes in BMI Z-scores. However, after completion of chemotherapy, weight Z-scores increase substantially, leading to high BMI Z-scores. Therefore, close monitoring of weight and height changes is important with nutritional support during therapy. For post-therapy weight gain, it is also necessary to continue providing multidisciplinary supports for healthy lifestyles, with appropriate diet and physical activities.

V239 SIOP19-1164 | Infection-Related Mortality in Childhood Acute Myeloid Leukemia in Limited Resources Setting: Experience with the Indonesian National Protocol

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Background/Objectives: Infection is still a major problem in the management of children with Acute Myeloid Leukemia (AML). Infection-related Mortality (IRM) is a major determinant of non-disease related mortality in pediatric AML. The IRM in Indonesia is considered high compared to high-income countries. Studies and documentation of IRM are still very few in low and middle-income countries. The objective of this study is to describe the characteristics and time of occurrence of IRM in children with AML treated according to the Indonesian National AML protocol.

Design/Methods: Medical records of 113 patients with AML from April 2012 – September 2018 treated at the Dr. Sardjito Hospital (Yogyakarta, Indonesia) according to the National Protocol were reviewed. Basic patient characteristics, time of IRM, and cause of death were recorded.

Results: There were 113 patients treated with National protocol, 95 meet the inclusion criteria. Out of 95 patients, 81 (85%) suffered from infection with total episodes of 144 times (mean 1.78x/patient). Death was seen in 60 (63%), with 31 (52%) IRM. Nearly half (45%) of all IRM occurred during induction. Sixty-two patients had neutropenic fever. The majority of infections was in the gastrointestinal tract 57 (40%), sepsis 36 (25%), and respiratory tract 33 (23%). Infection mostly occurred in the first induction 50 (35%) episode. There were 109 (76%) episodes of clinically documented infection, and 35 (24%) episodes of microbiologically documented infection. Culture was done in 85 episodes, and positivity of blood cultures was 16 (27%) samples. The majority of

bacteria detected was gram-negative 26 (74%), among them was *K. pneumonia* 8 (23%) and *E. coli* 7 (20%). *C. albicans* was 1 (3%).

Conclusions: Infections in children with AML in our center was the main cause of death. Infections during treatment mostly occurred in induction. The most common causative agent was gram negative. Further research into infection prophylaxis seems of utmost importance to improve the outcome for children with AML in resource limited settings

V240 SIOP19-1128 | Modeling Infant AML Using Human Pluripotent Stem Cells

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Background/Objectives: Infant leukemia (IL) is an aggressive cancer that develops *in utero* with very little somatic mutation. *KMT2A(MLL)*-fusions are present in 75% of cases, but fail to phenocopy IL in model systems. We previously demonstrated patients with IL possess a significant enrichment of rare, non-synonymous germline variants in histone modifying genes. We hypothesize these germline variants skew hematopoietic differentiation, which, in the presence of a somatic *KMT2A*-fusion, leads to leukemic transformation. To elucidate their contribution in fetal hematopoiesis and IL development, we have established patient-specific human induced pluripotent stem cell (hiPSC) models, transfected with a *KMT2A-MLLT3* transgene.

Design/Methods: Approved human embryonic stem cells (H1) were differentiated into primitive and definitive hematopoietic ontogeny according to the gold standard method developed by our collaborator, Christopher Sturgeon, PhD (Sturgeon et al. *Nature Biotech* 2014). Primitive CD34+CD43+ and CD34-CD43+ and definitive CD34+CD45+ and CD34-CD45+ progenitors were independently selected by flow cytometry at day 9 and 15 of *in vitro* differentiation, respectively. Selected populations were then transfected with retrovirus expressing *KMT2A-MLLT3* and, after 8 days of expansion, were plated into colony forming assays.

Results: Because little is known about the impact of *KMT2A*-fusions on primitive hematopoiesis, we first sought to establish the baseline role of *KMT2A-MLLT3* expression in H1 during *in vitro* differentiation. We found *KMT2A-MLLT3* expression in primitive CD43+ progenitors resulted in diminished erythroid precursors (CFU-E) in parallel with a commensurate expansion of granulocyte and monocyte progen-

itors (CFU-M and CFU-GM). We noted a similar result in CD34+CD43+ definitive progenitors.

Conclusions: In H1, *KMT2A-MLLT3* expression promotes granulocyte and monocyte differentiation at the expense of erythrocyte differentiation during *in vitro* differentiation. We expect to observe synergy between rare, non-synonymous germline variations and the *KMT2A-MLLT3* fusion in patients-specific hiPSC model. Such results would enable *in vivo* xenografts as pre-clinical models for novel therapeutic studies.

V241 SIOP19-1670 | Risk-Stratified Treatment for AML in Indian Children

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Background/Objectives: Outcome of AML in Indian children remains poor, partly due to high treatment-related mortality. In this observational study, we aim to learn if we can improve outcome by a cytogenetic-risk based therapy—offering allogeneic hematopoietic stem cell transplantation (SCT) to high-risk patients.

Design/Methods: Of the 105 AML patients seen over 10 years, we excluded 7 patients (APL, 6; refused treatment-1) and analyzed the outcome of 98 consecutively treated children. M:F, 49:49. The first 41 patients (group A) were treated without risk stratification on a modified MRC-10 protocol, followed by 3 months of metronomic maintenance therapy (with 6-thioguanine and etoposide), and without SCT. The next 57 patients (group B) were treated on a less intensive 7 & 3 induction, and three cycles of consolidation with high-dose cytarabine for good risk patients; and SCT for high-risk patients with a suitable donor.

Results: Overall, 46 of 98 patients (46.9%) are alive with a median follow-up of 35 months (range 2 to 100). The 3-year estimated survival rate (by Kaplan Meir analysis) was not statistically different between the two groups: 37% and 40% for group A and B respectively. Remission death rate was higher for group A. (20.7% vs 6.25%, $p=0.05$). There were no significant differences between the two groups in remission rate, induction mortality, and relapse rates. But for the 40 high-risk patients in group B, the overall survival rate was significantly better for those who had SCT: 13 of 16 (81.2%) with a median follow-up of 18 months (range, 8 to 53), compared to 8 of 24 (33.3%) for those who did not get SCT ($p=.009$).

Conclusions: MRC-10 regimen is associated with high treatment-related mortality in Indian children, and metronomic maintenance therapy does decrease the risk of relapse.

For cytogenetically stratified high-risk patients allogeneic stem cell transplant offers a higher chance of overall survival.

Haematology - Stem Cell Transplantation

V242 SIOP19-1161 | Outcome Predictors of Autologous Hematopoietic Stem Cell Transplantation in Children with Relapsed and Refractory Hodgkin Lymphoma: Single Center Experience in a Low Middle Income Country

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Background/Objectives: Children and adolescents with Hodgkin lymphoma (HL) have excellent long-term survival exceeding 95% after combined modality treatment. However, about 20% will either relapse or have primary refractory disease. Salvage high-dose chemotherapy followed by autologous hematopoietic stem cell transplant (AHSCT) is considered to be the preferential treatment. The aim is to describe the outcome (overall survival [OS] and event free survival [EFS]) and prognostic factors in pediatric patients with relapsed or refractory HL (r/rHL) who underwent AHSCT.

Design/Methods: We retrospectively included 43 pediatric patients with r/rHL who underwent AHSCT from 1st of July, 2007 till 31st of December, 2016 at the Children's Cancer Hospital of Egypt. Myeloablative conditioning (MAC) regimen given was CMV (Cyclophosphamide, Melphalan and Etoposide). Stem cells were obtained from peripheral blood in all patients using G-CSF.

Results: The median age at transplantation was 12 years. Time to 1st relapse ranged from 0 – 72 months with a mean of 18.5 months. Of the whole cohort, 88.4% of patients achieved CR, while 11.6% had a positive PET scan prior to transplantation. The 3-year OS and EFS were 85% and 70.6%, respectively. The 3-yr OS for patients >10 years was 94% versus 65.5% for patients 10 years of age or younger ($P=0.046$). Patients who received multimodality therapy before AHSCT had better 3-yr EFS than those who received chemotherapy only; 91.7% versus 62.9%, respectively ($P=0.116$). There is strong tendency towards better 3-yr OS for patients with negative PET scan as compared to those with positive PET scan before AHSCT; 89.4% versus 60%, respectively ($P=0.059$). This tendency is also applicable when looking at the 3-yr

EFS for the two groups; 78.3% versus 40%, respectively ($P=0.069$).

Conclusions: Poor predictors of OS were younger age and positive PET scan before AHSCT. The later, along with single modality treatment before AHSCT, were poor predictors of EFS.

V243 SIOP19-0764 | A Real-Time System to Optimize Discharge and Transfer of Patients Care From a Saudi Tertiary Care Referral Center – A Performance Improvement Approach

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Background/Objectives: Pediatric Non-Malignant Blood Disorders (NMBDs) section of King Faisal Specialist Hospital & Research Centre, Riyadh is a referral center for patients ≤ 14 years of age with hemostatic disorders, hemoglobinopathies & bone marrow failures. Sub-specialized transfers to treating institutions could be challenging but known to have impact on operational metrics.

Design/Methods: Performance Improvement (PI) project initiated as part of the institutional “All Commit to Improve-2018” initiative with an aim of increasing discharge / transfer of patients from service by 60% (120 in 2017 to 192 patients in 2018).

Results: Discharge and Transfer criteria developed that included patients with unmatched donors, >14 years of age, supportive services available at referral center; were cataloged into “>14 years of age” or “Tertiary care services – Not required” lists. An automated web-based dashboard utilizing REDCap software (Vanderbilt University) enabled weekly real-time tracking by the Clinical Nurse coordinator for transition of care arrangements with disease specific comprehensive management plans. An increase by 349% (120 to 539) in transfer / discharge of patients from the clinical service, increase in new cases by 4% and transplants for NMBDs by 8%, respectively observed during the year 2018.

Conclusions: In our experience, project had an impact on the following quality dimensions of care delivery: Safety through comprehensive management plans, Timelines as transfers / discharges were scheduled and Effectiveness characterized by increase in streamlined transition of care, further analysis to ascertain cost-effectiveness including but not limited to patient logistics is underway. System enabled virtual tracking and “no-donor” patients list resulted in alternate donor search, in addition to effective outpatient utilization. The project's design, innovation and outcome (s) was awarded the “Annual PI Award -2018 (2nd Place)” and similar

methodology / system is being applied to achieve Transition of care of oncology and post-stem cell transplantation patients through health outreach programs.

V244 SIOP19-0768 | Extracorporeal Photochemotherapy for Paediatric Patients with Graft-Versus-Host Disease After Haematopoietic Stem-Cell Transplantation: Experience of a French Center

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Background/Objectives: Graft-versus-host disease (GVHD) represents the first cause of morbidity and mortality after allogeneic stem-cell transplantation (HSCT) in children. Currently, for both acute and chronic GVHD, recommendations exist for initial treatment but subsequent therapeutic lines are not well defined in case of refractory or persistent GVHD. From the 1990s, extracorporeal photochemotherapy (ECP) started to be used in GVHD treatment as an interesting alternative by its immunomodulating action. One of the challenges in pediatric patients is the management of side effects in low-weight children. The aim of this work was to report the experience of our center on ECP treatment, to assess the effectiveness and try to identify predictive factors of response to this treatment.

Design/Methods: This monocentric and retrospective study enrolled 42 patients with acute or chronic GVHD after HSCT, treated by ECP because of corticoreistant, corticoddependent or refractory GVHD, from 2010 to 2017, in Robert Debré Hospital (France). Response evaluation was first assessed after 4 to 6 weeks of treatment, and then at cessation of ECP.

Results: More than 1,190 sessions were performed, and more than 80% of children showed an improvement of their GVHD symptoms thanks to ECP, especially in case of acute GVHD and/or skin involvement. However, long-term outcome showed only 54% of persistent complete remission at cessation of ECP. Low-grade GVHD, short time from GVHD onset to ECP starting and “early” response after 4 to 6 weeks of treatment seemed to be predictive factors for long-term response to ECP, in both acute and chronic GVHD. During ECP treatment, no major intolerance appeared, even in low-weight children (median weight of 32.5kg [11-90]). Complications of ECP were dominated by bacterial infections.

Conclusions: ECP appears as an interesting therapeutic alternative in children GVHD treatment after HSCT, especially in acute GVHD and skin involvement, and its early start seems correlated to a better effectiveness.

V245 SIOP19-0041 | Assessment of Chimerism and Immunomodulation to Prevent Post-Transplantation Relapse in Childhood Acute Myeloblastic Leukemia: Is It The Right Approach ?

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Background/Objectives: Relapse of acute myeloblastic leukemia (AML) after first allogeneic hematopoietic stem-cell transplantation (allo-HSCT) is a fatal complication.

Design/Methods: Sixty-five children transplanted for AML were included in a prospective national study from June 2005 to July 2008 to explore the feasibility of preemptive immune modulation based on the monitoring of blood chimerism. Chimerism monitoring was performed either by PCR testing for informative minisatellite regions or Taqman-based quantitative PCR. Prompt discontinuation of cyclosporin and the administration of donor lymphocyte infusions (DLIs) were planned in case of increased mixed chimerism.

Results: Sixty-five children transplanted for AML were included in a prospective national study from June 2005 to July 2008 to explore the feasibility of preemptive immune modulation based on the monitoring of blood chimerism. Chimerism monitoring was performed either by PCR testing for informative minisatellite regions or Taqman-based quantitative PCR. Prompt discontinuation of cyclosporin and the administration of donor lymphocyte infusions (DLIs) were planned in case of increased mixed chimerism.

Conclusions: Monitoring the kinetics of chimerism failed as a preemptive tool, either for detecting relapse or certifying long-term remission. Shortening the duration of cyclosporin treatment after allo-HSCT did not influence the risk of relapse. The early detection of relapse by monitoring MRD levels is probably more effective and the use of DLI in current clinical practice should be replaced by new drugs or CART cell targeting myeloid blasts.

V246 SIOP19-1002 | Favorable Evolution of Blastic Plasmacytoid Dendritic Cell Neoplasm after Hematopoietic Stem Cell Transplantation

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Background/Objectives: Blastic dendritic plasmacytoid cell neoplasm are exceptional pediatric cancers with very compromised prognosis due to the lack of therapeutic consensus and uncertain answer to the treatment.

Design/Methods: We report 2 cases of patients treated in the pediatric hematology unit of the Lille University Hospital Center (France). First patient had a had a tumefaction evolving since 6 months at the level of the calf. It was a blastic dendritic plasmacytoid cell tumor initially of the calf and secondarily pleural. The second patient had inguinal lymph nodes that appeared 5 months before the diagnosis of a blastic dendritic plasmacytoid cell neoplasm with leukemic component.

Results: The first patient received a very high risk (VHR) induction with vincristine, cyclophosphamide, asparaginase, prednisone and daunorubicine and then intensified consolidation with cyclophosphamide, cytarabine, mercaptopurine, vincristine, high dose methotrexate and asparaginase. But with a pleural evolution within 3 weeks that followed, the resumption of a treatment was done with bendamustine, bortezomib and dexamethasone followed by the hematopoietic stem cell transplant 4 months after the initial diagnosis. The second patient received VHR induction then consolidation with hematopoietic stem cell transplant 3 months after diagnosis. For both patients, complete remission was obtained sustainably after the graft with a very satisfactory evaluation at 1 year post transplant.

Conclusions: Intensive treatment towards high risk seems to be satisfactory in order to obtain a complete remission of blastic dendritic plasmacytoid neoplasm. However, this can only be sustainably maintained by combining the initial treatment with a hematopoietic stem cell transplant.

V247 SIOP19-0173 | Therapeutic Impact and Complications Associated with Surgical Lung Biopsy After Allogeneic Hematopoietic Stem Cell Transplantation in Children

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Background/Objectives: Hematopoietic stem cell transplantation (HSCT) in the pediatric population is associated with pulmonary complications in 25% of recipients. The role of surgical lung biopsy (SLB) remains unclear due to concerns about both the therapeutic impact and the morbidity associated with the procedure. We sought to delineate the risks and benefits of SLB in this vulnerable and complicated group of patients.

Design/Methods: A retrospective review of consecutive pediatric HSCT recipients at Dana-Farber and Boston Children's Hospital Cancer and Blood Disorders Center between 2006 and 2016 was performed. All recipients who underwent SLB during the study period were identified and charts reviewed for perioperative complications, histopathological findings and changes in therapy delivered.

Results: A total of 535 patients underwent 555 HSCT, among which 48 (8.6%) SLB were identified. Median follow-up time for patients who underwent SLB was 24 (interquartile range 9.7-32.7) months. Of the SLB specimens, 70.8% (n=34) resulted in a definitive diagnosis and included bronchiolitis obliterans (18.8%, n=9), noninfectious other than bronchiolitis obliterans (16.6%, n=8), infectious (22.9%, n=11) and other diagnoses (12.5%, n=6). Therapeutic changes based on pathologic findings were made based on 79.2% (n=38) of specimens. Overall, 83.3% (n=40) of SLB either provided a diagnosis or led to a change in therapy. Thirty-day postoperative morbidity was 16.7% (n=8) and 30-day postoperative mortality was 10.4% (n=5), though no mortalities were directly attributable to SLB.

Conclusions: SLB has an acceptable risk for perioperative complications given the illness severity of this population. In the majority of HSCT, SLB aids in defining the etiology of pulmonary infiltrates and can inform therapeutic decisions in patients where non-invasive diagnostic modalities have failed to provide a definitive diagnosis.

V248 SIOP19-1180 | Ten Year Activity and Outcome Data of Pediatric Haematopoietic Stem Cell Transplants from a Tertiary Cancer Centre in India and Relevance of Disease Risk Index

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Background/Objectives: Haematopoietic stem cell transplantation (HSCT) is indicated in management of various pediatric malignancies. We report the outcomes of HSCT in pediatric patients performed over a 10 year period. We also

retrospectively evaluate whether Disease Risk Index (DRI) can be applied to pediatric transplants.

Design/Methods: All consecutive patients aged <18 years, who underwent HSCT from November 2007 to November 2017 are included in this retrospective analysis. The patient characteristics, transplant details and outcomes were recorded. DRI was calculated for patients undergoing allogeneic HSCT and transplant outcomes were compared across patients with different DRI.

Results: A total of 116 patients (85 male, 31 female) with median age 11 (2-17) years underwent HSCT. Diagnosis were AML/MDS (n=19), ALL (n=25), CML (n=8), Hodgkin lymphoma (n=34), neuroblastoma (n=19), aplastic anemia (n=8) and others (n=3). Autologous (AuHSCT) and allogeneic (AHSCT) transplants were 54 (46.5%) and 62 (53.4%). Among AHSCT, 43 were matched sibling donors, 15 haplo HSCT and 4 unrelated donor transplants. Stem cell sources were PBSC (n=95), bone marrow (n=19), combined marrow and PBSC (n=1) and cord blood (n=1). Median follow up was 4.35 years. Five year OS and RFS for entire cohort was 54.5% and 43.7%; autologous- 52.3%, and 42.47%; allogeneic-56.7% and 44.7%, respectively. Disease wise 5 year OS and RFS were ALL-45.6% and 35.4%; AML-28.13% and 25%; HL-66.3% and 55.25%; neuroblastoma-27.4% and 16.6%, respectively. The total deaths were 49; 34 (70%) were relapse related. Non-relapse mortality of the whole cohort was 13%. Among AHSCT for malignancies (n=53), DRI was low in 6, intermediate in 28 and high/very high in 19. The OS and RFS in patients with low DRI was significantly better compared to those with intermediate/high DRI ($p = 0.05$ and 0.031)

Conclusions: In our cohort, patients with ALL (AHSCT) and Hodgkin lymphoma (AuHSCT) had best outcomes. More innovative approaches are required for patients undergoing AuHSCT for neuroblastoma. DRI is an important prognostic tool in allogeneic setting.

V249 SIOP19-0698 | Improved Outcomes of Allogeneic Hematopoietic Stem Cell Transplantation Including Alternative Donor Transplantation for Childhood Myelodysplastic Syndrome

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Background/Objectives: We investigated the outcomes of allogeneic hematopoietic stem cell transplantation (HSCT) in children and adolescents with myelodysplastic syndrome (MDS).

Design/Methods: Thirty-six patients underwent allogeneic HSCT over two decades (early cohort, 1997-2007, N=10 versus recent study period, 2008-2017, N=26). Refractory anemia, refractory cytopenia with multilineage dysplasia and refractory cytopenia of childhood were classified as “low grade MDS (N=24)”. Refractory anemia with excess blasts-1 and -2 were classified as “advanced MDS (N=12)”. The outcomes were analyzed according to disease status, cytogenetic risk, conditioning regimen, donor types and period of transplantation.

Results: The median age at transplantation was 10 years (range, 2-23). Thirty-two (89%) patients achieved neutrophil engraftment at a median of 11 days (range, 10-26). Cumulative incidence (CI) of grade II-III and grade III acute GVHD were 36% and 9%, respectively. No patient developed grade IV acute GVHD. Extensive chronic GVHD occurred in 4 patients (11%). At a median follow up of 61 months (range, 10-247), 4 patients died of TRM, leading to the CI of 12%, with significantly lower TRM in recent cohort than early study period (4% recent vs. 30% early, $P=0.021$). The probability of OS at 5-years was 77% for total cohort. The OS was significantly better in patients with low grade compared with advanced MDS (91% vs. 50%, $P = 0.005$), and patients who were transplanted in the recent period compared with early period (87% vs. 50%, $P = 0.006$). The survival rates were similar between matched sibling and alternative donor transplantation (OS, 68% matched sibling donor vs 82% matched unrelated donor vs 86% haploidentical family donor, and 67% cord blood transplantation, $P = 0.67$).

Conclusions: This study demonstrated an improved OS of childhood MDS in recent years, and HSCT from alternative donor showed favorable outcomes as comparable as HSCT from HLA identical related donor.

V250 SIOP19-1377 | Alternative Donor Stem Cell Transplant for Pediatric Patients: Which One To Choose?

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Background/Objectives: Haplo-identical stem cell (HISC) and umbilical cord blood (UCB) transplantation are common alternative donor strategies used when a matched related sibling donor (MRD) is not available. In Jordan, most patients

have a MRD available, making the use of alternative donor stem cell transplant infrequently used.

Design/Methods: We retrospectively reviewed the charts of pediatric patients who received HISC or UCB transplantation at our center between Jan 2003 and Dec 2016. Data collected included transplant indications, acute and chronic graft-versus-host disease (aGVHD and cGVHD) and cytomegalovirus (CMV) reactivation. Cyclophosphamide post unmanipulated stem cell infusion has been used for T-cell depletion after 2013 for HISC transplants.

Results: A total of 56 patients received either alternative donor transplant (HISC, 28 patients; UCB, 28 patients). Median age was higher in patients receiving UCB (HISC, 4.4 years; UCB, 8.1 years). Cytoablation consisted of myeloablative conditioning regimen (MAC) in 29 patients (HISC, 6; UCB, 23), reduced intensity (RIC) in 19 patients (HISC, 14; UCB, 5) or no conditioning in 8 patients who received HISC. Indications for transplant were malignancy (HISC, 9; UCB, 17), immunodeficiency (HISC, 10; UCB, 5), severe aplastic anemia (HISC, 3; UCB, 1), congenital bone marrow failure syndromes (HISC, 3; UCB, 3), or other indications including thalassemia, osteoporosis, inborn-errors-of-metabolism (HISC, 3; UCB, 2). CMV reactivation was similar in the 2 groups (HISC, 46%; UCB, 36%). Graft-versus-host disease were more common in HISC recipients: aGVHD (HISC, 12; UCB, 7) and cGVHD (HISC, 7; UCB, 3). Only Estimated 5-year-OS was similar (HISC, 47%; UCB, 54%). Transplant-related mortality (TRM) was higher in UCB recipients (HISC, 3; UCB, 10). Notably, steroids were removed from aGVHD prophylaxis after Jan 2012, leading to dramatic decrease in CMV reactivation and TRM. Cumulative costs of transplant calculated for both modalities until the end of one-year post-transplant were similar.

Conclusions: HISC and UCB transplantation are viable and life-saving alternative donor options. Improvement in post-transplant supportive care improved outcome though viral reactivation is still a challenge. Timely availability of Haplo-identical donors make this option plausible in places where umbilical cord transplant is not feasible. Modification of aGVHD prophylaxis lead to improved TRM, which was relatively high for our patients.

V251 SIOP19-0140 | The Effects of Inflammatory Priming on the Immunosuppressive Properties of Human Mesenchymal Stem Cells

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Background/Objectives: A number of preclinical and clinical trials of human mesenchymal stem cells (MSCs) are currently in progress worldwide; however, their clinical benefit is often limited. Therefore, strategies to enhance MSCs' immunosuppressive properties need to be sought. In this study, the effects of ex vivo culture conditions such as the presence of inflammatory stimuli including IFN- γ , TNF- α , and poly (I:C) on the immunosuppressive properties of MSCs were investigated.

Design/Methods: The gene expression profiles under IFN- γ , TNF- α , or poly (I:C) treatments were compared using RT-PCR analysis and microarray. In addition, the impact of IFN- γ treatment and regulation of IDO and PGES expression on MSCs' in vitro and in vivo function was analyzed.

Results: The expression of chemokine genes, immunomodulation-associated genes, anticancer effect-associated genes, and an adhesion-associated gene were significantly upregulated in IFN- γ -treated MSCs compared with TNF- α - or Poly (I:C)-treated MSCs. Furthermore, IFN- γ -treated MSCs significantly increased the survival rates of graft-versus-host disease (GVHD) mice compared with MSCs without IFN- γ stimulation. Downregulation of IDO in MSCs by shRNA resulted in restoration of T-cell proliferation in vitro and decreased the survival rates of GVHD mice. The toll like receptor 3 (TLR3) stimulant poly (I:C) increased prostaglandin E synthase (PGES) compared with IFN- γ and TNF- α , resulting in a significant increase in PGE2 levels. Reduced PGE2 levels decreased MSC's capacity to inhibit hPBMC proliferation. Administration of MSCs with inhibited PGES expression into mice with GVHD did not reduce mortality. These results indicate that upregulation of PGES via TLR3 is critical for BM-MSCs-mediated immunosuppression by PGE2 secretion via the COX-2/PGE2 pathway.

Conclusions: These results suggest that IFN- γ or Poly (I:C) priming during culture expansion could be an effective strategy to enhance MSCs' immunosuppressive properties for the enhanced cell therapy in GVHD, thereby controlling culture condition.

V252 SIOP19-1504 | Hematopoietic Stem Cell Transplantation in Children and Adolescents with Lymphomas: A Single-Centre, 25-Year Experience

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Background/Objectives: Hematopoietic stem cell transplantation (HSCT) in relapsed and refractory (R-R) lymphomas improves survival in definite subsets of patients but data in children are limited. The presented study summarizes 25-year single-centre experience in children and adolescents with R-R lymphoproliferative disorders that were transplanted in Raisa Gorbacheva Memorial Research Institute for Pediatric Oncology, Hematology and Transplantation.

Design/Methods: Children and adolescents (n=129) treated with HSCT for R-R lymphomas were retrospectively analyzed. Median age was 16 (1-19). Hodgkin lymphoma (HL) was diagnosed in 87 patients (67.4%), non-Hodgkin lymphoma (NHL) – in 42 (32.6%). Types of NHL were as follows: Burkitt Lymphoma (n=7), primary mediastinal B-cell lymphoma (n=11), diffuse large B-cell lymphoma (n=6), anaplastic large cell lymphoma (n=6), peripheral T-cell lymphoma (n=5), lymphoblastic lymphoma (n=7). Autologous HSCT (auto-HSCT) was administered in 100 (77.5%) patients and allogeneic HSCT (allo-HSCT) – in 29 (22.5%). Remission (complete or partial) prior to HSCT was achieved in 101 (78%) recipients. In auto-HSCT BEAM (carmustine or bendamustine, etoposide, cytarabine and melphalan) was the predominant conditioning regimen (n=52, 78%) and in allo-HSCT - combination of fludarabine and bendamustine (n=16, 55%). Graft versus host disease prophylaxis was based on post-transplant cyclophosphamide in 19 (65.5%) patients and on antithymocyte globulin – 10 (34.5%). Survival was calculated using Kaplan-Meier method.

Results: In children and adolescents with R-R HL (n=72) 10-year overall survival (OS) and progression free survival (PFS) after auto-HSCT were 44% and 36%, respectively. In R-R NHL (n=28) long-term OS and PFS after auto-HSCT were 78% and 55%, respectively. OS and PFS after allo-HSCT in R-R NHL (n=14) were 68% and 34%, respectively, and in R-R HL (n=15) – 76% and 50%, respectively.

Conclusions: Auto-HSCT is an important treatment option in children and adolescents with R-R lymphomas that enables cure for a substantial number of patients. Allo-HSCT demonstrates promising results in children and adolescents with R-R lymphomas.

V253 SIOP19-1089 | High Graft CD8 Cell Dose Decreased AGVHD Incidence in HLA-Haploidentical Hematopoietic Stem Cell Transplantation

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Background/Objectives: To characterize the impact of graft T-cell composition on outcomes of HLA-haploidentical

hematopoietic stem cell transplantation (haplo-HSCT) in children with hematologic malignancies

Design/Methods: We retrospectively studied 138 pediatric patients who underwent haplo-HSCT for a hematologic malignancy between 2014 and 2018 at the University of Soochow. Pediatric patients received unrelated cord blood (CB), bone marrow (BM) and peripheral blood (PB) in order. Numbers of transplanted lymphocytic subsets were correlated with overall survival (OS), relapse-free survival (RFS), acute graft-versus-host disease (aGVHD) cumulative incidence and chronic graft-versus-host disease (cGVHD) cumulative incidence. Participants received standard GVHD prophylaxis with cyclosporine and mycophenolate mofetil and/or methotrexate. Parts of participants received standard antimicrobial prophylaxis and daily granulocyte colony-stimulating factor until neutrophil engraftment.

Results: Naïve T cells (Tns) doses were associated with a lower risk for aGVHD including naïve CD3 T hazard ratio (HR, 0.269; $P = .0001$), naïve CD4 T hazard ratio (HR, 7.496; $P = .0001$), and naïve CD8 T hazard ratio (HR, 4.254; $P = .015$) with similar rates in OS, RFS, cGVHD. Transplantation of more Tns was associated with less grade 2 to 4 aGVHD. Conversely, analysis of grafts B cell (CD3-CD19+) and NK cell (CD3-CD16+CD56+) did not identify a donor cell subset significantly associated with OS, RFS, or cGVHD. A cutoff level of 1.04×10^8 CD8 cells per kilogram optimally segregated patients receiving CD8hi and CD8lo grafts with different aGVHD incidence ($P = .027$). Median donor age was 30 years old (range 3 to 46.9). Donor age did not correlate with graft CD8 dose (Pearson $r = .07$; $P = .931$).

Conclusions: Donor immune cells were associated with aGVHD incidence after haplo-HSCT. Donor grafts with more BM-derived T-cell favorably regulated post-transplantation immunity haplo-HSCT. Higher graft CD8 dose predicted a decreased aGVHD incidence in pediatric patients undergoing haplo-HSCT

V254 SIOP19-1560 | Day +100 Platelet Count Predicts Survival Post Allogeneic Hematopoietic Stem Cell Transplantation in Children with Hematologic Malignancies

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Background/Objectives: Recovery of platelet count by day 100 post Hematopoietic Stem Cell Transplantation (HSCT) is affected by many factors and has been reported to be a predictor of survival in a variety of diseases. We investigated

the correlation between day +100 platelet count and survival post allogeneic HSCT in pediatric patients with hematological malignancies.

Design/Methods: We conducted a retrospective study of 152 patients who underwent allogeneic HSCT at the Children's Cancer Hospital Egypt-57357 between 2009 and 2015 with a minimum follow up duration of one year post transplant. All patients received myeloablative conditioning and all had matched related donors. Patients who survived without relapse until day 100 post HSCT were divided into two groups: early platelet recovery (EPR) (platelet count ≥ 100 at day +100 post transplant) and delayed platelet recovery (DPR) (platelet count < 100 at day +100 post transplant).

Results: At day+100, 113 patients (74%) had EPR and 39 patients (26%) had DPR. With a median follow-up of 41 months (range 12 - 93 months), 41 patients (27.2%) died, 35 due to relapsed disease. The 3 year disease free survival (DFS) and overall survival (OS) were $68 \pm 7.84\%$ and $71.9 \pm 7.84\%$ respectively. The 3 year OS was 77.9% in the EPR group and 57.1% in the DPR group ($p = 0.006$). 3 year DFS of the EPR and DPR groups were $73.2 \pm 9\%$ and $54.8 \pm 16.3\%$ respectively ($p = 0.02$). Incidence of disease relapse for EPR and DPR patients was 22.6% and 39.5% respectively ($p = 0.04$). Multivariate analysis for survival identified delayed platelet recovery as a predictor of decreased survival ($p = 0.002$).

Conclusions: Our results suggest that patients with a robust platelet count at Day 100 are likely to do well, however patients failing to achieve a platelet count ≥ 10 have inferior long term OS and DFS and may require further evaluation at the Day 100 time point.

V255 SIOP19-0626 | Interest of Preventive Use of Defibrotide on the Occurrence and Severity of Sinusoidal Obstruction Syndrome in Hematopoietic Stem Cell Transplant in Children

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Background/Objectives: Sinusoidal obstruction syndrome (SOS) is one of the main causes of morbidity and death following hematopoietic stem cell transplant (HSCT). The incidence is higher in children, reaching about 20% of patients receiving HSCT, depending on the studies. Severe SOS is lethal in 80% of cases. The objective of this study is to describe if the preventive use of defibrotide helps to reduce the incidence and severity of SOS, in order to better determine which patients could benefit from this prevention.

Design/Methods: We retrospectively analysed the medical records of 128 patients, aged 0 to 19 years, who all received allogeneic HSCT after conditioning with busulfan and/or total body irradiation, in our comprehensive cancer centre, between 2013 and 2017. SOS prevention was mainly based on ursodesoxycholic acid and associated measures. Defibrotide was given for patients with probable or proved SOS, or in prevention for those presenting high risk of SOS (previous treatment with gemtuzumab ozogamicin, preexistent hepatic disease, or second HSCT). The diagnosis of SOS was based on Seattle or Baltimore criteria. The severity was retrospectively assessed according to 2017 EBMT criteria.

Results: Indication of HSCT was a malignant disease for 80 patients, and non-malignant disease for 48. Ten patients with high-risk of SOS received preventive defibrotide, in median during 24 days (18-35); 3 presented with mild to moderate SOS, and one had spontaneous cerebral bleeding under defibrotide. Among the 118 others, 37 presented with SOS (31.3%), and 21 received curative defibrotide because of severity criteria (17.7%). Five of them needed intensive care for SOS, including 3 who needed hemodialysis. One died because of SOS and septic shock.

Conclusions: SOS prophylaxis with defibrotide seems to reduce the incidence and severity of SOS for high-risk patients. The analysis of grades of severity will help to better determine which patients could most benefit from this preventive treatment.

V256 SIOP19-1518 | Outcomes of Cord Blood Transplantation in Pediatric Recipients with Hematological Malignant Disease / Risk Factors Associated With Survival - Retrospective Monocentric Study

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Background/Objectives: Over the last 25 years, umbilical cord blood (UCB) has become an established alternative source of hematopoietic stem cells (HSC) in allogeneic transplantation.

The main interesting characteristics of cord blood stem cells are the sufficient richness of the UCB, less demanding HLA-matching, the lower immunogenicity of UCB grafts and the low rates of graft-versus-host disease (GvHD) compared to partially matched bone marrow and peripheral blood stem cell transplants.

Design/Methods: A retrospective study based on the experience of 10 years of HSC transplantation (2006-2015) in one center. Our center performed annually about 20-25% of the total HSC pediatric transplantation in France.

We present results of cord blood transplants (CBT) for hematological malignant disease in 75 pediatric recipients and the risk factors associated with survival.

Results: Median age: 5.1years (0.48–15.3); diagnosis: Acute Lymphoblastic Leukemia (ALL) (36), Acute Myeloid Leukemia (AML) (28), and others (12); Disease status at UCBT: mainly in either Complete response 1 (CR1) (48) or CR2 (27). Median follow-up for patients: 21.5months (1 to 110 months); Conditioning regimen: All received myeloablative conditioning regimen followed by CSA based GvHD prophylaxis. Median total nucleated cells (TNC): $4.8 \times 10^7/\text{kg}$ (0.36–36); median CD34+: $2.4 \times 10^5/\text{kg}$ (0.16–34); and HLA match: 23 (6/6), 38 (5/6), 16 (4/6). Cumulative incidence of grade I acute graft-versus-host disease (aGVHD) by day +100 was 9.5%, grade II 28.7%, grade III 15%, grade IV 12% and chronic graft-versus-host disease was 14.5%. Incidence of aGVHD grade 0+I was 47.9% and aGVHD grade II+III+IV was 53.2% and cGVHD was 9.5%. Estimated 3-year overall survival is 60.8% (95% CI 30–71%), EFS is 58% and TRM CI is 22.2% (95%CI 14–34%).

Conclusions: The significant positive predictive factors that were shown by our univariate analysis was the sex match between the recipient and the donor, the CR status before UCBT and the number of TNC infused.

V257 SIOP19-1121 | Peripheral Blood Stem Cell Harvest- Effective Predictors in Pediatrics

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Background/Objectives: PBSC (peripheral blood stem cells) are used to restore hematopoiesis after high dose chemotherapy in solid tumors by aiding early stem cell recovery and reducing complications associated with prolonged neutropenia. PBSC collection is a time and resource consuming process as rapid appearance of CD34 cells in the circulation need immediate collection to achieve an optimal yield. In this setting, we would like to evaluate the role of peripheral blood monocyte count as a reliable surrogate marker to CD34 to optimize stem cell collection. We have also analyzed the factors affecting the stem cell yield as the pediatric literature is limited on poor mobilization.

Design/Methods: This is a retrospective study, from 2009–2018, collecting clinical, laboratory and technical data on autologous stem cell procedures at our center. Descriptive and statistical analysis of data was performed.

Results: One hundred and fifty five apheresis collections were performed on 132 children. Brain tumors (28%) and Neuroblastoma (26.5%) were the most common indications. We had 37 patients who mobilized poorly ($\text{CD34} < 5 \times 10^6/\text{KG}$) and 51% of which had infiltrating bone marrow disease ($p <$

0.01). The majority of remaining of the children had received platinum based therapy prior to apheresis ($p < 0.05$). The mean peripheral CD34 count was $140.66 \times 10^9/\text{L}$ and shows a positive correlation to the final product CD34 count (RR score of 0.7454, $p < 0.0001$). The chi square results comparing monocyte count ($>$ and $< 0.7 \times 10^9/\text{L}$) vs CD34 count ($>$ and $< 20 \times 10^6/\text{L}$) is 4.3961 with a p -value of 0.03.

Conclusions: A peripheral monocyte count of $> 0.7 \times 10^9/\text{L}$ on the day of stem cell collection helps in early detection of peripheral circulating CD34 cells and is a useful surrogate marker as it aids in optimizing progenitor stem cell collection. Other factors including, disease involvement of bone marrow, prior use of platinum therapy significantly influence the final product stem cell yield.

V258 SIOP19-0633 | Treatment-Related Mortality Contributes to Inferior Outcomes After Hematopoietic Stem Cell Transplant (HSCT) for Patients with T-Cell ALL: A Report From Children's Oncology Group AALL0434

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Background/Objectives: Relapse prevention is a top priority for patients with T-ALL. Although COG AALL0434 did not include an HSCT treatment arm, some patients received HSCT at investigator discretion. We retrospectively compared outcomes for patients who were taken off study to receive HSCT for reasons other than relapse.

Design/Methods: From 2007–2014, AALL0434 enrolled 1,596 T-ALL patients in a 2 x 2 pseudo-factorial randomization using a COG-modified BFM backbone. Patients randomized to receive escalating dose methotrexate without leucovorin rescue plus pegaspargase (CMTX) or High Dose MTX (HDMTX) with leucovorin rescue in a single Interim Maintenance phase, with or without six 5-day courses of nelarabine. Participants with $> 25\%$ marrow blasts (IF)

at end-induction were non-randomly assigned to receive HDMTX with nelarabine. All patients with intermediate risk, high risk or IF received cranial irradiation.

Results: For 1,385 eligible, evaluable patients for whom retrospective survey information was available, 333 (24%) were taken off therapy during induction; 32 (9.6%) subsequently underwent HSCT. For the 1052 patients who completed induction and underwent randomization/assignment to the four treatment arms, 43 (4.1%) subsequently came off study to receive HSCT. Multivariate survival analyses on all 75 patients, adjusting for treatment arm and risk group, and using time-dependent covariates for time to HSCT, showed worse outcomes for those who received HSCT versus those who received chemotherapy [Hazard ratio 3.46 (95% Confidence Interval 1.39 - 8.60); $P = 0.008$]. Altogether, 19 of 75 (25%) of patients who underwent HSCT died. Eleven deaths were from treatment-related mortality, while the remaining 8 patients (4 with IF) died from progressive/refractory disease.

Conclusions: Though this natural history study cannot compare outcomes for patients with T-ALL who underwent HSCT vs chemotherapy within specific indications, we found broadly that survival advantages favored those who received chemotherapy, and that treatment-related mortality with HSCT was a common cause of death.

Solid Non Brain Tumours - Bone Tumours

V259 SIOP19-0102 | Effect of Timing of Pulmonary Metastasis Occurrence on the Outcome of Metastasectomy in Osteosarcoma Patients

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Background/Objectives: Complete metastasectomy is the best predictor of survival in patients with osteosarcoma pulmonary metastases. The prognostic significance of the timing of occurrence of lung metastasis is controversial. Our objective was to investigate the prognostic value of the timing of identification of lung metastasis among patients who had metastasectomy for osteosarcoma

Design/Methods: We retrospectively reviewed the clinical course of all osteosarcoma patients with pulmonary metastases treated by metastasectomy in our hospital from January

2008 through December 2016. Each patient who underwent metastasectomy was placed into one of three groups based on whether lung metastases were present at initial presentation (Group 1), developed during chemotherapy (Group 2), or appeared after completion of chemotherapy (Group 3). Differences in the demographics and presenting characters between metastatic disease groups were evaluated by Pearson exact χ^2 test. Survival curves were created according to the Kaplan-Meier method and compared using log-rank test.

Results: We identified 170 patients with pulmonary nodules of whom 99 (58.2%) underwent at least one metastasectomy (149 thoracotomies). Eleven patients had benign pulmonary nodules and were excluded. The other 88 patients were classified as Group 1 (37), Group 2 (18) or Group 3 (33). The median follow-up was 35 months (range 8 to 99). Postmetastasis 5-year overall survival (OS) was $38.1 \pm 6.4\%$; event-free survival (EFS) was $25 \pm 5.3\%$. By group, postmetastasis 5-year OS and EFS were $34.3 \pm 13\%$ and $18 \pm 9.3\%$ in Group 1, $8 \pm 6.5\%$ and $6.5 \pm 5\%$ in Group 2, and $52 \pm 11.4\%$ and $25 \pm 9\%$ in Group 3 ($P = 0.001$). In univariate analysis, the only significant factors associated with survival were timing of occurrence of lung metastasis and the number of lung nodules found.

Conclusions: The timing of occurrence of lung metastasis is an important prognostic factor among osteosarcoma patients eligible for metastasectomy. Patients whose metastases occurred during chemotherapy had the worst survival.

V260 SIOP19-1517 | Pediatric Osteosarcoma Treatment Results: A-Single Center Experience

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Background/Objectives: Osteosarcoma (OS) is the most common type of primary malignant bone tumour. The main purpose of our study was to determine epidemiological characteristics, clinical features and prognostic factors of the patients with OS treated at our center.

Design/Methods: We evaluated the records of the patients with OS retrospectively, between 1994-2018 in our institution.

Results: A total of 68 patients were identified (52,9% male, 47,1% female with a mean age 13,2 years). The most common primary site of the tumour was femur ($n=41$). According to WHO classification 44 patients classified as conventional osteoblastic, 14 patients chondroblastic, 2 patients telangiectatic, 8 patients other types. Twenty four of these (35,3%)

had metastasis at the time of diagnosis. All were treated with Mayo Clinic (1995-2014) or EURAMOS protocol (2014-2019). Mifamurtid was used in addition to adjuvant chemotherapy treatment after 2016. The median surgery time was fifteen months (4-22 months). Fifty nine patients underwent limb salvage surgery whereas seven patients underwent amputation. Fifty-five patients were treated with prosthesis following tumor resection, four patients received extracorporeal irradiation and reimplantation. The median follow-up time was 53 months (2.5-265 months). Disease progression occurred in 11 patients and relapse occurred in 17 patients. The overall survival (OS) and event free survival (EFS) at 5 years were 60,3% and 54,4%, respectively. The estimated 5-year EFS rates of the patients without metastasis were 65,9% and those of the patients with metastasis 33,3% ($p = 0,006$). The EFS at 3 years in the patients who achieved $\geq 90\%$ tumour necrosis was higher than those who had $< 90\%$ of tumour necrosis (81,5%, 35,5%, $p = 0,006$). Among the patients who underwent limb salvage surgery or amputation, EFS rate was 59,3% and 28,6% respectively ($p = 0.000$).

Conclusions: This study is one of the largest single-center series of childhood patients with osteosarcoma in Turkey. Metastasis at the time of diagnosis and less than 90% tumour necrosis were associated with poor prognosis. High incidence of metastasis at the diagnosis might be associated with late admission to the hospital. Our results of survival analysis were similar to literature.

V261 SIOP19-1348 | Targeting Metastasis in Ewing Sarcoma with T Cell Receptor-based Immunotherapy

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Background/Objectives: Ewing sarcoma (EwS) is characterized by low immunogenicity. In addition, T cell checkpoint inhibition and chimeric antigen receptor T cells are not sufficient to target metastasis, the major cause of death from cancer. Chondromodulin-I (CHM1), is a direct downstream target of the EwS oncogenic driver EWS-FLI1. CHM1 is selectively expressed and sustains metastasis in EwS. Native EwS do rarely express programmed cell death ligand 1 (PD-L1).

Design/Methods: We assessed HLA-A* 02:01/CHM1-specific T cell receptor (TCR) transgenic CD8⁺ T cells

against EwS focusing on PD-L1 expression utilizing a TCR recognition-sequence for CHM1 peptide 319 (CHM1³¹⁹). Four refractory HLA-A2+ EwS patients (pts) were treated with engineered T cells. Pt derived cell lines (PDCL) were established in all cases. Pts received up to 10⁷/kg TCR transgenic CD8⁺ T HLA-A2- cells. All pts were treated with the same TCR CDR3 recognition-sequence for CHM1³¹⁹.

Results: All PDCLs displayed persistent HLA-A2 expression. Transgenic T cells showed specific *in vitro* lysis of all PDCLs. Therapy was well tolerated and did not cause graft versus host disease (GvHD). Patients #1 #3 and #4 showed delayed progression, whereas patient #2, while having bone marrow (BM) involvement and accessible multifocal disease, showed partial metastatic regression associated with T cell homing to involved lesions. Tested PDCL were PDL-1 negative and became PDL-1 positive after exposure to 100 U/ml interferon *in vitro*. In addition, HLA-A2 expression was strongly upregulated. *In vivo*, transgenic T cells became trackable in peripheral blood after application of a PD1-inhibitor.

Conclusions: In conclusion, CHM1319-TCR transgenic T cells may home to affected BM and may cause partial remission. They proliferate *in vivo* without causing GvHD. EwS may undergo PDL-1 mediated immune-evasion when put under immunological pressure with CHM1319-TCR transgenic T cells. This finding suggests implementation of checkpoint-inhibitors to enhance TCR transgenic T cell mediated antitumor responses in an *a priori* non-immunogenic sarcoma.

V262 SIOP19-1718 | Preliminary Tolerability Assessment of Naxitamab (Humanized Anti-GD-2 Monoclonal Antibody) Therapy in a Phase 2 Osteosarcoma Trial

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Background/Objectives: The high prevalence of GD2 positivity in osteosarcoma (OS), and clinical activity of anti-GD2 therapy in pediatric solid tumors, prompted an ongoing phase 2 clinical trial of naxitamab (Hu3F8) in relapsed OS. Naxitamab is a fully humanized anti-GD2 monoclonal antibody with improved pharmacokinetics and increased cytotoxic activity. Early phase pediatric trials of naxitamab demonstrated tolerability and clinical activity. However, the toxicity and tolerability profiles of naxitamab therapy in comparably older osteosarcoma patients remain undescribed.

Design/Methods: OS patients with recurrent disease and in $\geq 2^{\text{nd}}$ complete remission were eligible for this single institution phase II trial of naxitamab in combination with GM-CSF. Patients must have adequate organ function and performance status, and could have previously received anti-GD-2 therapy. Enrolled patients received naxitamab in the outpatient setting for 3 days augmented with GM-CSF constituting 1 cycle administered every 3-4 weeks for a maximum of 5 cycles.

Results: Twenty-five patients have been enrolled to date with a median age of 15.7 years (range 8.8 - 29.5). Grade 3/4 toxicities were observed in 80% (N=20 Grade 3, N=3 Grade 4) of patients but were all clinically manageable. Toxicities were as previously reported for naxitamab and included pain, hypo- and hypertension, fever, nausea, urticaria, and transaminase elevation. No long term or delayed toxicities have been observed. A majority of patients were able to receive therapy in an outpatient setting (76%, N=19). Human antihuman antibody (HAHA) positivity developed in 40% (N=10) of patients with 60% (N=6/10) occurring after 1 cycle of naxitamab, significantly higher than observed in neuroblastoma (9%).

Conclusions: Despite the higher incidence of treatment-related toxicity, naxitamab can be safely and tolerably administered to osteosarcoma patients in an outpatient setting and with a manageable toxicity profile. Determining the clinical impact of naxitamab on disease control and prognostic significance of HAHA positivity in osteosarcoma is ongoing.

V263 SIOP19-1278 | Assessing Early Response to pre-Operative Chemotherapy for Early Limb Osteosarcoma Using Magnetic Imaging Delta-Radiomic

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Background/Objectives: Standard of care for osteosarcoma includes neoadjuvant chemotherapy, large surgery, and adjuvant chemotherapy according to histological findings. Early response assessment to adjuvant chemotherapy could be crucial for treatment optimization. Radiomic technic represents a new automatic method for increasing the number of quantitative features extracted from image (and modification/filter or new calculated matrix). Promising results of radiomics have been reported in many cancers such as a prognostic value in lung cancer. Here, we studied magnetic resonance imag-

ing (MRI) based delta-radiomics (or textural modification) as early biomarker for chemotherapy response assessment.

Design/Methods: All patients with a histologically proven localised limb osteosarcoma, treated from May 2007 to September 2015 in our Center and enrolled in the prospective OS2006 trial, were included in the current study. They were all evaluated by MRI at the time of diagnosis and one month after start of chemotherapy (T1 weighted MRI fast spin echo without contrast). Features from first order and second order (co-occurrent matrix, using 0°, 45, 90°, 135° axis and neighbourhood = 7) were extracted. We studied the association between ratio of delta-radiomics (between these 2 MRIs) and histological tumor response (poor response if 10% or more viable tumour cells in operative specimen).

Results: Among the 34 study patients, 24 had a poor histological response. Delta-radiomics in percent based on contrast from 3D co-occurrent matrix was statistically associated with the histological response (p=0.036). Moreover, when using a 7.4% threshold for this delta-radiomics feature, we found a sensibility of 40% and a specificity of 100%. All patients with less than this threshold presented a good histological response (9/9, 100%) whereas only 15 patients over 25 (60.0%) presented a good histological response (p=0.034).

Conclusions: Early MRI delta-radiomics assessed during the neoadjuvant chemotherapy seems to be associated with chemotherapy response. Validation on an independent set is requested.

V264 SIOP19-0506 | Systematic Review of Phase-I/II Trials Enrolling Refractory and Recurrent Ewing Sarcoma: Actual Knowledge and Future Directions to Optimize the Research

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Background/Objectives: To analyze phase-I/II trials in recurrent/refractory Ewing Sarcoma (ES) to improve future trials design.

Design/Methods: Comprehensive review of clinical trials registered on 5 trial databases (who.int/trialsearch, clinicaltrials.gov, clinicaltrialsregister.eu, e-cancer.fr, umin.ac.jp) and/or published in PubMed/ASCO/ESMO websites, between 2005-2018, using the criterion: (Ewing sarcoma OR bone sarcoma OR sarcoma) AND (Phase-I or Phase-II).

Results: Among the 146 trials identified, 77 phase-I/II, 67 phase-II and 2 phase-II/III, tested targeted therapy (34%), chemotherapy (24%), immunotherapy (19%) or drug combination (23%). Twenty-three trials were ES specific, 48 had a specific ES stratum. Although usually metacentric (88%), few

trials were international (30%). Inclusion criteria cover the recurrent ES age range only for 12% of trials and allow only measurable diseases according to RECIST criteria (at least one extra-osseous lesion ≥ 1 cm). Single-arm design was the most frequent (88%), testing mainly single drug (61% vs. 39% combination). Primary phase-II outcome was response rate (RR=CR+PR; Complete + Partial response) (n=116/146; 79%), rarely progression-free or overall survival (16% PFS, 3% OS). H0 and H1 hypotheses were very variable (RR=5-20% and 20-35%, respectively). Only 5% of the trials were randomized. The 60 fully/partially published trials enrolled 930 ES (93% evaluable for RR). RR was poor (9.7%; 15 CR=1.7%, 68 PR=7.9%). Stable disease was the best response in 175/863 patients (20%). Progression disease (PD) occurred at first evaluation in 67% (580/863) of the patients. The median PFS/OS were of 1.9 (1.3-14.7) and 7.6 months (5-30), respectively. 32/60 (53%) trials had RR=0% and 16/60 trials (27%) PD=100%. Eleven (18%) published trials were considered positive, with median RR/PFS/OS of 15% (7-30%), 4.5 (range 1.3-10) and 16.6 months (range 6.9-30), respectively.

Conclusions: This review and the lack of reliable historical data support the need to develop international randomized phase-II trials across all age ranges with primary endpoints including RR and PFS for patients without measurable disease.

V266 SIOP19-1643 | Phase 1 Combination Dose-Finding/ Phase 2 Expansion Cohorts of Lenvatinib + Etoposide + Ifosfamide in Patients Aged 2 to ≤ 25 Years with Relapsed/Refractory Osteosarcoma

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Background/Objectives: Lenvatinib is a multikinase inhibitor of VEGFR1-3 and other targets. We report data from a phase 1b dose-finding and phase 2 expansion cohorts of lenvatinib + etoposide + ifosfamide in patients with relapsed/refractory osteosarcoma.

Design/Methods: Patients aged 2 to ≤ 25 years with relapsed osteosarcoma and < 2 prior VEGF-targeted therapies received phase 1b combination regimen (starting dose: lenvatinib 11 mg/m²/day + ifosfamide 3,000 mg/m² + etoposide 100 mg/m² daily/3 days). On determination of recommended phase 2 dose (RPh2D) of lenvatinib + chemo, patients were enrolled into the phase 2 expansion cohort. Primary endpoints: phase 1b – RPh2D; Phase 2 - 4 months progression-free survival.

Results: In the phase 1b dose-finding cohort (n=23), patients received lenvatinib 11mg/m² (n=7) and 14 mg/m² (n=16) + chemo. Dose-limiting toxicities were: G4 thrombocytopenia (n=1; lenvatinib 11 mg/m²), G4 thrombocytopenia and G3 epistaxis (n=1; lenvatinib 14 mg/m²), G2 oral dysesthesia, G3 muscle spasm and G2 back pain (n=1; lenvatinib 14 mg/m²). RPh2D was lenvatinib 14 mg/m² + chemo. In the expansion cohort (n=18), median number of cycles received was 3 (range: 1-7). Most common treatment-emergent adverse events (TEAEs) were anemia, platelet count decreased (38.9% each), nausea, neutropenia (33.3% each), neutrophil count decreased, white blood cell count decreased (27.8% each), abdominal pain, ALT increased, asthenia, diarrhea and headache (22.2% each). Most common Grade ≥ 3 TEAEs were: neutropenia and platelet count decreased (33.3% each), neutrophil count decreased and white blood cell count decreased (27.8% each), anemia (22.2%), and thrombocytopenia (16.7%). Two patients discontinued treatment due to TEAEs (in the dose-finding cohort). There are no treatment-related fatal serious adverse events. Efficacy data will be presented during the meeting.

Conclusions: The combination of lenvatinib + chemo had a manageable safety profile. RPh2D is lenvatinib 14 mg/m² + chemo.

V267 SIOP19-1110 | IGF1R in Ewing's Sarcoma- Revisited: Association with Prognosis and Expression of S6 Kinase

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Background/Objectives: Ewing's sarcoma is an aggressive malignancy of bone and soft tissue in children and young adults. Despite advances in modern therapy, metastasis can occur and results in high mortality. IGF1R and S6 kinase are signaling proteins that regulate the proliferation of tumor cells.

Design/Methods: We have studied the immunohistochemical expression of these proteins in 32 tumor samples from adult and pediatric patients with Ewing's sarcoma in correlation with patients' age, gender, clinical stage and survival information (overall and disease-free survival). Tissue microarrays slides were stained with antibodies against IGF1R β and p-S6 kinase proteins.

Results: Patients had an age range of 12-72 years and 8 (25%) were pediatric (≤ 20 years). After a follow-up to 14 years, the overall survival ranged from 25 – 5,065 days. High expression of IGF1R β and p-S6 kinase, defined as staining stronger than positive control, was seen in 25% and 68.75% of cases respectively. Statistical analysis revealed IGF1R β high expression had a significant association with bad outcome ($p=0.0048$), shorter overall survival ($p=0.0398$) and a slight association with advanced stage tumors ($p=0.0534$). Expression of S6 kinase exhibited a trend towards shorter survival ($p=0.0934$).

Conclusions: High expression of IGF1R β in Ewing's sarcoma may identify cases with a more aggressive phenotype, highlighting its role in targeted therapy. More definitive studies with in vitro biologic data are needed to confirm whether the high expression of S6 kinase can be predictive of the prognosis in Ewing's sarcoma tumors.

V268 SIOP19-0947 | Impact of Doxorubicin Dose on Osteosarcoma Outcomes

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Background/Objectives: We implemented new clinical practice guidelines (CPG) for patients with osteosarcoma starting in Jan2009. These guidelines were based on standard EURAMOS regimen which includes 6 cycles of doxorubicin with a cumulative dose of 450mg/m². Aiming to reduce cardiac toxicity at our center, we opted to reduce the cumulative dose of doxorubicin to 375mg/m².

Design/Methods: We conducted a retrospective analysis of children (<18years) with osteosarcoma who presented to our center from Jan2009 until Dec2017 and were treated according to our institutional CPG. Data collection and analysis were done in Mar2019.

Results: We identified 79 patients (38 males) with a median age of 12.8 years at diagnosis. Patients were followed for a median of 35 months (range, 2-122). Most tumors were

located in extremities (n=75). Fifty eight patients (73%) had localized disease, 15 (19%) had lung only metastasis, and 6 (8%) had multiple sites metastasis. Local control was done by surgery for 69 patients: Limb-salvage (N=51), amputation (N=16), hemipelvectomy (N=1), and resection (N=1). Of those who had surgery for local control, necrosis was $\geq 90\%$ in 31 patients (45%). The 5-year-EFS and OS were $50 \pm 6.2\%$ and $63 \pm 6.3\%$, respectively. Absence of metastasis, extremity tumor site, and necrosis $\geq 90\%$ were associated with better 5-year EFS ($P=0.0012$, $P=0.022$ and $P=0.01$, respectively), while only absence of metastasis and extremity site were associated with a better 5-year OS ($P=<0.0001$ and $P=0.026$, respectively). Patients with extremity non-metastatic tumor who had necrosis $\geq 90\%$ (n=20) had the best survival (5-year-EFS and OS of 82 ± 9.7 and 86 ± 9.5 , respectively). No patient developed cardiac dysfunction during the study period.

Conclusions: We achieved cure rates that were in parallel with EURAMOS trial using reduced doxorubicin cumulative dose. This approach can be particularly useful in countries with limited resources where screening for cardiac dysfunction can be suboptimal. Also, this regimen deserves evaluation in a randomized trial to prove non-inferiority to the standard regimen.

V269 SIOP19-1306 | Prognostic Factors and Outcome of Pulmonary Metastatectomy in Pediatric Cancer Patients at National Cancer Institute, Egypt

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Background/Objectives: Metastatic tumors account for approximately 80% of all lung tumors in children.

aim: Assessment of prognostic factors of pulmonary metastatectomy in pediatric solid tumors as age, number, size, site, laterality, resectability of pulmonary nodules and number of Thoracotomies. Calculate OS among Patients who underwent pulmonary metastatectomy

Design/Methods: Retrospective study include all patients with metastatic solid tumors to lungs treated at pediatric oncology and surgical departments, national Cancer Institute, Cairo University from 2008 to 2014 with resectable lung disease based on C.T chest and lung is the only site of metastasis

Results: Fifty five patients were included, 43 were Osteosarcoma (78.2%), 5cases Synovial sarcoma (9.1%), 2 cases Rhabdomyosarcoma (3.6%), 2 cases Ewing Sarcoma (3.6%), 2 cases Germ cell tumor (3.6%) and 1 case was Wilms tumor

(1.8%). There were 30 male (54.5%) and 25 female 45.5%. The mean age was 15 years ranging from (4.5- 23) years. All of them underwent complete surgical resection of the primary disease with negative margin, 22 of the osteosarcoma patients did local control with tumor necrosis less than 90% in 40 cases. Regarding type of local control OS in limb salvage with -ve margin was 81 months mean compared to 46 months in amputation group with p-value < 0.001%. The patients were grouped into four groups according to time of diagnosis of pulmonary metastasis: 1. metastatic at presentation were seen in 13 patients (21.8%), 2. diagnosed during treatment time were 16 (30.9%), 3. diagnosed within first year follow up were 18 patients (32.7%) and 4. diagnosed after first year follow up were 8 patients (14.5%). OS was 64.5 months in initially metastatic patients, 50 months in patients who developed mets during treatment, 64 months in patients who relapsed by lung nodules before 1 year follow up and 114 months in patients who relapsed after 1 year follow up with p-value < 0.001%. There were no perioperative deaths and minimal encountered complications were detected. 3 year OS rate was 86.5% and 5 year OS was rate 74.8%.

Conclusions: Pulmonary metastasectomy is a mandatory procedure for pediatric cancer patients.

V270 SIOP19-1232 | Etoposide-Ifosfamide-Induced Haemolytic-Uremic Syndrome Successfully Treated With Eculizumab: One Pediatric Case Report

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Background/Objectives: Well-known chemotherapeutic agents have been associated with haemolytic-uremic syndrome (HUS). The monoclonal anti-C5 antibody eculizumab (ECU) has been successfully tested in certain drugs-associated HUS.

Design/Methods: We reported the case of a 13-year-old girl with localised high-grade osteosarcoma of the right distal femur. She developed during neoadjuvant chemotherapy two episodes of HUS. Following the first cycle of etoposide-ifosfamide, she presented confusion and thrombocytopenia, haemolytic anaemia with schistocytes, acute kidney injury. The dosages of complement proteins were normal. A diagnostic of HUS was established and the patient was treated by plasma exchange. Clinical and biological symptoms disappeared after two days. After the second cycle of etoposide-ifosfamide appeared recurrence of HUS: the patient developed the same symptoms and a hypertension appeared.

Results: HUS was treated by ECU, and disappeared in a few days, except persistent renal failure. ECU was continued during the neoadjuvant and adjuvant chemotherapy, without any recurrence of HUS. A moderate chronic renal failure persisted. Because of a tumoral progression during neoadjuvant chemotherapy, the patient was treated with a second-line and has been in complete persistent oncologic remission for 8 months. ECU was well tolerated: there was no infectious complication. For this patient we did not identify any classical genetic alteration associated with HUS.

Conclusions: Etoposide-ifosfamide-induced HUS has not previously been described. It is not possible to determine which of these two agents induced HUS. Etoposide was reintroduced as adjuvant treatment with ECU therapy, without HUS recurrence. Ifosfamide was not reintroduced because of the switch for the second-line chemotherapy. ECU was also effective, well tolerated and allowed to continue chemotherapy program in order to obtain a persistent oncologic remission.

V271 SIOP19-1741 | Functional Genomics of Metastatic Ewing Sarcoma

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Background/Objectives: Pediatric cancers are mostly driven by a small number of recurrent somatic events. These aberrancies that encompass copy number alterations, DNA rearrangements and global transcriptional reprogramming have rendered the identification of driver events in such malignancies more challenging. An example of such cancers is Ewing sarcoma (ES), a malignant bone and soft tissue tumour of high metastatic potential. ES neoplasms strikingly converge on a recurrent initiating event, which is a chromosomal translocation that generates a fusion transcript between the EWSR1 gene and the ETS family of transcription factors, most commonly FLI1 (85%). After 20 years since the discovery of the EWS-FLI1 fusion, ES remains a clinical challenge with unacceptably low survival rates, which is primarily due to metastasis.

Design/Methods: To address this issue the LentiHop technology was used to engineer ES cell models. LentiHop combines the genome-wide insertional mechanism of transposons and the transduction efficiency of lentiviruses. Human mesenchymal stem cells (hMSC), the putative cells of origin of ES,

were genetically modified to constitutively express EWS-Flt1. Transformed hMSC-EWS and a cohort of non-metastatic ES cell lines were engineered to harbor loss of function and gain of function gene traps mediated by a conditionally-expressed highly active transposase.

Results: Upon initiating the system, transposon-mediated mutagenesis activated oncogenes and inactivated tumor suppressor genes. Increased cell proliferation rates were evident and implanted cells were capable of engraftment in-vivo, which lead to tumor evolution in recipient mice. Xenografted tumors were resected and analysed for SRBCT histological hallmarks. Recipient mice are followed up for development of distant metastases. Upon occurrence, matched primary and metastatic tumors are sequenced and pathway-oriented bioinformatic analysis is performed to reveal candidate metastasis genes.

Conclusions: The EWS-Lentihop system was successful in generating stable cell lines that model Ewing sarcoma. Further experimentation is on-going to harvest metastasis samples from NRG-ES mice for proceeding with the analysis.

V272 SIOP19-0779 | Initial Experience of Compressed Cycle Chemotherapy Feasibility in Pediatric Ewing Sarcoma from a Developing Country

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Background/Objectives: Children with cancer in low-middle-income countries (LMICs) have inferior outcomes than those in high-income countries. The factors responsible for this survival gap, are not well identified and understood. In the past as an institution we were treating our pediatric patients as per the EuroEwing99 (EE99) protocol. Given that the Children Oncology Group (COG) compressed chemotherapy cycles were shorter in total duration and would help with our inpatient admission constraints we decided to switch protocol to the Vincristine, Doxorubicin, Cyclophosphamide, Etoposide and Ifosfamide (VDC/IE) compressed regimen.

Design/Methods: We retrospectively collected data on a cohort of pediatric Ewing sarcoma (ES) patients presenting to the hospital from June 2017 to June 2018, who were started on the VDC/IE regimen. The aim was to determine if this regimen is feasible in our setting and tolerated by our patients.

Results: There were a total of 24 patients seen within the given 12-months. Among these 10 were girls and 14 were boys. The mean age was 10.2 years. The most common site was extremity (54%) followed by the pelvis (16.6%) and spine (12.5%). Twenty patients (83.3%) were able to complete chemotherapy on time. The average tumor volume was 485ml (range 5-1978). There was an average of 2.5 fever &

neutropenia (F/N) episodes. Nine patients (37.5%) got salvage surgery and four (16.6%) had amputations. Tumors (n=11; 45.8%) not amenable to surgery were treated with radiation for local control. Seventeen (70.8%) are well and were alive at their last follow-up. Three (12.5%) relapsed post treatment. Three (12.5%) children died due to sepsis during chemotherapy and 1 (4.2%) died because of anthracycline induced cardiac failure

Conclusions: This is a single-institution study of a small cohort of patients treated as per the COG compressed chemotherapy regimen. We are able to deliver chemotherapy on time. Long term follow up is needed to assess efficacy.

V273 SIOP19-1562 | Distant Bone or Skip Metastases in Osteosarcoma at Diagnosis: Experience of the OS2006 Study

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Background/Objectives: We aimed to describe the characteristics and outcome of patients with an osteosarcoma presenting with skip or bone metastases at diagnosis.

Design/Methods: Description of all patients prospectively enrolled in the French OS2006 study between April-2007 and December-2015, for a newly diagnosed high-grade osteosarcoma with skip (in the primary bone site) or distant bone metastases (including transarticular skip metastases) at diagnosis. Detection method of the bone metastases, treatment, pathological response and survival related data were analyzed.

Results: From the 646 study patients, 63 patients (median age=13.8; range, 4.7-45.6) had skip metastases only (N=38) or distant bone metastases (N=25, including 6 patients with also skip metastases). Among patients with distant bone

metastases, 9 had a unique lesion in addition to the primary, and 16 had multifocal lesions. Twenty two patients had lung metastases. Skip metastases were diagnosed by MRI in 44/44 patients. Surgery of the primary tumour was performed in 50 patients. A poor histological response was reported in 21/49 evaluable patients (43%) not significantly different from patients without bone metastases (37%, $p=0.58$). A complete remission was obtained in 39 patients after polychemotherapy combined with local treatment of primary site and metastatic lesions. Only 19 patients are still alive free of progression/relapse at last follow-up, leading to a 5-year PFS of 29% (SE=6%) on the entire series: 36% (SE=8%) in patients with skip metastases only, and 17% (SE=8%) in patients with distant bone metastases (logrank, $p=0.04$). In multivariate analysis adjusted for lung metastases, the hazard ratio of progression/relapse was 1.7 (95%CI, 1.1-2.6) in patients with skip metastases only and 2.7 (95%CI, 1.7-4.4) in patients with distant bone metastases, compared to patients without bone metastases. Overall survival was 42% (SE=7%).

Conclusions: Initial bone metastases are rare in osteosarcoma. The outcome of these patients remains poor even in patients with skip metastases only.

V274 SIOP19-1239 | Prognostic Factor of Hemogram Parameters in Patients with Osteosarcoma Treated with High Dose Methotrexate and Etoposide/Ifosfamide Chemotherapy

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Background/Objectives: Besides metastatic status and histologic response, previous studies have shown that neutrophil to lymphocyte (NLR) ratio at diagnosis and early lymphocytes recovery on doxorubicin-based chemotherapy, may impact outcome in osteosarcoma. The aim of this study was to evaluate the prognostic value of hemogram parameters in patients with osteosarcoma treated with high-dose methotrexate and etoposide/ifosfamide (M-EI) chemotherapy.

Design/Methods: We retrospectively analyzed the prognostic value of various hemogram parameters at diagnosis and at different time points during therapy in a multicentric cohort of patients with osteosarcoma included in the French OS2006 trial and treated with M-EI chemotherapy.

Results: We analyzed 164 patients. Median age was 14.7 years (IQR: 11.6-17). Primary tumor location was limb in 137 patients (84%) and 71 patients (44%) presented metas-

tasis. 106/158 evaluable patients (67%) had good histological response. Median follow-up was 5.6 years (4.8-6.2) and 65 patients had relapse/progression. Three-years event-free survival (EFS) and overall survival (OS) were 71% (95%CI, 63.5-75.5%) and 86.5% (80-91%), respectively. In univariate analysis, blood count parameters at diagnosis and early lymphocyte recovery at day 14 had no impact on survival outcomes. Conversely, high Neutrophil/Lymphocyte Ratio (NLR) ratio at day 1 of the 1st EI chemotherapy (NLR-W4) was associated with reduced OS in univariate ($p=0.0055$) and multivariate analysis (HR=1.3, IC95% [1.1-1.53], $p=0.0019$), after adjustment on histologic response and metastatic status. An increase of NLR of 1 was associated with an increased risk of death of 30%. A cut-off of 2 had the higher sensibility and specificity (47% and 40%, respectively) on Youden index.

Conclusions: This study identifies a relevant prognostic association of NLR-W4 with survival outcomes for osteosarcoma patients treated with M-EI chemotherapy. Early identification and risk stratification therapy based on the NLR-W4 may improve outcome. Prospective studies are needed to confirm this finding along with a better understanding of the immunology of the disease.

V275 SIOP19-0112 | Clinical Characteristics and Outcomes of Pediatric Osteosarcoma in Thailand: Single Institutional Experience

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Background/Objectives: In developing countries, outcomes of pediatric osteosarcoma are significantly inferior since most patients encounter difficulty in receiving optimal treatment due to limited resources and disease abandonment. The objective of this study is to identify outcomes and explore barriers to achieve effective treatment including surgery type and/or chemotherapy regimens effecting outcomes of pediatric osteosarcoma.

Design/Methods: Medical records from newly diagnosed osteosarcoma between January 1, 1996 and December 31, 2016 were retrospectively reviewed and analysed.

Results: There were 29 patients with male to female ratio of 3:1 and mean age of 10.3 years. Common primary sites include femur (n=14, 50%) and tibia (10, 35.7%), respectively. Histopathology was conventional type osteosarcoma for 62.1% (n=18) and majority (n=19, 65.5%) were localized stage at diagnosis. Lung was the most common site of metastasis for 70% (n=7). Abandonment rate was 21% (n=6). Twenty-six (92.9%) patients underwent chemotherapy

and 23 (82.1%) of those had methotrexate containing chemotherapy regimen. Twenty-three (82.1%) patients underwent surgery including amputation and limb salvage in 6 (26.1%) and 17 (73.9%) of those respectively. Allograft and autograft were performed in 12 (70.6%) and 5 (29.4%) patients. At the end of study period: 11 (37.9%) patients alive with no disease, 5 (17.2%) alive with disease, 6 (20.7%) died from disease, 1 (3.4%) died from secondary malignancy. Chemotherapy included methotrexate was the significant factor associated with less relapse rate ($p=0.015$). Patients who underwent surgery had superior survival outcome than chemotherapy alone ($p=0.002$). Amputation versus limb salvage surgery either using allograft or auto-recycling graft were not affected survival outcomes ($p=0.64$ and 0.57) and relapse rate ($p=0.483$ and 0.597). The 2-year event-free survival and overall survival were 68% and 73%, respectively.

Conclusions: Surgery combined with methotrexate containing chemotherapy regimen remained essential for pediatric osteosarcoma patients regardless of types of surgery. Barriers to appropriate treatment needs to be identified and addressed.

V276 SIOP19-0670 | Clinical Characteristics in Children with Ewing Sarcoma Between 2010 and 2018 at the Instituto Nacional de Enfermedades Neoplásicas Lima – Perú

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Background/Objectives: Ewing Sarcoma is the second most frequent osseous tumor, the treatment is based on chemotherapy, surgery and radiotherapy, most patients in Perú are diagnosed with advanced disease, metastatic tumors, associated to intense pain and functional limitations, conservative surgery is rarely possible due to the size of the tumors. The principal objective of this study is to know the clinical characteristics of children with Ewing Sarcoma at diagnosis in our institution.

Design/Methods: This is a retrospective, descriptive study. All children younger than 15 years with Ewing Sarcoma diagnosed at the Instituto Nacional de Enfermedades Neoplásicas (INEN) between January 2010 and December 2018 were included. We had a sample size of 47 patients, STATA 14 was used for the statistical analysis.

Results: A total of 47 patients were identified, 28 patients were male (59.6%), nineteen patients were female (40.4%). The age ranges were between 1 month and 15 years, twenty three patients (48.9%) were metastatic at diagnosis, twenty seven patients (57.4%) were from the coast of Peru. Regarding the location of the tumor, 24 (51%) had axial location and 23 (49%) were appendicular, thirty patients (63%) had tumors bigger than 8 cm at diagnosis, 22% of the patients had surgical treatment at diagnosis.

Conclusions: Ewing Sarcoma is an extremely aggressive disease, our results showed a high percentage of metastatic diseases, this results encourage us to look for the causes of the diagnosis delay, evaluate the surgical management and response to chemotherapy and radiotherapy.

V277 SIOP19-0096 | TAE226, A Dual Inhibitor of Focal Adhesion Kinase and Insulin-Like Growth Factor-I Receptor, is an Effective Treatment for Ewing Sarcoma

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Background/Objectives: The outcomes for relapsed and metastatic Ewing sarcoma (EWS) is extremely poor. Therefore, it is important to identify the tumor-specific targets in these intractable diseases. High focal adhesion kinase (FAK) transcript expression levels in EWS cell lines are known. TAE226 is a dual inhibitor of FAK and insulin-like growth factor-I receptor (IGF-IR), while PF-562,271 is a dual inhibitor of FAK and proline-rich tyrosine kinase 2.

Design/Methods: We compared the cytotoxicity of TAE226 and PF-562,271 toward three EWS cell lines. Furthermore, we investigated the efficacy of TAE226 as well as its mechanism of action against EWS. TAE226 strongly inhibited proliferation of three cell lines when compared with PF-562,271. A stable EWS cell line with FAK and IGF-IR knocked down was established, and microarray analysis revealed dysregulated expression in various pathways.

Results: TAE226 strongly inhibited proliferation of three cell lines when compared with PF-562,271. TAE226 treatment of EWS cell lines induced cell cycle arrest, apoptosis, AKT dephosphorylation, and inhibition of invasion. We demonstrated that TAE226 drastically inhibits the local growth of primary tumors and metastasis in EWS using mouse models. Furthermore, the combination of TAE226 and conventional chemotherapy proved to exert synergistic effects.

Conclusions: TAE226 may be a candidate single agent or combined therapy drug to be developed for patients who have relapse and metastatic EWS tumors in future.

V278 SIOP19-1316 | Combined Analyses of Hypoxic Biomarkers and MRI Necrotic Volumes Might Predict Outcome in Pediatric Osteosarcomas at Diagnosis

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Background/Objectives: Despite the remarkable advances, osteosarcoma remains a bone cancer, where there is no objective marker able to predict at diagnosis the response to neoadjuvant chemotherapy or outcome. Therefore, the aim of this study is to correlate with patient outcome diagnostic MRI features (tumor volume and necrotic zones in the tumor) and hypoxic biomarkers' study on tumor specimens.

Design/Methods: A retrospective analysis was performed in our center on 30 patients diagnosed for high grade osteosarcoma (11 females, 19 males, 6 metastatic diseases). Parameters of diagnostic 1.5T MRI and tumors samples were collected. Volumetric measures of the entire tumor and the necrotic parts were performed on each T1 Fat suppressed post-contrast image of the tumor (slice thickness of 5 mm). A final volumetric 3-D reconstruction was calculated with Universal Viewer software (General Electric) for each tumor. The necrotic zones were defined as non-enhanced tumor parts. Immunohistochemistry was assessing the status of mTor and HIF1 alpha expressions in paraffin-embedded samples at diagnosis. Kaplan Meier analyses, Khi2 and Anova tests were used to evaluate marker impacts

Results: The population had a median OS of 48.5 months (8-122) and median EFS of 41 months (8-122). Seven patients relapsed with a mean time of 17.6 months (10-23). The higher necrotic volume (> 20 mL) was significantly linked to a worst 5-year EFS, 57% +/-13% (p=0.02). The mTor expression was present in 70% of the samples. The higher necrotic volumes tend to be linked to the mTor expression above 50%, as the HIF1 alpha expression above 5% (observed in 60% of the patients) tends to be linked to a higher proportion of tumor cellular part (p=0.08). No correlations were found between survivals or treatment responses and these hypoxic biomarkers.

Conclusions: The volume of tumor necrotic zones seems to be one of the prognostic markers that might be used in pediatric osteosarcomas.

V279 SIOP19-1532 | Treatment Outcomes of Pediatric Patients with Ewing Sarcoma Treated According to Euro Ewing 99 Protocol in Romania Between 2005-2015: A Single-Institution Experience

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Background/Objectives: The treatment of Ewing sarcoma (ES) requires specialized centers and multidisciplinary approach. From 2005 the Pediatric Oncology Department of the "prof. dr. Ion Chiricuta" Cancer Center in Cluj-Napoca, Romania, treated patients according to the Euro EWING 99 protocol. The aim of this study was to identify the treatment outcomes of pediatric patients with ES treated in our center.

Design/Methods: This is a retrospective study that reviewed the medical records of pediatric patients with ES treated between 2005 and 2015, in the Pediatric Oncology Department of the "prof. dr. Ion Chiricuta" Cancer Center in Cluj-Napoca, Romania, with follow-up until March 2019.

Results: A total of 23 pediatric patients (pts) with ES were included in this study. The median age at diagnosis was 12.9 years, 69.5% were male, and 30.4% were female. The primary tumor was in the extremities 13 pts (56.5%), the pelvis 7 pts (30.4%). Seventeen patients (73.9%) had localized disease at the time of presentation. All the patients received chemotherapy, 30.4% patients underwent only surgical resection and 34.78% only radiation therapy for local control. Out of 13 pts with the primary tumor in the extremities, 9 pts had limb sparing surgery. Two patients underwent high dose chemotherapy with autologous stem cell transplantation, both patients relapsed and died. At the end of treatment 82% pts were in complete response, 3 had progressive disease and 1 partial response. Six pts had relapsed. The overall survival (OS) at 5 years was 65%, with a median follow-up of 85.9 months. The OS at 5 years for patients with localized disease was 71%, and 69% for extremities tumors.

Conclusions: The treatment of patients in a reference center using international protocols and multidisciplinary teams improved the treatment outcomes and quality of life (more limb sparing surgeries) of patients with ES in Romania.

V280 SIOP19-0821 | Pazopanib, a Multikinase Angiogenesis Inhibitor, in Patients with Relapsed or Refractory Advanced Pediatric Sarcoma: Single Institutional Experience

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Background/Objectives: Given the importance of angiogenesis in sarcoma (PS), Pazopanib, an oral angiogenesis inhibitor that targets vascular endothelial growth factor receptor and platelet-derived growth factor receptor was explored

in children and adolescents with advanced bone and soft tissue sarcoma.

The aim of the study was to clarify the efficacy of pazopanib for refractory and recurrent sarcoma in children and adolescents.

Design/Methods: Between 2016–2018, children and adolescents diagnosed with recurrent or refractory bone or soft tissue sarcoma received Pazopanib with the objective of treating local recurrence and / or metastasis.

Patients (pts) with pediatric sarcoma with documented progression after > 2 chemotherapy salvage protocols, with adequate performance status, and good organ function were eligible. Pazopanib at a dose of 400 - 800 mg was given daily. The primary end point was progression-free survival (PFS) at 12 weeks. Secondary end points were response and safety.

Results: Nine pts were enrolled, median age 12 years (y), (1.5y–18y). Histological diagnosis included bone sarcoma in 4 pts (2 pts with Ewing sarcoma, 2 pts with osteogenic sarcoma), rhabdomyosarcoma in 3 pts, undifferentiated sarcoma in 2 pts, both local relapse and metastases were observed in 4 pts, metastases only were documented in 5 pts. The most frequent drug-related toxicities were hair discoloration (white), transaminase and CPK elevation (grade 2), nausea and vomiting (grade 1), diarrhea (grade 1), no grade 3 - 4 toxicity was noted. Median PFS: 5.1 months (2m–8.5m). Four pts are still alive on therapy, 1 pt with osteogenic sarcoma in CR, 2 pts with ewing sarcoma in partial response, 1 pt with ewing sarcoma with progressive disease, 5 pts died.

Conclusions: Pazopanib was well tolerated in patients with relapsed, advanced pediatric sarcoma and demonstrated interesting activity that warrants additional studies in a larger population.

V281 SIOP19-1596 | Addition of Mifamurtide to Standard Chemotherapy for Osteosarcoma: A Single Centre Experience

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Background/Objectives: The outcome of paediatric patients with osteosarcoma has remained unchanged in the last few years and the complex biology of the tumour makes it difficult to find new effective directed therapies. Mifamurtide is a synthetic lipophilic analogue of muramyl dipeptide, which stimulates immune responses via production of proinflammatory cytokines and adhesion molecules and is currently indicated for the treatment of high grade resectable non metastatic osteosarcoma in combination with standard chemotherapy.

Design/Methods: We performed a retrospective analysis of the patients treated for localised osteosarcoma at Birmingham

Children's Hospital between June 2011 and July 2018. The aim was to evaluate the outcome of our patients and the possible role of mifamurtide in the results.

Results: 21 patients were diagnosed with osteosarcoma between the selected time period. 14 of these patients had a localised tumour and all of them received mifamurtide as part of their treatment at 2 mg/m² twice weekly for 12 weeks, followed by once-weekly treatments for an additional 24 weeks. 2 patients are still receiving treatment and 12 completed therapy. Currently all 14 patients continue to be in complete remission (follow up 0–80 months). The most common side effect noticed was headache, but no other complications were detected during or after infusions.

Conclusions: Mifamurtide is a safe and well tolerated drug that has previously demonstrated an increase in overall survival (OS) in non-metastatic patients. In our cohort, the current OS is 100% which is higher than previously published in the literature for non-metastatic patients (50–70%). Further randomised prospective studies should be made to support the conclusions and eliminate possible confounding factors. The limitations of this review are the small number of patients and the short follow up period for some of them.

V282 SIOP19-1561 | Leucoencephalopathy is a Common Complication in Patients Treated with High Dose Methotrexate

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Background/Objectives: Methotrexate encephalopathy is a severe complication due to high dose methotrexate (HDMTX). Little is known on its incidence and long-term outcome in osteosarcoma patients.

Design/Methods: We analyzed incidence of neurologic complications, neurocognitive performance and brain MRI during and after treatment in osteosarcoma patients treated with HDMTX and etoposide-ifosfamide (EI) according to OS2006 protocol in the pediatric department of Gustave Roussy between 2007 and 2015. All patients who had received ≥4 courses of MTX and could have at least one brain MRI during or after the treatment were eligible. Leucoencephalopathy (LE) was defined by the presence of hypersignal of the periventricular white matter on sequence T2 FLAIR and graded according to Wilson staging system.

Results: Among 60 patients included in OS2006 trial, 54 met eligibility criteria. At least one episode of neurological complication due to MTX was reported in 40 (74%) patients. It was

limited to headaches or severe depression in 37 and regressed in most patients within a few days or months.

LE was detected on at least one MRI in 50 patients (92%) (7 grade (G) G1, 16 G2 and 22 G3; missing 4). In 45 patients with brain MRI performed after treatment (median delay 3 years), LE was detectable in 36 (8 G1, 15 G2, 13 G3).

Results of neuropsychological assessment performed during treatment and at least one year after its end were compared in 32 patients. The median scores obtained at first and second evaluation were 103 and 106 (NS) for verbal IQ, 90 and 96 ($p=0.03$) for performance IQ, 86 and 95 for working memory ($p=0.012$) and 86 and 95 for processing speed ($p=0.077$).

Conclusions: Neurotoxicity is a frequent complication in patients treated with HDMTX-EI. It is associated with a high incidence of LE and moderate alteration of cognitive functions which improves after the end of the treatment.

V283 SIOP19-0022 | Clinical Characteristics ANS Survival of Pediatric Patients with Metastatic Osteosarcoma at the Hospital Civil de Guadalajara Dr. Juan I. Menchaca

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Background/Objectives: Osteosarcoma (OS) is the most common primary bone tumor in the pediatric age, it is located mainly in the metaphyseal region of long bones, 20% of patients have metastasis at diagnosis. (1-2). The objective is to describe the clinical characteristics of pediatric patients with metastatic disease

Design/Methods: An analytical cross-sectional study that included patients under 18 years of age, characteristics such as age, size and tumor location, fracture at diagnosis, pain, chemotherapy, tumor necrosis, response to treatment, survival were evaluated. The variables were compared between localized OS and metastatic, descriptive analyzes were performed by using frequencies, the variables were compared using the T-student test. All calculations were made in the SPSS 20 program.

Results: We evaluated 37 pediatric patients from January 1, 2007 to December 31, 2016; 13 (35%) presented metastatic disease, the median age for both groups was 13 years (SD: 2.8), no significant differences were found with respect to gender ($p=0.627$), tumor size ($p=0.2$), fractures ($p=0.42$), a statistically significant difference was found in the duration of pain ($p=0.046$), response criteria (0.000), adjuvant chemotherapy (0.027).

Conclusions: 35% of the patients treated in the institution debutan with metastatic disease at diagnosis, contrasts with what is reported in the literature that is 20% (2-4). The complete response was presented in 58% vs 30%. Overall survival and event-free survival was 30% in metastatic disease compared to patients with localized disease who achieved an OS of 58% and an SLE of 30%.

V284 SIOP19-1721 | Multicentric Study of Interval-Compressed-Multiagent Followed by Maintenance with Metronomic Chemotherapy for Metastatic Ewing Sarcoma (ES): Results of the Latin American Pediatric Oncology Group (GALOP) Trial

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Background/Objectives: High rate of metastatic ES and the limitations in care delivery are still frequently observed in developing countries. The need to develop adapted regimens in these settings motivated pediatric oncologists to design GALOP trial.

To report preliminary results with the primary endpoint to investigate the feasibility, and event free survival (EFS) of combined modality therapy with interval-compressed VDC (vincristine, doxorubicin, cyclophosphamide)/IE (ifosfamide/etoposide), and metronomic chemotherapy (MC).

Design/Methods: Prospective phase III trial. Between August 2011 and August 2018, 181/ 463 (39%) patients with metastatic ES were enrolled in GALOP Trial, across 34 centers of Argentina, Brazil, Chile, and Uruguay. Therapy consisted of 9 alternating cycles of Induction every 14 days, followed by local and metastatic site control, and 5 cycles of consolidation every 21 days followed by MC (cyclophosphamide/vinblastine) for 1 year. Toxicity was assessed according to CTC-criteria v2.0.

Results: Median age was 12 years (range 1-31). According to the primary site 63.5% were axial, size was ≥ 8 cm in 68.5% and had bone origin 74.9% of patients.

Overall Response rate after induction was 89.1%. Local and metastatic site control was performed in 58.5% and 46.9% of patients, respectively.

With a median follow up of 31.8 (range 1-92.1) 5-year OS and EFS was 31.7% and 29.3%, respectively.

Metastasis site was lung in 45% of pts, extra-lung in 28.9%, Bone Marrow in 2.8%, and combination (Lung + others) in 23.3%. The 5-year OS and EFS according to metastatic site was 48.8% and 35.4%, 31% and 28.9%, 25% and 25%, 18.4% and 16.4%, respectively. ($p=0.03$; and 0.044 respectively, lung vs other sites).

Conclusions: Implementation of a multi-institutional protocol in 4 countries in South-America was feasible. Although our series showed a higher rate of metastatic disease, 5-year OS and EFS was similar to those reported by cooperative groups in high-income countries.

V285 SIOP19-0126 | A Systematic Review and Meta-Analysis of the Signs and Symptoms of Bone Tumours in Children and Young People

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Background/Objectives: Bone tumours in children and young people are often associated with significant diagnostic delay. Experience from the HeadSmart campaign showed that a national awareness campaign based on high quality evidenced based guidance can promote earlier diagnosis. We conducted a systematic review and meta-analysis on bone tumours in order to understand the core signs and symptoms.

Design/Methods: Medline, Pubmed and Embase databases were searched without language restriction from January 2005 – August 2015. Key words were “bone tumour (s)”, “bone tumor (s)”, “bone neoplasm (s)”, “diagnosis”, “signs (s)”, “symptom (s)”, “presentation (s)”. All references were restricted to “all child”. All papers discussing bone tumour presentation and time to diagnosis were included. A standard data extraction form was used. Pooled proportions (%) of children with each sign or symptom at diagnosis were estimated. Subgroup analysis of Osteosarcoma and Ewing sarcoma was undertaken.

Results: The search strategy identified 15477 papers. 713 papers were reviewed in full; 11 met the inclusion criteria, describing the symptoms and signs at diagnosis in 1246 children. 29 symptoms and signs were recorded but only those that occurred in 2% or more of patients are reported. These were pain (76%), swelling (21%), fever (4%), history of

trauma (3%), functional limitation (3%), palpable mass (3%), pain and swelling (2%), volume increase (2%), limp (2%) and pathological fracture (2%). The key finding in subgroup analysis was fever in Ewing sarcoma ($n=733$) but no fever in Osteosarcoma ($n=435$).

Conclusions: This is the first systematic review on paediatric bone tumours to our knowledge. It provides strong evidence of the most common presenting symptoms and will form the basis of a new clinical guideline in the assessment and investigation of suspected bone tumours. This will form key messaging in our new national awareness campaign called ChildCancerSmart, raising awareness of symptoms amongst the public and healthcare professionals for earliest possible diagnosis.

V286 SIOP19-1712 | Multicentric Study of Interval-Compressed Multiagent and Metronomic Chemotherapy for Patients with Ewing Sarcoma: Results of the Latin American Pediatric Oncology Group Trial for Metronomic Chemotherapy

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Background/Objectives: The current Latin-American Pediatric Oncology Group trial examined whether a maintenance metronomic chemotherapy (MC) administration of continuous, low-dose, low-toxicity chemotherapy with vinblastine 3 mg/m² intravenous weekly and 25 mg/m² daily oral cyclophosphamide after standard chemotherapy, would improve event-free survival (EFS) in patients with non-metastatic and metastatic Ewing sarcoma.

Design/Methods: The study design included 14 cycles of interval-compressed chemotherapy with vincristine, doxorubicin, cyclophosphamide alternated with ifosfamide, etoposide; surgery and/or radiotherapy for local treatment. After completing conventional chemotherapy, patients with localized tumors were randomized according to gender, age, site of primary tumor and tumor size to receive 1 year of

MC or follow-up. Metastatic patients received 14 cycles of chemotherapy and received 1 year of MC. Primary endpoint was 5-year event-free survival (EFS)

Results: Four hundred sixty-three patients were enrolled from August 2011 to August 2018, median follow-up 32.3 months (0.2-105 months). For 282 patients with localized tumors, 104 were randomized to MC, 84 completed treatment. Five-year EFS was 69.2% for MC vs 69.3% for conventional chemotherapy alone ($p=0.751$). According to gender 5-year EFS was 66.9% for males vs 69.4% females ($p=0.937$); age 73.4% ≤ 14 years-old vs 61.2% > 14 years-old ($p=0.081$); primary site 65.8% non-pelvic vs 81.8% pelvic tumors ($n=11$) ($p=0.423$); tumor size 74.1% ≤ 8 cm vs 66.1% > 8 cm ($p=0.247$). For 181 metastatic patients, 71 received MC; 5-year EFS was 44.4%. The most common grade 3-4 toxicity for MC was neutropenia, 26.9% of cycles; vs 47.2% of conventional chemotherapy cycles for nonmetastatic and 49.3% for metastatic patients.

Conclusions: According to current follow-up, EFS with addition of MC is not statistically superior to chemotherapy alone in patients with localized Ewing sarcoma. Further analysis is necessary to determine if there are specific subgroups that would benefit from this approach.

Acknowledgements to Data Managers: Eric Warriner, Argentina; Fernanda Lima, Brazil; Mariela Fuenzalida, Chile; Anaulina Silveira, Uruguay.

V287 SIOP19-0272 | Clinically Significant, Novel Biological Classification of Osteosarcoma Based on Gene Expression Profiling

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Background/Objectives: Osteosarcoma is classified based on clinical features or pathological findings. Most osteosarcoma gene expression profiling studies have compared sample groups defined by clinical characteristics such as outcome or initial metastasis. However, since biological features never achieve perfect one-to-one predictions of clinical features, unsupervised clustering with expression profiles could be a better approach to defining biological groups. We aimed to classify osteosarcoma according to gene expression profiles and find novel target genes that characterize each group.

Design/Methods: Clinical characteristics of clusters post unsupervised consensus clustering on expression profiles of 53 osteosarcoma samples deposited in Gene Expression Omnibus (GSE21257) database were compared. We further conducted differential expression analysis between the clusters to identify characteristic gene expression of each cluster.

Results: Unsupervised consensus clustering based on gene expression status revealed 2 distinct clusters that did not exhibit significant correlations with gender or histology. Compared to cluster B, cluster A was associated with significantly worse event-free-survival ($p<0.01$, log-rank test) and overall-survival ($p=0.037$). Cluster A was significantly associated with higher rate of metastasis at the time of their initial diagnosis. Moreover, further analyses in cases without metastasis at the time of initial diagnosis revealed that cluster A was associated with significantly faster events than cluster B ($p=0.027$), indicating that cluster A showed worse prognosis even without initial metastasis. Genes which showed significantly high expression in cluster A included several oncogenes such as *YES1*, *YAP1*, and other potentially targetable genes, which may be responsible for the aggressive features of the cluster. The same clustering was also applicable to an expanded cohort (GSE42352).

Conclusions: Although validation in other cohorts is warranted, our analysis with unsupervised clustering method has revealed a clinically significant, novel biological classification in an osteosarcoma cohort.

Solid Non Brain Tumours - Germ Cell Tumours

V288 SIOP19-0623 | Malignant Germ Cell Tumors in Children: Results of the TGM 95 Protocol at the Pediatric Hematology and Oncology Department of Rabat- Morocco

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Background/Objectives: Malignant germ cell tumors (MGCT) in children constitute a group of rare diseases, which are characterized by big clinical, radiological, biological, anatomo-pathological, and cytogenetic heterogeneities. Our objectives are to report the results obtained in patients treated with the TGM 95 protocol, to evaluate the treatment tolerability by studying the acute toxicity; and the effectiveness of treatment by studying survivals.

Design/Methods: It is a retrospective descriptive study of children with extracerebral malignant germ cell tumors who were treated according to SFOP/SFCE TGM 95, followed at the Department of Pediatric Hematology and Oncology (DPHO) at Rabat, between January 2005 January 2016.

Results: Sixty cases were included, representing 1.64% of the cases of all pediatric tumors followed by DPHO, the median age was 30 months and the M/F ratio was 0.6. The locations were gonadal in 60% and sacrococcygeal in 21.7%

of cases. The predominant histological types were: yolk sac tumor (51%), immature teratoma (15%), and mixed GCT (15%). Ninety-five percent of patients had received chemotherapy with 82% of them had a surgical treatment. Surgery was the only treatment for 5% of patients. The rates of toxicity grade 3-4 were 75% and 39% for the group of patients treated by VIP (Etoposide, Ifosfamide, Cisplatin) and VBP (Vinblastine, Bleomycin, Cisplatin) respectively. The hematological and digestive toxicities were the most recorded. The complete remission rate was 60% of cases, the relapse was 8.3%, the tumor progression was 11.7%, and the death was 3.3%. 16.7% of patients had abandoned treatment. Overall survival at 5 years was 89.1%.

Conclusions: Therapy results of gonadal MGCT were good compared to others extracranial locations. The relapse or refractory diseases after chemotherapy have a dismal prognosis; therapeutic strategies remain to be defined in such situations.

V289 SIOP19-0780 | Neonatal Choriocarcinoma: Experience of the "Société Française de Lutte Contre Les Cancers et Leucémies de L'Enfant et de L'Adolescent" and Review of the Literature

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Background/Objectives: Neonatal choriocarcinoma is an exceptional and poorly known malignant trophoblastic tumor of the new born. It is the result of the metastatic evolution of maternal placental choriocarcinoma. Rapidly fatal without appropriate treatment, choriocarcinoma is nowadays curable with polychemotherapy, based on germ cell tumor treatments. Diagnosis is based on abnormal increase of Human Chorionic Gonadotropin (HCG). The aim of this study was to describe clinical, therapeutic and evolutive presentation of new borns and infants presenting with neonatal choriocarcinoma.

Design/Methods: Patients presenting with neonatal choriocarcinoma in France from 2000 to 2015 were retrospectively included, and 4 patients, aged 0 to 6 months, were found. Were studied clinical and paraclinical presentation, used therapeutics and evolution of each of them. Survival prognostic factors were then searched, helped by a complete review of the literature.

Results: Digestive and/or haemorrhagic signs were most of the time the first symptoms of neonatal choriocarcinoma.

Despite always increased HCG, imaging could also show « vascular » lesions in invaded organs. Overall survival over the past 60 years was dark, with a median survival of 3 months, but tended to improve since the 1990s. Two of the four patients included in the study survived without sequelae. A long diagnostic delay, polymetastatic disease and brain or pulmonary involvement seemed to be poor prognostic factors.

Conclusions: Diagnosis of new born choriocarcinoma must be evoked in front of any unexplained neonatal haemorrhagy, and systematically in case of maternal placental choriocarcinoma. Biopsy and/or initial surgery are strictly prohibited because of major haemorrhagic risk, and HCG increase is sufficient to confirm diagnosis. Chemotherapy, based on platinum salts, is a therapeutic emergency, and adjuvant surgery must be discussed case-by-case.

V290 SIOP19-0923 | Pediatric Gastric Teratoma: 6 Cases in a Limited Resources Center

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Background/Objectives: to describe the clinical manifestations, treatment and outcome of patients with gastric teratoma.

Design/Methods: Case series.

Results: from 2011 to 2016, we had 6 cases of pediatric gastric teratoma: 5 boys and 1 girl. Median age is 12.5 months (2 days- 64 months). Clinical manifestation mainly was abdominal mass. All tumor was removed via laparotomy: 5 cases had partial gastrectomy and 1 case had distal esophagectomy combined with partial gastrectomy. Post-operative was uneventful. There were 2 case of mature teratoma, 4 immature teratoma (two grade 2 and two grade 3), no chemotherapy was given. Mean time follow-up was 80.2 months (36-96 months, one loss of follow-up). No signs of recurrence was noted.

Conclusions: Gastric teratoma is a rare pediatric primary gastric tumors. Operation is the treatment of choice.

V291 SIOP19-0366 | Disorder of Sex Development with Germ Cell Tumor: Who is the First Uncovered?

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Background/Objectives: Disorders of sex development (DSD) are rare conditions, known to predispose to gonadal or mediastinal germ cell tumors (GCT), but few is known about the timing of DSD discovery.

Design/Methods: Patients with DSD included in 2 consecutive French pediatric GCT protocols (TGM95 and 13) were analyzed with focus on the timing and symptoms leading to DSD discovery.

Results: Fifteen patients were identified among 226 ovarian, 157 testicular and 24 mediastinal GCTs. Ten phenotypic females (aged 6 to 18 year) had 46, XY karyotype and developed gonadal GCTs (bilateral in 4 cases). All but the one aged 6, had signs of pubertal development and none had sexual ambiguity. One had menstruation. Tumors were seminomatous in 8 cases, non seminomatous (NSGCT) in 2 cases. Karyotypes were made after GCT diagnosis in 8 cases (the reasons were: bilateral tumors (4), associated gonadoblastoma/streak gonad/absence of egg follicles (3), or systematic for seminomatous histology (1)). For the 2 remaining cases, it was made for nuchal translucency thickness and polymalformative syndrome, respectively 5 and 15 years before the diagnosis of GCT. One patient had an ambiguous male phenotype (hypospadias) leading to 46, XY/45, X0 mosaicism discovery before the diagnosis of testicular NSGCT at age 16. The remaining 4 males (aged 10 to 17y) presented with mediastinal NSGCT (metastatic in 2 cases) uncovering the Klinefelter syndrome, despite a typical phenotype with atrophic testicles and big size in all cases.

Conclusions: DSD are often uncovered at the time of GCT diagnosis. This should prompt oncologists to rule out a DSD in patients with GCT at mediastinal and ovarian site. Lack of genital ambiguity and presence of pubertal development precludes from precancerous diagnosis in 46, XY phenotypic females. Conversely, recognition of clinical signs of Klinefelter by local physician could potentially lead to earlier GCT detection.

V292 SIOP19-0822 | Favorable Outcomes for Children with Biopsy Proven Malignant Extracranial Germ Cell Tumours 1990-2015: A First National Report by the South African Children's Cancer Study Group (SACCSG)

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Background/Objectives: Malignant extracranial germ cell tumours (MEGCTs) require a comprehensive, multidisciplinary team approach to achieve good survival rates and good quality survival. In preparation for harmonised national treatment protocol development, a national retrospective analysis was performed to evaluate treatment outcomes of children and adolescents with MEGCTs.

Design/Methods: Retrospective data from nine South African paediatric oncology units was analysed to determine 5 year overall survival (OS) and prognostic factors. JEB (carboplatin, etoposide, bleomycin) and BEP (bleomycin, etoposide, cisplatin) were most frequently used regimens and long term toxicities are described.

Results: Between January 2000 and December 2015, 217 children and adolescents were diagnosed with MEGCTs, 64 males (median 25.67 months) and 153 females (median 98.33 months). Stage significantly affected 5 year OS: Stage 1 (95.9%), stage 2 (94.3%), Stage 3, (75.2%) and Stage 4 (59.8%) (p=0.00002, CI 95%). Protocol use also impacted outcome: JEB 87.6%, BEP 80.5%, PEb 66.5% and other 49.6% (p=0.002). Only 6/82 (7.3%) patients who received cisplatin-based chemotherapy had a documented glomerular filtration rate (GFR) at diagnosis and only 10/82 (12.2%) an audiogram. Thirteen patients receiving cisplatin-based chemotherapy developed hearing deficits, 4 were severe. Causes of death in 36 patients included disease progression (30), infection (3), pulmonary fibrosis (1), secondary acute myeloid leukaemia (1) and surgical complications (1).

Conclusions: In the largest cohort of MEGCTs from sub-Saharan Africa, we demonstrate a five year OS of 80.3% with Stage 4 patients having only achieved a 59.9% OS. Protocol use impacted survival, with JEB showing clear superiority. Of concern, GFR and audiogram assessment pre-chemotherapy was performed in a minority of patients.

Development and implementation of a standardised national protocol is intended to improve survival, especially for those with advanced disease, and will standardise the management of patients with long-term sequelae.

V293 SIOP19-0107 | Neonatal Ovarian Cysts: Clinical Characteristics, Treatment Choice and Outcome

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Background/Objectives: The treatment choices of neonatal ovarian cysts are challenging and various in literatures. To analyze and discuss the clinical features, treatments and outcomes of neonatal ovarian cysts can help to standardize treating-process.

Design/Methods: The medical records of 86 children under 3 months of age who were diagnosed with neonatal ovarian cysts from January 2011 to March 2018 in our center were collected and retrospectively analyzed.

Results: AFP were physiologically elevated in all cases. 76.9% of children had a high E2 level, and 68.4% of children had a high FSH level. 77 patients were followed up, 39 patients were treated conservatively, and 38 patients underwent surgery. 71.1% of the patients received ovarian cystectomy, others were underwent oophorectomy or salpingo-oophorectomy. The mean diameters of cysts in conservative group and surgical group were 30.3 ± 15.4 mm and 54.2 ± 18.9 mm respectively, while the difference was significant ($P < 0.001$). In the conservative group, 82.1% of the cysts completely resolved. The Kaplan-Meier survival curve indicated that the median time for complete regression of cysts was 4 months. 95% of cysts completely resolved in 18.2 months, and there was no significant difference in the regression time between simple cysts and complex cysts ($p = 0.519$). Only one patient relapsed after conservative treatment.

Conclusions: The outcome of neonatal ovarian cysts is fairly good. When the cyst is large (>5 cm) and complex, it tends to be treated surgically. Smaller cysts or simple cysts tend to be conservative and have a high rate of regression. Too aggressive surgical exploration is not recommended for small and asymptomatic complex cysts.

V294 SIOP19-1440 | Testicular Surveillance Following Orchidopexy and the Stage of Cancer at Presentation in Adult Patients who Underwent Previous Orchidopexy

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Background/Objectives: Undescended testicles are a recognised risk factor for testicular cancer. Orchidopexy is one of the commonest operations performed in Paediatric Surgery. A successful orchidopexy achieves a number of goals including making the testicle accessible for surveillance. Paediatric surgeons are expected to counsel patients about the potential risk and need to self examine in adulthood. The study objectives were to examine if Paediatric surgeons are giving such advice and if adult patients with testicular cancer and previous orchidopexy present with early stage disease.

Design/Methods: This was a five-year observational, retrospective collaborative study between a tertiary Paediatric surgical unit and its regional Adult testicular cancer service, examining the nature of counseling given if any and if it was influenced by the location of the testicle in children. The local incidence of cancer in adults with previous orchidopexy is estimated and the stage of disease is recorded for five years.

Results: At our institute orchidopexy was performed in 228 patients who completed a mean follow up of 11.9 (1-40) months. Of these 22 (9.6%) underwent a staged surgery whilst the rest had a single operation. Twenty-two patients (9.6%) had documented advice to self examine from puberty onwards. The advice was not influenced whether the surgery was staged or single ($p = 0.39$). During the five years 133 adults were diagnosed with testicular cancer, 6 (4.5%) were cases of previous cryptorchidism, seminoma ($n=5$) and Non Seminoma Germ Cell Tumour (NSGCT) ($n=1$). All seminoma cases were stage I, NSGCT was stage IIa, half of the cancer cases needed chemotherapy.

Conclusions: In our study the incidence of cryptorchidism in testicular cancer was 4.5%, with all cancer patients presenting with early disease. Despite documented advice to self examine being low (9.7%), it is likely that verbal advice was given and not documented and patients were self-examining.

V295 SIOP19-0622 | Pure Pediatric Ovarian Immature Teratomas: The French Experience

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Background/Objectives: To describe characteristics and outcome of pediatric ovarian immature teratomas (IT), to better define the place of chemotherapy.

Design/Methods: Children with ovarian IT enrolled in TGM95 and TGM2013 studies were analysed. Norris grading and FIGO (International Federation of Gynecology and Obstetrics) staging system were used. Gliomatosis peritonei (GP) and mature teratoma peritoneal implants did not result in upstaging, whereas IT peritoneal implants did.

Results: Thirty-seven cases were identified at a median age of 11 years (range=1-18), 36/37 stage I (17 stage IA, 14 stage IC and 5 stage IX), including 7 patients with GP, and 1 stage IIIB (IT peritoneal implants). Histological review was performed in 31 cases: 14 Norris low-grade (I) and 17 high-grade (II/III) tumors. All patients had surgery first: 22 underwent unilateral oophorectomy, 14 unilateral adnexectomy and 1 bilateral cystectomy. No extensive GP surgery was performed. Seven patients received adjuvant VBP (vinblastin, bleomycin, cisplatinum). The reasons for chemotherapy were tumor rupture (n=6, 2 had GP) and stage III (n=1). After a median follow-up of 27 months (range=3-238), 2 events occurred: 1 bilateralization (initial stage IX, grade I) and 1 TI peritoneal relapse (initial stage IA, grade II), 10 and 11 months after diagnosis, respectively. Both were successfully treated with platinum-based chemotherapy and delayed surgery. No stage-IC-patients treated without adjuvant chemotherapy relapsed (4 grade I and 3 grade III). None of the 7 GP patients suffered from progressive disease. Two-year EFS and OS were 94% (95%CI= 80-98%) and 100%. No significant impact of grading on EFS was observed (p=0.73).

Conclusions: The current series confirms the excellent prognosis of pediatric ovarian IT, even with GP or rupture, pleading for conservative surgical approach in GP and against systematic adjuvant chemotherapy, even in ruptured tumors.

Acknowledgment: All participating SFCE centers.

V296 SIOP19-0624 | Survival Outcomes and Long-Term Follow-Up in Children Treated for Ovarian Non Seminomatous Germ Cell Tumors in the French TGM-95 Study

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Background/Objectives: To analyze characteristics and outcomes with actualized very-long-term follow-up data from patients treated for ovarian non seminomatous germ cell tumors (NS-GCT).

Design/Methods: Children (≤ 18 years) treated for ovarian NS-GCT in 1995-2005 in France and Belgium were included in TGM-95. Primary gonadal resection was recommended whenever feasible. Patients with localized-completely-resected tumors (Figo-stage IA) had no adjuvant treatment (low-risk, LR). Patients with advanced-stage (Figo-stage $\geq$ IC) received 3-5 VBP cycles (vinblastin-bleomycin-cisplatinum) in intermediate-risk disease (IR: Figo-stage IC-II-III and AFP $<$ 15,000ng/ml) or 4-6 VIP (etoposide-ifosfamide-cisplatinum) in high-risk (HiR: metastatic and/or AFP $\geq$ 15,000ng/ml).

Results: 77 patients were included (median age=12 years, 43 with pure yolk-sac tumor and 34 with mixed NS-GCT). Primary surgery was performed in 55/77 patients. Fourteen patients were LR (12 stage IA, 2 retrospectively stage IC), 26 IR (12 stage IC, 12 stage II-III, 2 not-available) and 37 HiR (8 metastatic, 29 loco-regionally advanced, including 24/29 AFP $\geq$ 15,000ng/ml). After a median follow-up of 13 years (range=1-23), 9 events (including 5 relapses/bilateralizations and 2 secondary acute-myeloid-leukemias) and 6 deaths occurred. All relapses/bilateralizations occurred in LR (n=4, including the 2 retrospectively-stage-IC) and IR groups (n=1), within 2 years post-diagnosis. Four cases of contralateral mature teratoma were observed, within 8 years after diagnosis. Five-year EFS and OS were 89% (95%CI=80-95%) and 95% (95%CI=87-98%). Bilateral gonadectomy was performed in 6/77 patients. At a median age at last news of 26 years (range=12-35), 28 pregnancies were reported in 19 patients (25 natural, 3 medically-assisted), leading to 23 healthy-born children. Three patients treated with ifosfamide/platinum-based chemotherapy suffered from chronic-kidney-disease. Long-term hearing function was evaluated in 19/69 patients treated with cisplatinum: 7 Brock-grade-1 and 1 grade-2 were described.

Conclusions: Ovarian NS-GCT have an excellent prognosis even in advanced cases with conservative surgery and platinum-based chemotherapy, with few long-term complications. The risk of contralateral mature teratoma makes monitoring of the single ovary remaining necessary.

Acknowledgment: All SFCE and Belgian participating centers.

V297 SIOP19-0040 | Leydig Cell Tumors In Children: A Study of Rare Testicular Tumors Over A Period of 15 Years in a Single Institute

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Background/Objectives: Testicular tumors in children are rare comprising 1% of all childhood tumors. Sex-cord stromal tumors are very uncommon heterogeneous group of them and Leydig cell tumors are rare subtypes comprising 7-10 of them.

This study aimed at reporting and studying Leydig cell tumors treated in the Main Children's Hospital of Alexandria, University, Egypt over a period of 15 years.

Design/Methods: All cases of Leydig cell tumors reported were studied concerning the following: age, ways of presentation, the laboratory data including serum testosterone level and tumor markers (AFP&HCG). Imaging modality used for diagnosis was also reported.

Treatment procedures for the cases were reported and studied.

Results: Nine cases of Leydig cell tumors were reported: 5 were retrospective and 4 were prospective. Eight cases with age range 4-7 years and only one case was 8 months old. All cases presented with manifestations of pseudo-precocious puberty in the form of enlarged penis and supra-pubic hair. Scrotal examination revealed unilateral testicular mass. Serum testosterone level was high in all cases and tumor markers (AFP&HCG) were negative in all cases. US revealed unilateral solid testicular swelling in all cases.

All cases were treated surgically in the form of total orchiectomy in 8 cases and testicular sparing surgery in one case. Histopathological study revealed benign Leydig cell tumors in all cases. Follow-up revealed regression of the pseudo-precocious puberty within a period of 8-11 months

Conclusions: *Leydig cell tumors should be put in mind in our clinical practice once we are confronted with a boy presented by pseudo-precocious puberty.

*Testicular tumors in pre-pubertal boys with negative tumor markers (AFP&HCG), Leydig cell tumors should be considered and differentiated from other germ cell tumors including testicular carcinoma.

V298 SIOP19-1516 | Malignant Germ Cell Tumors (MGCT) in Children: Retrospective Study in the Center of Tunisia

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Background/Objectives: Malignant Germ cell tumors (MGCT) of childhood are rare and include a highly heterogeneous tumors regarding to their clinical and histological appearance. The aim of this study is to describe the clinical characteristics and evaluate the therapeutic results in the center of Tunisia.

Design/Methods: This is a retrospective study including 36 cases of MGTC treated between 1999 to 2017 at the medical oncology department of Farhat Hached University Hospital of Sousse Tunisia according to TGM95 SIOP protocol.

Results: The median age was 8 years old (1 month to 16 years) with a sex ratio of 0.4. Swelling and pain were the most frequent symptoms with a median delay of 3 months for consultation. AFP levels were elevated in most cases (75%). The most common pathological tumor types were Yolk sac tumor (25%), immature teratomas (25%) followed by Dysgerminoma (19%), and mixed tumors (11%). Gonadal tumors were observed in 52%. For extragonadal tumors, sacrococcygeal presented 30.6% of cases. Locally advanced disease stage (III, IV) was observed in 50% of cases. The treatment consisted of neoadjuvant chemotherapy for 08 patients with partial response. Surgery was performed for 80% with R0 resection in 44.4% of cases. Thirteen patients received adjuvant chemotherapy. Adjuvant Radiation therapy was indicated in two patients. Ten patients had a local recurrence, treated by chemotherapy added or not to surgery. The median disease free survival (DFS) was 7.5 months. The Overall survival (OS) and (DFS) at 5 years were 70% and 69% respectively.

Conclusions: The multidisciplinary approach has improved survival rate but in our limited resource countries we need more efforts for diagnosis and treatment to achieve a complete remission of all our children.

Solid Non Brain Tumours - Liver Tumours

V299 SIOP19-0895 | Post-Chemotherapy KI-67 Index Might be an Important Indicator in Predicting Recurrence After Surgery in Pediatric Patients with Hepatoblastoma

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Background/Objectives: Ki-67 has been recognized as a biomarker for cell proliferation. Previous studies have shown that its expression is associated with malignancy of tumors and prognosis. However, little is known about

its clinical significance in the prognosis of hepatoblastoma. This retrospective study investigated the prognostic value of post-chemotherapy ki-67 in pediatric patients with hepatoblastoma.

Design/Methods: Patients with primary hepatoblastoma who were treated and followed up in our centre from March 2010 to February 2017 were identified. All received neoadjuvant chemotherapy and surgery. Ki-67 index was measured in all cases. Diseases were closely monitored with both serum and imaging studies after surgery. Histology, PRETEXT staging, demographic information, ki-67 index, and survival were analyzed.

Results: A total of 46 patients were identified. Twenty-nine patients experienced no recurrence after surgery with a median follow-up of 52 months (range, 24 to 87 months). Relapse occurred in 17 patients within 2 years after surgery. Median time to relapse after initial tumour resections was 5 months (range, 1 to 21 months). No statistically significant difference was found in PRETEXT staging ($p=0.079$), histology ($p=0.321$) and gender ($p=0.683$) between patients with recurrent diseases and those without. Children with relapse were older at surgery (mean age, 43 vs 20 months; $p<0.001$). Post-chemotherapy ki-67 index was significantly higher in the relapse group (mean, 43.2%; range, 25-90%) than that in the recurrence-free group (mean, 20.2%; range, 2-80%) ($p<0.001$).

Conclusions: A high post-chemotherapy ki-67 index is associated with recurrence after surgery. Ki-67 might be used as a parameter in risk stratification for children with hepatoblastoma.

V300 SIOP19-0051 | Treatment of Childhood Hepatoblastoma at a Single Children's Hospital in Shanghai China 2009-2017

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Background/Objectives: We reviewed the clinical patterns and outcomes of children with hepatoblastoma (HB) treated at Shanghai Children's Medical Center to improve our understanding of this issue and serve as a historic control for our future HB study.

Design/Methods: Newly diagnosed patients treated under a uniform institutional protocol were included from 2009 to 2012. Pretext/Posttext staging system and orthotopic liver transplantation were not included in the protocol during this period. Maximum resection of the liver tumor is considered if it is feasible. Patients were stratified into two risk groups: low-risk group (Evans stage I or II, and AFP ≥ 100 ng/ml at

diagnosis) and high-risk group (Evans stage III or IV, or AFP <100 ng/ml).

Results: Ninety-four patients (58 boys, 36 girls) were enrolled with a median age of 1.6 years: 32 (34%) in low-risk group and 62 (66%) in high-risk group. Nine patients (9.6%) had metastatic disease at presentation. Forty patients had primary liver tumor complete resection at diagnosis and 52 had their maximum liver tumor resection after 2~7cycles of chemotherapy. The 3-year event-free survival (EFS) for the entire group was $83\pm 4.2\%$ with a median follow-up time of 29.4 months. After a median 5 cycles of C5V, patients in low-risk group achieved a $93.6\pm 4.3\%$ EFS. After a median 8 cycles of C5VD followed by ICE, patients in high-risk group achieved a $78.1\pm 5.7\%$ EFS. Fourteen patients had an event: disease progression ($n=7$), tumor relapse ($n=5$), abandonment of treatment during therapy ($n=2$). Seven patients died as a result of tumor failure. Two of 9 patients with metastatic pulmonary disease at presentation did not clear after chemotherapy and died afterwards. Patients ≥ 3 years have a worse outcome.

Conclusions: Although the institutional protocol yielded an 80% cure rate, a more individual approach based on a precise risk stratification system is required to treat highly heterogeneous HB.

V301 SIOP19-1069 | Margin of Resection in Advanced Hepatoblastoma (HB) When Less is More

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Background/Objectives: Complete tumor removal remains central for cure. For some with POSTEXT II and III tumors obtaining >1 cm negative margin might mean a shift to liver transplant. Our aim is determining whether a slim negative resection margin affects local relapse.

Design/Methods: We used institution review board approved standard retrospective clinical research form to identify children treated between January 2006 and December 2015 at the center. Demography, PRETEXT, risk group, platinum-based therapy, type of surgery, pathology report, thickness of negative margin and local relapse were analyzed. A multi disciplinary team made all management decisions. Statistical analysis using Medcalc software, fishers exact test and Chi square. kaplan-Meier plots for event free survival (EFS) and overall survival (OS).

Results: We identified 37 children. Two died prior to treatment. 30 children received neoadjuvant chemotherapy and

delayed surgeries were eligible for analysis; 16 standard, 14 high risk. After 2-4 cycles 60% reduction in tumor size resulted in PRETEXT down staging in 37%. Complete anatomical tumor resection was achieved in 28 (24 were POS-TEXT II-III), 2 referred for transplant. Twenty three who had negative margin on pathology were divided into 2 groups for further analysis; 12 > 1 cm, 11 < 1 cm thickness. Both were comparable. Viable tumor present in all. No difference in vascular injury (13%) and bile leak (20%). During follow up 3 children died; 1 with aspiration pneumonia, 1 with biliary sepsis and 1 from disease progression in the lung. No local relapse was recorded.

Conclusions: This review provides evidence that a slim negative margin following neoadjuvant chemotherapy is not associated with increased rate of local relapse. Few were spared transplant. The importance of Multi disciplinary team management and expertise in liver surgery in a referral cancer center cannot be emphasized enough as pillars of success. Short term surgery related mortality was minimal and avoidable. EFS and OS were comparable.

V302 SIOP19-1711 | Survival of Hepatoblastoma with Lung Metastases in Chile, 1997-2018

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Background/Objectives: Hepatoblastoma (HB) is the most common malignant liver tumor in childhood. Overall survival (OS) continues to be low in metastatic patients. Combination of chemotherapy and surgery reaches an OS of 27-62%. With complete resection is up to 79%. Chile had developed a National Oncology Program to treat Cancer in Children (PINDA). The aim was to study the OS of patients with HB with pulmonary metastases treated under PINDA Program.

Design/Methods: After ethical committee approval, patients under 18 years of age with HB and pulmonary metastases (PM) were treated under PINDA protocol, from 1997 to 2018. They were staged according to PRETEXT. One patient received a primary hepatic tumor resection and in 31, resection was performed after cyto-reduction. Three were treated with Siopel-3 and 29 with Siopel-4 protocol. Resection of PM

was performed after chemotherapy. Those who progressed received salvage treatments.

Results: Seventy-nine patients had high-risk HB, 32 had PM. Fifteen women. Age at diagnosis 30 months. Main primary symptom was abdominal mass. They presented with at least 3 lung lesions at diagnoses. Median AFP was 60.500 µg/dl. Associated genetic syndromes: trisomy 21 (1), Beckwith Wiedemann (1) Familial Adenomatous Polyposis (1) and 2 pre-Term. PRETEXT II: (10), III: (13) and IV: (9) patients. Median follow-up 65 months. Fourteen patients presented disease progression (44%) and 3 died due to infection during chemotherapy (9%). Fifteen patients responded to chemotherapy, 6 with negative PM after chemotherapy. These 15 patients received hepatic resections (3 transplants) and in 9 with residual pulmonary disease, received also a PM resection. Twelve are alive (OS and EFS of patients who responded to chemotherapy 80%). Three died due to lung relapse (1 transplant). Of all 32 patients with PM at diagnoses, EFS and OS was 38%.

Conclusions: Chemosensitivity and total surgical resection, have an important role in Overall Survival.

V303 SIOP19-1719 | Children's Hepatic International Collaboration Staging System in Hepatoblastoma in Chilean Children Treated from 1997 To 2018

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Background/Objectives: Hepatoblastoma (HB) is the most common malignant liver tumor in childhood. Stratification (PRE-treatment EXTent of tumor) PRETEXT system was introduced in 1992. CHILDREN'S HEPATIC INTERNATIONAL COLLABORATION (CHIC) created a new risk stratification to help design future treatment protocols adjusted for survival and late effects. The aim was determining the risk stratification in patients treated for HB from 1997 to 2018, analyzed with CHIC's staging system

Design/Methods: Multicentric retrospective study of the Chilean group between 1997 to 2018. Patients under 18 years of age with HB were admitted. They were re-staged according to CHIC's prognostic factors: Age < 3 years, between 3 to 7 years and > 8 years; PRETEXT I, II, III and IV; α fetoprotein (AFP) <100 ng/dL and PRETEXT annotation

factors: metastatic disease (M), macrovascular involvement all hepatic vein (V), or portal bifurcation vein (P), contiguous extrahepatic tumor (E)), multifocal tumors (F), spontaneous rupture (R). Enrolled patients: 121, 110 were analyzed. Exclusion criteria were: lack of PRETEXT images, unknown histology, unknown AFP levels and death by biopsy. Patients were treated by Siopel-3 and Siopel-4 protocols

Results: One hundred ten patients were analyzed. Median age of 2 years, 57% were male. In the previous stratification system 30% were low risk and 70% were high risk. Under CHIC's system: 4% were very low risk, 35% low risk, 24% intermediate risk and 38% high risk.

Conclusions: Currently, OS in Chile is 94% in low risk and 62% in high risk patients. With this new system, 39% of patients would received less chemotherapy, decreasing late drugs effects, and 1% may increase chemotherapy, hoping to increase survival.

V304 SIOP19-1070 | Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia

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Background/Objectives:

The objective of our work is to describe the epidemiological, Cytogenetic, and evolutive profile of patients followed for Ph+ALL.

Design/Methods: We included patients younger than 20 years of age followed for Philadelphia chromosome-positive acute lymphoblastic leukemia from May 2006 to December 2016

Results: From May 2006 to December 2016, 395 patients were diagnosed ALL, 10 (2, 5%) with Ph+ALL, median age was 16 years (4-13), sex ratio M / F to 1, the median of white blood cells (G / L) was 45,9 (2-386), according to immunostaining 8 (80%) patients were LALB, on the karyotype 9 (90%) patients had t (9.22), 2 (20%) patients had BCR/ABL transcript at diagnosis, nine (90%) patients received the TKI, no patient stopped imatinib, 2 (20%) have made a hepatic toxicity grade II, seven patients (70%) had remission after induction therapy, 1 (10%) patient has died in induction, and 1 patient was in failure. After a mean follow up of 21, 5 months (1-55), 4 (40%) patients have relapsed, who all died, and 1 (10%) patient was allografted.

Conclusions: Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ALL), remains rare, and poor prognosis, and several progress remains to be made in our countries especially in diagnosis and surveillance.

V305 SIOP19-0720 | Feasibility of Hepatoblastoma Diagnosis Based on Alpha-Fetoprotein in Children Before Preoperative Chemotherapy

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Background/Objectives: Children with high preoperative tumor staging (PRETEXT) hepatoblastoma need to undergo preoperative chemotherapy to reduce the size of tumor before complete resection. Pre-chemotherapy pathological biopsy is gold standard approach for the diagnosis of hepatoblastoma. However, in this case, children will undergo two operations and are at risk of surgery, especially when the tumors are large and the patients are in poor condition. The aim of this study is to determine the feasibility of clinical diagnosis based on alpha-fetoprotein (AFP) without pathology biopsy.

Design/Methods: A retrospective analysis was made on 80 cases of liver space-occupying lesions, including 49 cases of hepatoblastoma and 31 non-hepatoblastoma. The sensitivity and specificity of AFP in the diagnosis of hepatoblastoma and consistency of two diagnostic methods were analyzed. Child patients who started chemotherapy according to diagnosis by AFP were in the non-pathological chemotherapy group, while children by pathologically confirmed before chemotherapy were as the pathological chemotherapy group. Event-free survival (EFS) and overall survival (OS) were compared between the two groups.

Results: The sensitivity and specificity of AFP in the diagnosis of hepatoblastoma in children were 98%, 100% respectively. The actual consistency of diagnosis based upon AFP with pathological diagnosis was 98.75% ($P < 0.05$) by kappa test. KM curve showed that the EFS and OS were higher in the group with pathological chemotherapy, but there was no significant difference in the EFS and OS between the two groups by Log-rank test. (P values were 0.142 and 0.759). In view of that proportion of stage III /IV was higher in the non-pathological chemotherapy group, only EFS and OS were compared on patients of stage III and IV, there was no significant difference between the two groups.

Conclusions: The clinical diagnosis of hepatoblastoma in children based on AFP is credible, which can guide preoperative chemotherapy without pathological biopsy.

V306 SIOP19-1613 | Outcome of Children with Hepatoblastoma: Analysis of a Single Center Experience Over the Last 23 Years

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Background/Objectives: Hepatoblastoma (HBL) is the most common liver tumor of early childhood. According to the SIOPEL group; perioperative chemotherapy followed by surgical resection has improved the outcome for more than 90% and the challenge is to desescalate treatment without losing efficacy.

The aim of the study was to describe the clinical characteristics of our population and the survival

Design/Methods: This is a retrospective study of 21 cases of HBL treated in our center during the last 23 years (1995 - 2017). The data was collected retrospectively and analysed with SPSS19.0

Results: The mean age at diagnosis was 2.2 years (2 months-8 years) with a sex ratio of 0.9. The most common presenting symptom was abdominal mass (66.6%) and the median Alpha Fetoprotein (AFP) level at the time of diagnosis was 296,500 ng/ml (250-2183130 ng/ml). All patients benefited from the couple ultrasound / TDM for the diagnosis. Liver biopsy was performed in 17 cases. Lung metastases at diagnosis were found in 3 cases. Tumors were unifocal in 17 patients and multifocal in 4 patients. Neoadjuvant chemotherapy was performed for 17 patients (81%). Surgery was performed in 14 children (66.6%) followed by chemotherapy in 9 cases. The median follow-up was 53 (1 day-21 years). Evolution has been marked by a complete remission in 9 cases, local recurrence in 3 cases, and 5 cases lost of seen.

Conclusions: The prognosis of children with hepatoblastoma was improved substantially during the past few years through the efforts of all the cooperative study groups. In limited resource country, outcome need more care for multidisciplinary management.

V307 SIOP19-0106 | Intraoperative ICG Fluorescence Navigation is Useful to Evaluate Vascular Invasion of Hepatoblastoma

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Background/Objectives: When performing hepatectomy, we sometimes face almost no surgical margin from hepatic vessels. We have performed navigation surgery using indocyanine green fluorescent method (ICGF) for hepatectomy, liver transplantation and metastasectomy of hepatoblastoma. This

method can visualize even a diameter of 0.05mm of hepatoblastoma tissue intraoperatively. We found ICGF useful to find extremely small residual tumors on or inside the hepatic vessels and to contribute a determination of whether the vessels should be preserved or extirpated.

Design/Methods: Three patients with hepatoblastoma were corresponded. Retrospective review of radiological image findings, pathological findings and operation records and videos were performed. All operations included hepatectomy. Intraoperative ICGF was done by intravenous administration of 0.5mg/kg of ICG 3 days before operations and fluorescence was detected by a detector within an infrared ray radiator (PDE neo^R).

Results: Case 1: After an extended right hepatectomy, ICGF demonstrated some micro residual tumor lesions on the residual left hepatic vein wall. After careful removal of these lesions, ICG demonstrated no residual tumors and the vein was preserved. Case 2: After a left trisegmentectomy, ICGF demonstrated a residual tumor lesion inside the right hepatic vein. Because a posteroinferior hepatic vein was intact, we decided to resect the invaded right hepatic vein. Case 3: After a right trisegmentectomy, ICGF demonstrated a small tumor thrombus in the portal vein trunk. We decided to resect the portal vein and made a Rex-shunt using a residual umbilical vein. Each of the patients underwent postoperative chemotherapy and had no tumor recurrence.

Conclusions: ICGF is useful for intraoperative determination whether hepatic vessels should be preserved or not. This method sometimes contributes to avoid liver transplantation like case 1.

V308 SIOP19-0507 | Clinical Profile and Treatment Outcomes of Hepatoblastoma in Children: 10-Year Experience from a Developing Country

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Background/Objectives: Rapid advances in the fields of chemotherapy, hepatic surgeries, paediatric liver transplantation and supportive care have vastly improved survival in children with hepatoblastoma (HB). However, limited financial resources, lack of awareness and difficulty in accessing healthcare contribute to poorer outcome of HB in developing countries. We review the clinical profile and outcomes of HB treated in our institute over the last 10 years.

Design/Methods: Retrospective study of all children (< 16yrs) with HB treated in a tertiary care hospital in South India comprising paediatric oncology, paediatric liver surgery AND transplantation unit between January 2009 to December 2018. Data regarding the clinical presentation, pre-operative management, surgical treatment, post-operative course and outcomes was extracted from a prospectively managed database.

Results: During the study period, 50 children were treated for hepatoblastoma (HB) in our hospital, out of which 19 children were high risk (risk stratified as per SIOPEL protocol). Fifteen children were PRETEXT 4, 19 were PRETEXT 3, 15 were PRETEXT 2 and one was PRETEXT 1. All but one child received neoadjuvant chemotherapy before surgery followed by adjuvant chemotherapy. Thirty-three children underwent hepatectomy, while 12 underwent primary living donor liver transplantation. Five children poorly responded to chemotherapy and died due to progressive disease. Five children had disease relapse, out of which 4 died. At a median follow-up of 48 months, 41 of the total 50 children continue to be in remission with an overall survival of 82% (97% in Standard Risk, 57% in High Risk).

Conclusions: Excellent treatment outcomes can be achieved in children with HB, even in developing countries when managed in centers with facilities for pediatric oncology, liver resection and liver transplantation.

V309 SIOP19-1065 | Hepatic Malignant Tumors in a High Complexity Health Care Center in a Middle Income Country

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Background/Objectives: In pediatric population, hepatic tumors correspond to 5% of solid organ tumors. Hepatoblastoma (HB) and hepatocellular carcinoma (HCC) are the most common among malignant hepatic tumors. The aim of this study was to review the diagnosis and treatment of pediatric liver tumors from 2011 to 2018 In Fundacion Valle de Lili, a high complexity and reference center for pediatric hemato-oncology and hepatic transplantation in Cali, Colombia.

Design/Methods: The medical records of all pediatric patients with liver tumors diagnosed between January 2011 and December 2018 were reviewed. Considering age, place of origin, histopathologic findings, staging, previous management, interinstitutional treatment; including chemotherapy, surgery and/or hepatic transplantation.

Results: 43 pediatric patients with malignant hepatic tumors who came from different sites of the country including neighboring countries. 34 patients with HB with an average age of

3 years (1,7-5). 4 patients with HCC with 6 to 12 years old and 5 patients with sarcoma between 4 and 13 years.

Depending on the tumor stage and the previous treatment at time to referral, patients were treated with chemotherapy and/or surgical resection or transplant. 60% patients received five or more chemotherapy cycles previous and after surgery.

2 patients with HCC had liver transplant with 2 cycles of presurgical chemotherapy and after transplant 1 cycle, 2 had metastatic disease at diagnosis and were referred to palliative care.

Conclusions: Hepatic tumors in pediatric population although not frequent, can cause high mortality and morbidity rates.

Early referral to a high complexity and experienced health centers in hemato-oncology, hepatobiliary and transplant surgery, as soon as possible is important to avoid unnecessary chemotherapy cycles.

V310 SIOP19-1318 | EXON3-Associated B-Catenin Mutations Impede the Negative Regulation of WNT Signaling by Striatin-3 in Hepatoblastoma

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Background/Objectives: Hepatoblastoma (HB) is the most common form of liver cancer in children. It is characterized by an abnormal activation of the Wnt pathway due to mutations in β -catenin/CTNNB1 gene. Recently, our team reported the decrease of miR-624-5p in hepatoblastoma and its capacity to directly regulate β -catenin (Indersie et al, *Hep Comm* 2017). Since *Striatin3* (*STRN3*) gene hosts *MIR624*, we investigated the role of STRN3 in Wnt pathway and liver carcinogenesis.

Design/Methods: *STRN3* transcript expression was analyzed by RTqPCR in 32 HB and adjacent normal livers (NL). Gain- and loss-of-function experiments were performed using different hepatoma cell lines with mutated (MUT) or wild-type (WT) β -catenin. Deregulation of β -catenin mRNA and protein was studied by RTqPCR and Western blot. Wnt signaling activity was evaluated using the TOPflash reporter assay and through changes in Wnt-associated genes expression. Cell proliferation, apoptosis and survival were measured using cell-based assays. Finally, the human *STRN3* transcript was injected in *Xenopus* oocytes to assess its function in Wnt pathway *in vivo*.

Results: *STRN3* mRNA was dramatically decreased in HB compared to NL. RNA-induced *STRN3/MIR624* silencing increased β -catenin protein and mRNA levels in tumoral cells.

Inversely, STRN3 protein down-regulated β -catenin, strongly impeded Wnt signaling activity and inhibited the growth of WT *CTNNB1* tumoral cells reflecting a pronounced loss of β -catenin oncogenic functions. Very interestingly, MUT cells were resistant to STRN3 action. Finally, human *STRN3* significantly counteracted the Wnt8-induced dorsal axis duplication in *Xenopus* oocytes, therefore demonstrating the capacity of STRN3 to inhibit the Wnt pathway during the embryonic development.

Conclusions: We report that *STRN3/MIR624* gene inhibits β -catenin and Wnt pathway through a double mechanism associating both STRN3 protein and miR-624-5p. Given the key role of Wnt pathway in carcinogenesis, our results may find new applications in the treatment of HB and many other cancers.

V311 SIOP19-1465 | Pronostic Factors of Pediatrics Hepatocellular Carcinoma in France

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Background/Objectives: Little is known about pediatric hepatocellular carcinoma (HCC) which constitute an heterogeneous group of disease. The objective of the study was to describe clinical presentation, histology and outcome of childhood HCC.

Design/Methods: Data of 23 French pediatric patients diagnosed as HCC between 1999 and 2017 and included in the national HEPATOBIO database were retrospectively analyzed.

Results: Median age at diagnosis was 13.6 years. After central histological review, 12 were diagnosed as fibrolamellar (FL) carcinoma, 9 non FL HCC, and 2 unclassified. Three were reclassified as hepatoblastoma with HCC features, 1 adrenocortical carcinoma. In addition 11 patients (47.8%) had an extra-hepatic involvement including lung metastases in 6, bone lesion in 1, and abdominal extra-hepatic disease including lymph nodes involvement in 4. The incidence of metastases tended to be higher in FLC (57.1%) than in the other patients (66.7% versus 22.2% ($p = 0.0805$)). Surgery was performed in 19 patients (82.2%) leading to complete resection in 17 (89.5%). Sixteen patients (69.6%) received chemotherapy (Doxorubicin and Cisplatinum +/- Sorafenib). Five-year EFS and OS were respectively 46.8% and 58.3%. Non fibrolamellar carcinomas exhibited greater survival as compared to fibrolamellar subtype (82.5% vs. 36.4%, respectively $p = 0.0138$). Significant correlation was found between metastasis and OS ($p = 0.0021$). Complete resection significantly improved OS compared to incomplete resection (72.7% vs. 28.6%, respectively).

Conclusions: The small scale of the study does not allow to draw conclusions about the worst survival of FLC even if the number of metastasis forms is higher in this group. Histology and radiology reviewing is essential to confirm the influence of histology on the prognosis.

V312 SIOP19-0665 | Retrospective Study of Pediatric Undifferentiated Embryonal Sarcoma of Liver From Beijing Children Hospital's Experience

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Background/Objectives: Pediatric undifferentiated embryonal sarcoma is one rare maglinant carcinoma in children. It is considered an aggressive neoplasm with an unfavorable prognosis. This study is to to present a single center experience in the treatment of children with UESL.

Design/Methods: 16 Children suffered from UESL were treated in Beijing Children Hospital (BCH) from 2008-2018. There were 9 males and 7 females with an age range of 5 to 11 years.

Results: 12 patients were successfully treated with surgery. Right hemihepatectomy (n=6), midlobectomy (n=2), left hemihepatectomy (n=1), left lateral lobectomy (n=1) and irregular hepatectomy (n=2) were performed. Tumor rupture occurred in 7 cases before operation. 6 patients underwent primary complete resection without preoperative chemotherapy. Adjuvant chemotherapy was administered in 10 patients (CDDP+VP16/VCR+DOXO+IFO, VDC/IE/ PLADO), Tumor reduction (n=4) or hemorrhage control (n=2) occurred in 6 patients after chemotherapy, 4 cases were ineffectual after chemotherapy. 10 patients received postoperative chemotherapy (VCR+CTX+THP/ VCR+CTX+CDDP+VP16/ VCR+CTX+TPH+5-FU/ VCR+IFO, IFO+DDP+VP16, VCR+DDP+5-FU+ADR, TOPO+CTX/VCR+CTX+EPI). During follow-ups, 2 patients were lost to follow-up, 3 patient died of hemorrhage and recurrence, the remainder had tumor free survival.

Conclusions: Excellent results with long-term survival can be achieved in children with combined therapy of surgery and chemotherapy in UESL.

V313 SIOP19-0996 | Hepatoblastoma, Treatment Outcome in 2006–2017: Chemotherapy Induced Down-Staging, Surgical Complications and Survival

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Background/Objectives: In the retrospective analysis, we studied local PRETEXT and POSTTEXT staging (including VPEFR annotation) in hepatoblastoma (Hb) in respect to down-staging of tumour, survival and surgical complications.

Design/Methods: From 2006 to 2017, 22 patients with Hb were treated at our institution. Median follow-up was 7.0 years (2.1 – 9.63). Event-free survival (EFS) a overall survival (OS) were analyzed using Statistica® program.

Results: At diagnosis, median age of patients was 1.44 (0 – 6.46) years. Hb PRETEXT stage I had 4 patients, II 5, III 10, IV 3 patients, VPEFR positivity had 13 patients (V 10x, P 10x, E 0x, F 3x, R 1x), lung metastases 3 children. Preoperative chemotherapy (SIOPEL-3 and SIOPEL-4) was used in 18/22 patients (82%), in 15 patients (68%) POSTTEXT analysis could be performed. Down-staging of tumour was observed in 9/15 (60%) patients, positivity of VPEFR diminished in 3/10 (30%). Final pre-operative staging (PRETEXT and POSTTEXT: stage I 6 patients, II 10, III 4, IV 2, VPEFR positive 11 patients. Surgical complications: 1x severe bleeding and 3x biliary leak were present in stage I 0/5, II 3/10, III 1/4, stage IV 0/1 (p=0.09), no statistical difference was found in VPEFR. Overall number of peri-operative transfusions: stage I 9.8 transfusion, II 7.4, III 6.0, IV 6.0, p=0.17. Three patients died (I stage 1, III 1, IV 1), 1 locally relapsed and survived, 1 developed secondary malignancy; EFS 77.3%, OS 86.4%. In term of EFS, no statistical significance was found: pre-operative stage p=0.15, VPEFR p=0.66, R0 resection p=0.8, histology p=0.45, except of metastatic tumour at diagnosis (p=0.006).

Conclusions: Pre-operative chemotherapy down-stages Hb in children, but very likely due to low number of patients, we did not find any significant difference in survival between PRETEXT/POSTTEXT stages, VPEFR positivity and surgical complications. Supported by MH CZ – DRO, Motol University Hospital, Czech Republic 00064203.

V314 SIOP19-0398 | Refractory and Recurrent Hepatoblastoma: Epidemiology, Current Treatments and Outcome: The French Experience

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Background/Objectives: Refractory and recurrent hepatoblastoma are rare and data about these children are limited. We analyzed the clinical characteristics, treatments and outcome of children with refractory or recurrent hepatoblastoma in France.

Design/Methods: From 1990 to 2018, 41 children were registered in HEPATOBIO, the French pediatric liver tumors national register: 24 with progression during initial treatment, 17 with relapse after complete remission (11 metastatic relapses and 6 local relapses).

Results: Median age was 3.5 years old (0.7-17.7 y). Initial PRETEXT staging was PRETEXT IV in 12, III in 16, II in 12, I in 1 and 21 patients had metastasis disease at diagnosis. The median time from the initial diagnostic to the relapse/progression was 8.1 months (2-157 m). Second-line treatment included chemotherapy for 33 children, surgery for 25, radiotherapy for 9 and radiofrequency ablation for 5. Median follow-up was 32.8 months (1-270 m). Among the 24 children with refractory hepatoblastoma, 4 received molecularly targeted therapy (1 sorafenib, 1 temsirolimus, 2 sirolimus). Overall, 26 children died with a median survival of 8.2 months (0.3–20.7 m) and 15 children are still alive in second complete remission including 2/24 children with refractory disease, 7/11 children with a metastatic recurrence and all 6 children with local relapse. One-year overall survival is 44% (95% Confidence Interval (CI) 32%-62%). Three-years overall survival is 33% (95% CI 20-49%).

Conclusions: Prognosis of refractory hepatoblastoma is still poor despite second-line treatments whereas a multimodal treatment achieves a good survival rate for local and metastatic recurrence.

V315 SIOP19-0088 | A Potential Therapeutic Target Molecule of WNT Signaling Promotes the Development of Hepatoblastoma by Suppressing TGFB Signaling

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Background/Objectives: The β -catenin mutation is frequently observed in hepatoblastoma (HB), but mechanism underlying the involvement of Wnt/ β -catenin signaling in HB formation is unknown. We explored downstream targets of Wnt/ β -catenin signaling and analyzed its function and mechanism in HB development.

Design/Methods: RNA-sequencing analyses were performed in HepG2 cells with β -catenin siRNA to screen for novel

downstream target genes of Wnt/ β -catenin signaling. The expression of a specific nuclear factor (SNF; patent pending) identified as a downstream target of β -catenin was examined immunohistochemically in HB tissues (n=11) and using a public dataset of patients with HB. We investigated the involvement of SNF in HB cell proliferation and survival using siRNA or the CRISPR-Cas9 system. Downstream mechanisms regulating cell proliferation by SNF were analyzed by molecular biological methods. Using model mice harboring HB-like tumors induced by the forced expression of β -catenin, YAP, and c-Met (BYM), the SNF expression and effects of shRNA-mediated SNF knockdown on liver tumor formation were investigated. To assess the feasibility of SNF as a therapeutic target, we synthesized amido-bridged nucleic acid (AmNA)-modified antisense oligonucleotides (ASOs) targeting human SNF and injected ASOs into mice with HepG2-induced liver tumors.

Results: We identified SNF as a downstream target of Wnt/ β -catenin signaling in human HB. SNF was overexpressed in tumor lesions of 10/11 HB tissues (90.9%) and in the public dataset. SNF depletion decreased the HepG2 cell proliferation and survival. SNF interacted with Smad2/3 and competed with p300, resulting in the inhibition of TGF β -dependent cytotaxis. Liver tumors induced by BYM upregulated the SNF expression along with HB-specific markers, and SNF knockdown suppressed the expression of HB marker genes and tumor formation. SNF depletion by ASOs suppressed HepG2-derived liver tumor formation.

Conclusions: These findings clarify the previously unrecognized involvement of the Wnt/ β -catenin-SNF-Smads axis in HB pathogenesis, suggesting that SNF represents a potential therapeutic target for β -catenin-driven HB.

V316 SIOP19-1098 | Application of Indocyanine Green Fluorescence Imagine Technique in Precise Hepatectomy for Hepatoblastoma

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Background/Objectives: To investigate the imagine characteristics of near-infrared technology guided by indocyanine green (ICG) in hepatoblastoma, and the value of this technique for the identification of small lesions, the definition of tumor margin and the surgical navigation.

Design/Methods: From March to June 2018, 8 patients of hepatoblastoma received hepatectomy were treated in our hospital. ICG was injected intravenously at least 24 hours before operation. The detection of liver small lesions, definition of tumor margin and surgical navigation were performed intraoperation.

Results: There were 4 male and 4 female patients with average age of 33 months (range 5-132 months). Among these patients, one patient was tumor recurrence, one patients received chemotherapy after biopsy, 4 patients received chemotherapy without biopsy and 2 patients had primary hepatectomy. According to the classification of fluorescence, total fluorescence was in four patients, 2 of whom had primary tumor resection, one of whom received chemotherapy after biopsy and one of whom was recurrent patient with the history of hepatitis and liver mild sclerosis which had full fluorescence of the tumor accompanied by diffuse nodular imaging of the liver. Partial fluorescence was in another four patients who all had preoperative chemotherapy. Results of pathologic examination indicated that the fetal hepatoblastoma include 4 total and 1 partial fluorescence image, and mixed fetal and embryonic hepatoblastoma was in one patient with partial fluorescence image. The tumor margins were negative in all patients, which were confirmed by ICG and pathology.

Conclusions: Intraoperative ICG fluorescence imaging for patients with hepatoblastoma was feasible and useful and the type of fluorescence imaging is related to preoperative chemotherapy. However, ICG fluorescence imaging has some limitations in the identification of deep small tumor foci and the application in liver cirrhosis patients.

V317 SIOP19-1731 | Clinical Outcome of Hepatoblastoma with Multimodality Treatment Based on a Novel Risk Stratification

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Background/Objectives: Risk stratification and treatment strategies in hepatoblastoma have yet to be unified. This study integrated various definite prognostic factors of hepatoblastoma to propose a new stratification suitable for practising in China. Additionally, the effect of a new chemotherapy regimen on high-risk patients was explored.

Design/Methods: Children and adolescents under 18 years old were enrolled. According to stage, serum AFP level, pathological subtype and other factors, patients were stratified into very low-risk, low-risk, intermediate-risk and high-risk groups. The patients at very low-risk were treated with surgery plus C5V (cisplatin + 5-FU + vincristine) regimen for 4 courses. The patients at intermediate-risk were treated with surgery plus C5VD (cisplatin + 5-FU + vincristine + adriamycin) regimen for 6-8 courses. And the patients at high-risk were treated with surgery plus alternate C5VD/IIV (ifosfamide + irinotecan + vincristine) regimen for 8 courses.

Results: A total of 100 patients were enrolled from September 2014 to September 2018. There were 65 males and 35 females,

with 2 at very low-risk, 10 at low-risk, 51 at intermediate-risk and 37 at high-risk. The objective response rate of first-line chemotherapy was 78.3% in the 83 evaluable patients. With a median follow-up of 17 months, 30 relapses and 27 deaths occurred. The 2-year progression-free survival (PFS) rate was 69.2% and the overall survival (OS) rate was 72.0% in the whole cohort. Among them, the two-year PFS rate were 100%, 88.9%, 75.3% and 43.2% in patients at very low-risk, low-risk, intermediate-risk and high-risk, respectively.

Conclusions: The risk stratification of hepatoblastoma in this study is feasible and suitable for individualized diagnosis and treatment of hepatoblastoma in developing countries. C5VD/IIIV chemotherapy regimen is well tolerated in high-risk patient, but the long-term efficacy is dismal.

V318 SIOP19-0899 | 5-Hydroxymethylcytosine (5HMC) Profiles of Cell-Free DNA (CFDNA): Novel Liquid Biopsy Biomarkers for Children with Neuroblastoma

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Background/Objectives: 5-hydroxymethylcytosine (5hmC) is an epigenetic marker associated with active gene expression. Recently, we demonstrated the prognostic significance of tumor-derived 5hmC whole genome profiles in children with neuroblastoma (Applebaum et al, JCO Precision Oncology, in press). To develop a biomarker more suitable for monitoring disease response, we profiled 5hmC in cfDNA from children with neuroblastoma and healthy controls using nano-hmC-Seal, a novel highly sensitive technology.

Design/Methods: Plasma was collected from 32 children with neuroblastoma at various time points and 34 well children. 5hmC sequencing libraries were generated using 10ng of extracted cfDNA. Gene body read counts were determined using featureCounts and normalized with DESeq2, which also identified genes with differential 5hmC between patient groups.

Results: cfDNA 5hmC profiles were generated from 66 samples from 27 high-risk, 3 intermediate-risk, and 2 low-risk patients. Hierarchical clustering of the top 347 genes with differential 5hmC between newly diagnosed patients and well children identified 3 clusters that correlated with disease burden. Cluster 1 was comprised of cfDNA from patients with known metastatic disease (7 newly diagnosed and 2 with relapse). Cluster 2 was comprised of samples from patients with focal relapse (n=6), high-risk patients undergoing induc-

tion therapy (n=3), patients in clinical remission who subsequently relapsed (n=2), and 1 patient with newly diagnosed stage 4S disease. Cluster 3 was comprised of cfDNA from patients in clinical remission (n=34), well children (n=34), or those with minimal disease burden on clinical imaging (n=13). More than one sample was collected from 15 neuroblastoma patients, and the 5hmC profiles tracked closely with changes in disease status. Cluster 1 and 2 samples from patients with *MYCN*-amplified tumors had significantly higher *MYCN* 5hmC compared to all other samples (padj<0.05).

Conclusions: cfDNA 5hmC profiles correlate with clinical disease status in children with neuroblastoma and may serve as ideal biomarkers for monitoring response.

V319 SIOP19-0968 | SIOPEN Prospective Study Registry of Peripheral Neuroblastic Tumors Presenting with Spinal Canal Involvement

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Background/Objectives: Spinal canal invasion (SCI) occurs in 10-15% of children with peripheral neuroblastic tumors (PNTs). These patients have favorable clinical and biologic features at diagnosis and excellent survival but are prone to late neurologic and orthopedic sequelae. The optimal treatment for these patients has not been decided yet. This study/registry is collecting data to describe the natural history of PNTs presenting with SCI, evaluate the combined effects

of clinical and treatment-related risk factors on neurologic and orthopaedic outcome.

Design/Methods: We expect to collect prospective data on at least 150 symptomatic and/or asymptomatic patients. Internationally approved scales are used to grade type and severity of symptoms.

Results: One-hundred and seven patients have been registered from 15 countries, with an M/F ratio 1:1.2. Seventy-one% were <36 months old, and 59% had L2 disease. The most common histology was NB poorly differentiated (66%) and 8% of the patients had MYCN amplification. 47% had >66% SCI. 66% of the patients were symptomatic (71% <36 months, 50% ≥36 months); motor deficit was present in 53% of patients (in 39% reported as moderate/severe). Patients were treated by SIOPEN/institutional protocols. Chemotherapy was the prevalent approach; early neurosurgery was performed in 24% of patients and the decision to operate was significantly associated with the presence ($p=0.003$) but not severity of symptoms. Improvement of symptoms, if any, was observed within the first 6–12 months. Few asymptomatic patients developed late symptoms. After a median 1-year follow-up the prevalence of motor deficit reduced to 32% with “only” 16% of patients experiencing moderate/severe deficit.

Conclusions: This international prospective study/registry aiming to evaluate the effects of different risk factors on neurologic functioning and orthopedic outcome of PNTs presenting with SCI. Recruitment is still open and we encourage institutions to contribute to reach an adequate sample size for final statistical analysis.

V320 SIOP19-0258 | Uncovering Sympatho-Adrenal Microenvironmental Triggers of Neuroblastoma Metastatic Dissemination

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Background/Objectives: Neuroblastoma (NB), one of the most common childhood extracranial solid tumor, is a neural-crest derived malignancy that arises from the sympatho-adrenal lineage. NB aggressive forms are usually diagnosed with already established metastases, resulting in low survival rate and lack of understanding of early steps of the dissemination process. Our previous work conducted in a novel avian NB model revealed that the embryonic environment profoundly impacts the gene program of NB cells preparing for metastasis within the primary tumor (Delloye-Bourgeois *et al.*, Cancer Cell, 2017). Our present objectives are to iden-

tify the molecular signals provided by the sympatho-adrenal microenvironment which modify NB cell gene program to trigger their detachment and switch on their migratory potential.

Design/Methods: To do so, we set up an *in vitro* system that models NB cohesive primary tumors and allows assessing NB cell disaggregation behavior. We exposed these NB cohesive masses to medium conditioned by sympathetic chains dissected (symp^{CM}) out at different developmental stages.

Results: Interestingly, we observed that symp^{CM} obtained from E6 to E8 drastically affects NB cell mass cohesion properties, triggering an invasive-like behavior. Proteomic analyses of symp^{CM} combined with RNASeq analyses of NB cells revealed a list of candidate mediators of this scattering effect. Functional validations by gain and loss of function will be conducted on selected candidates.

Conclusions: These findings should bring us one step closer to the discovery of key microenvironment-derived players and the design of novel therapeutic targets of aggressive NB.

V321 SIOP19-1392 | The value of FDG PET-CT in Neuroblastoma Imaging

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Background/Objectives: In a proportion of neuroblastoma patients, lesions show no or low MIBG uptake. In these cases, FDG PET-CT is performed as an alternative imaging technique to investigate metabolic active disease.

Design/Methods: Patients referred for both MIBG and FDG PET-CT were retrospectively investigated. Included for analysis were patients with the diagnosis of neuroblastoma and a MIBG and FDG PET-CT performed within 2 weeks of each other. Results of scans were compared using SIOPEN score for skeletal localization and absolute number of soft tissue lesions for primary tumor and soft tissue metastases.

Results: Twenty-four patients with the diagnosis neuroblastoma were identified that had both an FDG PET-CT and MIBG scan performed within 2 weeks. In this cohort MIBG-SIOPEN score was 0 in 17 patients and positive with a mean score 17 (range 1 - 31) in 7 patients, for FDG the SIOPEN score was 0 in 17 patients and positive with a mean score of 11 (range 1 - 27) in 7 patients. In 13/24 (54%) patients both MIBG and FDG SIOPEN score was 0, in 2/24 (8%) patients both scans detected bone metastases, in 4/24 (17%) patients FDG was positive whilst MIBG-SIOPEN score was 0 and in 5/24 (21%) patients MIBG detected bone metastases whilst FDG SIOPEN score was 0. In 9/24 (38%) of patients, MIBG-non avid soft tissue lesions were detected, 8 out of

these 9 patients had FDG PET-CT positive disease. Overall, compared to MIBG, FDG PET-CT detected more soft tissue lesions in 12, equal number in 8, and less in 4 patients.

Conclusions: In this selection of patients FDG PET-CT detected more soft tissue lesions than MIBG. Moreover, FDG PET-CT detected bone metastases that were not detected with MIBG in 17% of patients.

V322 SIOP19-1425 | Characterization of Minimal Residual Disease in Patients with High Risk Neuroblastoma Using ddPCR and RTQ PCR

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Background/Objectives: The actual problem in patients with neuroblastoma is the detection of minimal residual disease (MRD) and its correlation with the progression or relapse of the disease. The popular method MRD monitoring is real-time PCR (RTQ-PCR) based on the detection of mRNA of genes which are expressed predominantly in neuroblastoma cells. Three specific markers have been recommended by SIOPEN group for the MRD monitoring: *TH*, *DCX* and *PHOX2B* genes. In some cases, with low tumor burden, the droplet digital PCR (ddPCR) could be more precise method for quantitative measuring of MRD.

Design/Methods: The group of patients consists 13 children (age 0-8 years) with the diagnosis of high-risk neuroblastoma. The bone marrow (BM) aspirations were examined for four times during the treatment according to the NB2004 protocol: before starting the therapy, after second and fourth block and in conclusion of the induction treatment. RNA from BM cells was subjected to reverse transcription and used simultaneously in RTQ PCR and ddPCR.

Results: All 13 patients had initial detectable BM involvement: in specimens of 10 patients it was detected by both RTQ-PCR and ddPCR, while in BM of 3 children subtle BM disease was traced only by ddPCR. After the second block of chemotherapy only 2 patents became MRD negative by both techniques, and 5 patients had MRD detected only by ddPCR. After the fourth block of chemotherapy only 6 patients had double-negative MRD results. This means that ddPCR is more sensitive technique to evaluate MRD in high risk neuroblastoma patients.

Conclusions: Simultaneous MRD detection in neuroblastoma by both RTQ PCR and ddPCR seems to be appropriate in high risk group patients and helps the clarification of MRD changes during the treatment. Patients from high risk group shows slow elimination of tumor cells from BM, that can be detected in the most cases only by ddPCR method.

V323 SIOP19-0114 | Nucleosome Footprinting Enables Inference of Differential Expression Profiles in Circulating Tumor DNA from Neuroblastoma Patients

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Background/Objectives: In neuroblastoma (NB), significant amounts of circulating tumor DNA (ctDNA) enable the detection and sequential analysis of tumor cell-specific genetic alterations based on next-generation sequencing technologies. In NB, expression profiles are also of importance to detect prognostic or disease evolution. We now sought to make use of ctDNA to infer expression profiles in sequential plasma samples. Indeed, it has been shown that gene expression levels are reflected by nucleosome positioning. Differences in nucleosome organization at transcription start sites (TSS) leads to differential clipping of fragments upon ctDNA release, leading to differential ctDNA nucleosome footprints depending on the expression of the given genes in the originating cells.

Design/Methods: To establish nucleosome footprinting and infer expression profiles, we isolated ctDNA from plasma at diagnosis (n=43) and during follow up (complete remission, n=2; progressive disease, n=5) from 43 NB patients. A target capture was designed to encompass the TSS of 34027 known coding genes (8,7Mb). For each patient, the primary tumor DNA, germline DNA and ctDNA samples were submitted to target sequencing. For 18 patients, diagnostic tumor expression profiles were available as controls.

Results: To predict the expression status of individual genes, we trained a machine learning model (SVM) on a set of 680 housekeeping genes and 680 unexpressed genes in most tissues. Normalized coverage from -200bp to +200bp with respect to the TSS was used as input. We then performed a cross-validation that resulted in a mean accuracy of 94%. The preliminary result show as expected an expression of gene involved in NB and unexpressed in blood cells such as MYCN, ALK, PHOX2B, KIT in 91% of cases. For one case with a relapse, 6023 became expressed and 62 unexpressed compared to the cfDNA diagnosis.

Conclusions: Our study expands a new utilization of the ctDNA and allows the sequential expression profile of the tumor.

V324 SIOP19-0600 | Identification of A-N-Catenin as a Novel Tumor Suppressor in Neuroblastoma

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Background/Objectives: Neuroblastoma remains as a difficult tumor to treat. The lost expression of α -catenin has been found in cancers, and reinstalling α -catenin inhibits tumor growth; however, its potential role in neuroblastoma is unknown. Here, we hypothesized that the α -N-catenin, a homologous member of α -catenin and neural-specific expressed, functions as a novel tumor suppressor in neural crest-derived tumor, neuroblastoma.

Design/Methods: We correlated CTNNA2 (encodes α -N-catenin) expression to neuroblastoma disease relapse-free survival probability using human neuroblastoma datasets in R2 platform. Human neuroblastoma cell lines, SK-N-AS (non-MYCN amplified) and BE (2)-C (MYCN-amplified), were stably-transfected with CTNNA2- or control plasmids. Tetrazoleum-based proliferation assay, adherent colony formation, and soft agar colony formation were performed. Subcutaneous xenograft model was used to determine the function of α -N-catenin in vivo. EMSA was used to measure nuclear NF- κ B activity. PTGS2, IL8, IL6, and MYC were our downstream markers of NF- κ B signaling. ELISA was performed to quantify secreted IL-8. HUVEC tubule formation was our surrogate marker of angiogenesis.

Results: The expression of CTNNA2 negatively correlated to relapse free survival in patients with non-MYCN amplified neuroblastoma. Overexpressing CTNNA2 suppressed the neuroblastoma cell proliferation as measuring by the clonogenesis, inhibited anchorage-independent growth with soft agar colony formation assay. It also decreased cell migration and invasion. Further, CTNNA2 overexpression reduced the secretion of angiogenic factor IL-8 and HUVEC tubule formation. Interestingly, this was only observed in SK-N-AS xenografts with non-amplified MYCN, and not in BE (2)-C xenografts. Mechanistically, α -N-catenin attenuated NF- κ B responsive genes by inhibiting NF- κ B transcriptional activity.

Conclusions: Our data, for the first time, show that α -N-catenin functions as a tumor suppressor in neuroblastoma and that NF- κ B signaling pathway is critically involved with this process. Restoring the expression of α -N-catenin could be a novel therapeutic approach for neuroblastoma patients who have the deletion of CTNNA2 and non-MYCN amplification.

V325 SIOP19-1277 | Phase II Study of 131I-MIBG with Five Days of Topotecan for Patients with Relapsed or Refractory Neuroblastoma (NB): Results of the French Study MITOP

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Background/Objectives: The objective of this multicenter study was to estimate objective response rate (ORR, complete or partial response) according to International Neuroblastoma Response Criteria 6 weeks after treatment, event-free survival (EFS), overall survival (OS) and tolerance of ¹³¹I-MIBG infusions coupled with topotecan in children with relapsed/refractory neuroblastoma.

Design/Methods: Patients <18 with relapsed or refractory MIBG-avid neuroblastoma and stem cells available were eligible. Patients received one or two courses of intravenous infusion of ¹³¹I-MIBG with concomitant topotecan to receive a whole-body radiation dose (WBD) of 4 Gy. Peripheral blood stem cells were given on day-31.

Results: 30 patients were included, median age 5.5 years (range: 2-20). 21 had refractory NB including 13 first line refractory metastatic NB (VHR NB), 9 had relapsed NB. Median modified SIOPEN score at inclusion was 8.5 (range, 2-55). Median number of previous lines of treatment was 3. All but 5 patients received 2 MIBG/¹³¹I courses. Estimated median WBD was 3.9 Gy (1.85-4.9). Immediate tolerance was good with non-hematologic toxicity limited to grade-2 vomiting/nausea in 8 patients. One patient developed late grade-1 hypothyroidy. ORR was 19% (4/21) for refractory and 0/9 for relapsed disease. Two-year OS and EFS rates were 40% (95%CI, 23-57%) and 13% (4-28%), respectively. Among the 13 VHR NB, 10 with at least SD after MITOP received further therapy: 8 received BuMel and maintenance therapy; 3 of them are alive (median FU=7 years), and 2 received another treatment; 1 of them is alive after 9 years.

Conclusions: MITOP has an acceptable safety profile in a group of heavily pretreated patients with a very poor prognosis but response rate was lower than expected. However in patients with first line refractory disease and no prior HDT, MITOP followed by BuMel resulted in encouraging survival rates. This schedule is actually evaluated in the randomised trial VERITAS.

V326 SIOP19-0240 | LINC01105 Acts as a Novel Oncogene in the Development of Neuroblastoma

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Background/Objectives: Our previous research revealed that Linc01105 is associated with neuroblastoma proliferation and apoptosis, its expression is correlated with the International Neuroblastoma Staging System (INSS) stage. The purpose of this study was to investigate functions of Linc01105 in neuroblastoma.

Design/Methods: Lentivirus-mediated Linc01105 knock-down was performed in the neuroblastoma cell line SH-SY5Y. The expression levels of Linc01105 and other relative genes were measured using qRT-PCR. CCK8 and flow cytometry were used to determine cell viability and apoptosis. The levels of proteins were detected using western blot. Bioinformatics analysis and luciferase reporter assays were applied to analyze the relationship between linc01105, miR-6769b-5p and VEGFA. Tumor angiogenesis was measured using a tube formation assay.

Results: HIF-1 α overexpression promoted the transcription of Linc01105 by acting as a transcription factor. Down-regulation of Linc01105 inhibited neuroblastoma cell viability, migration and induced apoptosis. Moreover, Linc01105 also affected the expression of p53 and Bcl-2 family proteins and activated the Caspase signaling pathway. Further studies revealed that Linc01105 could promote the expression of the miR-6769b-5p targeted gene VEGFA by acting as a sponge of miR-6769b-5p.

Conclusions: Linc01105 up-regulation contributes to neuroblastoma genesis and development. The interplay between the p53/caspase pathway and Linc01105- miR-6769b-5p-VEGFA axis may play an important role in the development of neuroblastoma.

V327 SIOP19-1389 | Downregulation of MIR128A Expression Reveals a Novel Subgroup of Unfavorable Neuroblastoma and Together with Tert Overexpression Predicts Adverse Outcome

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Background/Objectives: Clinical heterogeneity is a hallmark of neuroblastoma. Rearrangements of *TERT* gene with its correspondent hyper-expression are known to be an adverse prognostic markers, while significance of microRNA profile in neuroblastoma is undiscovered.

Design/Methods: RNA samples from 103 fresh-frozen neuroblastoma tissues were reverse transcribed and used in quantitative PCR for *miR128A* and *TERT* expression evaluation. 25 samples were subjected to the whole-transcriptome profiling for the verification of unraveled expression aberrations. The correspondence of gene's expression to event-free survival (EFS) was analyzed by ROC-analysis and established threshold levels (TL) were applied for group separation in subsequent survival analysis. Median of follow-up time achieved 5.8 years.

Results: Downregulation of *miR128A* was associated with specific gene expression signature with the *ECEL1*, *SYT3* and *CTAG1A* as the most differentially expressed genes. Both downregulation of *miR128A* and abundant *TERT* expression were connected with the superior rate of adverse events ($p=0.027$, $TL=4.7E-3$ and $p=0.004$, $TL=4.6E-2$ respectively). Based on the presence of expressional abnormalities patients were separated into four groups. EFS in group of patients with *TERT* expression above $4.7E-3$ (group TERT) was $0.66SE0.07$, in patients with *miR128A* expression below $4.6E-2$ (group miR128A) was $0.64SE0.15$, patients harboring both *TERT* overexpression and lack of *miR128A* expression (group miR128A/TERT) had dismal outcome: EFS $0.29SE0.11$, comparing to patients without these abnormalities (group "neither"): EFS $0.92SE0.06$, $p<0.001$. Analogously cumulative incidence of progression in the group TERT was $0.32SE0.07$, miR128A – $0.36SE0.15$, miR128A/TERT – $0.71SE0.11$, "neither" – $0.08SE0.06$, $p<0.001$. Expressional biomarkers retained prognostic significance in *MYCN* single-copy patients where EFS rates were as follow: group miR128A/TERT ($0.40SE0.15$), miR128A ($0.60SE0.15$), TERT ($0.74SE0.08$) and group "neither" $0.92SE0.06$, $p<0.001$.

Conclusions: Level of *miR128A* expression allows separation of patients with neuroblastoma into groups with unequal outcome and together with *TERT* expression could be a useful prognostic biomarker for the initial risk definition.

V328 SIOP19-1052 | Neuroblastoma as Perinatal Tumors: When Surgery is Not Essential. Our Experience

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Background/Objectives: Neuroblastoma (NB) is the most frequent malignant tumor in pediatrics. The most important prognostic factors are age, stage and MYCN gene amplification. Children under 12 months with localized tumors have a survival > 90% at 5 years. This is why many studies have endorsed observation as a safe alternative for infants with small perinatal tumors.

We described our experience in perinatal Neuroblastoma, which the primary therapeutic option was watch and wait.

Design/Methods: From march 2014 to march 2018, we analyzed neonatal patients with suspected Neuroblastoma in the Hospital Italiano de Buenos Aires.

After histological confirmation, C T scan, MIBG tracing, bone marrow biopsy and urinary catecholamines were performed. In patients with localized tumors, observation was made as primary therapy and controls were performed with ultrasound and urinary catecholamines up to 18 months.

Results: Ten patients were evaluated, 8 male, media age, 30 days (7d- 7m) Nine presented adrenal mass (one bilateral) and one presented cervicothoracic localization. Sixty percent were localized and 30% were classified as 4S. Eight has catecholamines positive. Two patients underwent immediate surgery, one of them had a diagnosis of low risk NB. In the remaining 8 patients, observation was made: One patient underwent surgery at 12 months due to pulmonary sequestration; and 2 patients after 18 months, histology revealed Ganglioneuroma and Neuroblastoma (4S). In three patients the lesion disappeared and 2 patients with NB 4S presented regression of the lesions, so they continue to be observed.

Conclusions: Clinical observation in infants with small masses is possible, survival gives encouraging numbers, even in patients with NB 4S. Working in cooperative groups is essential since it is a viable treatment strategy and cost effective even for developing countries.

V329 SIOP19-0838 | HSA-MIR-323A-3P Induces G1-Cell Cycle Arrest and Apoptosis in Neuroblastoma Cells

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Background/Objectives: **Background:** The treatment of patients with high-risk neuroblastoma is unsatisfactory due to clinical obstacle posed by drug resistance mechanisms. MicroRNAs (miRNAs) are small, endogenous, non-coding

RNAs that reduce the translation of target mRNAs. Recently, multiple microRNAs are implicated in the modulation of drug resistance in cancers. Our previous research have identified downregulation of *miR-323a-3p* in the post-chemotherapy neuroblastoma cell lines as compared to matched pre-chemotherapy neuroblastoma cell lines. *MIR-323a-3p* microRNA lie in the 14q32 chromosome location, which is frequently downregulated in human cancers. In addition, *miR-323a-3p* was found downregulated in stage 4 vs stage 1-2 in a cohort of 226 primary neuroblastoma tumors.

Design/Methods: **Methods:** In this study, RT-qPCR assay was used to quantitate the basic expression of *miR-323a-3p* in Kelly, SH-SY-5Y and SKNBE (2)-C cell lines. The functional role of *miR-323a-3p* in neuroblastoma cell lines was evaluated by alamar blue-cell viability; flow cytometry and western blot assays. Luciferase reporter assay, RT-qPCR and western blotting techniques will be further used for *miR-323a-3p* target identification and quantification in the neuroblastoma cell lines.

Results: Over-expression of *miR-323a-3p* led to significant inhibition of cell viability in Kelly, SH-SY-5Y and SKNBE (2)-C. In addition, overexpression also caused G1-cell cycle arrest in Kelly, SH-SY-5Y and apoptosis in Kelly, SH-SY-5Y and SKNBE (2)-C.

Conclusions: Our preliminary results provide new insights into the role of previously unknown *miR-323a-3p* in neuroblastoma tumorigenesis and warrants further investigation into the functional targets of this microRNA.

V330 SIOP19-1118 | Use of Dinutuximab/Dinutuximab Beta in Patients with High Risk and Relapsed Neuroblastoma. Experience in Argentina

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Background/Objectives: Dinutuximab/Dinutuximab Beta is a monoclonal antibody specific to the disialoganglioside GD2, an antigen overexpressed in neuroblastoma (NBL) cells. The incorporation of immunotherapy into standard maintenance treatment for patients with high-risk neuroblastoma has been reported to improve overall survival. Dinutuximab/Dinutuximab Beta has also shown promising efficacy and tolerability in patients with relapsed or progressive neuroblastoma/To report the experience of the use of Dinutuximab/Dinutuximab Beta for maintenance treatment of high-risk NBL and for treatment of relapsed neuroblastoma (NBL) in 4 institutions in Argentina

Design/Methods: We describe retrospectively clinical and epidemiological features, feasibility to access, administration form, different infusion regimens elected, adverse effects and outcome of pediatric patients with high risk and relapsed NBL treated with Dinutuximab and Dinutuximab beta between December 2016 and March 2019 in Argentina.

Results: Patients (p): 11 Mean age 36 months (range: 15-50). Boys 9. Maintenance treatment (with isotretinoin): 9p. Treatment at relapse (together with VIT scheme): 2p. Infusion in a public system institution: 5p. Number of cycles (c): 29 (r: 1-5). Dinutuximab (17,5 mg/m²/day in 8 hours for 5 days) 4p/11c. Dinutuximab Beta (20mg/m²/day in 10 hours for 5 days) 4p/14c. Dinutuximab Beta (10mg/m²/day in continuous infusion for 10 days) 3p/5c. All patient received medication by a central venous access and continuous intravenous morphine by another access. Adverse effects: fever 11p, neuropathic pain 10p, capillary leak syndrome grade IV 1p, hematology toxicity 3p (grade I-II 9p- grade IV 1p). Evolution and outcome: 3p are still in treatment, 2p are out of treatment (1p relapsed/1p in complete remission), 1p refused to continue with Dinutuximab Beta and 5 died for disease progression (2p treated at relapse).

Conclusions: In our experience the administration of Dinutuximab/Dinutuximab Beta was feasible. One p had a severe adverse effect (capillary leak syndrome). The rest of the adverse effects were well controlled with morphine and antitermics. Although the importation of the drug demanded a great effort and central drug administration interventions it was possible in public and private institutions.

V331 SIOP19-1503 | Immune Features Correlate with Neuroblastoma Risk Groups Using Multiplex Platforms

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Background/Objectives: Neuroblastoma outcomes vary from spontaneous regression to metastatic with high mortality rates. The tumor microenvironment (TME) may play a significant role in this disease. Further analysis is needed to analyze the TME comparing high-risk (HR) and low-risk (LR) groups. Using publicly available data on R2, Genomics Analysis and Visualization Platform we find high expression of immune markers including CD8A, HLA-DRA and PDCD1 (PD1) predict poor relapse-free survival. In this study, we evaluate the TME comparing HR to LR patients at the tissue level using multiplex platforms.

Design/Methods: Two tissue microarrays (TMA) were created from 41 patients treated at Columbia University Irving Medical Center (CUIMC), including 17 HR, 7 intermediate-risk (IR) and 15 LR patients. Five micron slides were cut and stained for 34 proteins using Digital Spatial Profiling (DSP, nanoString) and a subset of 23 patients were analyzed including 11 HR, 4 IR and 8 LR. TMAs were also stained using quantitative multiplex immunofluorescence (qmIF) for CD3, CD8, CD68, HLA-DR, PDL1, and Chromogranin A. Statistical analysis performed using Mann-Whitney t-test.

Results: With DSP we find HR tumors express significantly more HLA-DR compared to LR tumors ($p=0.016$). We next evaluate CD8 expression per total CD45 finding a trend toward higher CD8/CD45 in HR compared to LR tumors ($p=0.059$). Interestingly, we find that PD1 and PDL1 expression is similar in all groups with no significant difference comparing LR to HR ($p=0.778$ and $p=0.310$, respectively).

Conclusions: Unlike other tumors, increased immune markers in TME correlate with poor prognosis in neuroblastoma. Using DSP we find that markers of immune activity including HLA-DR and CD8A tend to be upregulated in HR neuroblastoma. To further characterize the TME in neuroblastoma, qmIF analysis is underway, evaluating concatenated immune cell density (i.e. CD3+CD8+) and spatial arrangements of immune cells.

V332 SIOP19-0795 | Unveiling Early Differentiation Induced by Histone Deacetylase Inhibitors in Neuroblastoma Cell Lines: A Single-Cell Transcriptomics Approach

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Background/Objectives: The process of tumorigenesis cannot be fully explained solely by genetic alterations. Epigenetic regulation is an underinvestigated basal cause initiating and sustaining cancer cells development. In this context, Histone deacetylases (HDACs) play a fundamental role in remodeling chromatin and thus regulating gene expression towards cell proliferation and de-differentiation (PMID 21416059). Currently, there are more than 20 HDAC inhibitor drugs approved for cancer treatment or in clinical trials. These inhibitors can promote cell differentiation and apoptosis and ultimately reduce cancer cell growth, infiltration and angiogenesis. However, little is known on the early transcriptional response induced by HDAC inhibitors, particularly in Neuroblastoma, where HDAC inhibition has been proven favorable in reducing tumor features in cell line models (PMID 28671573). Current quantitative transcriptomics techniques (microarrays and bulk RNA-Seq) measure average gene expression across many cells, but ultimately lack the ability to understand short-term

transcriptional responses at a single cell resolution (PMID 29643510).

Design/Methods: We measured transcript expression from unsynchronized MYCN-amplified Neuroblastoma-derived cell lines, both untreated and treated with an HDAC pan-inhibitor. We separated 1000 cells for each experimental group using the 10x Genomics Emulsion technology. We then sequenced polyA transcripts in each cell using Illumina Sequencing.

Results: Our analysis of single-cell gene expression profiles detected an increased proportion of cells in G1 phase in inhibitor-treated Neuroblastoma cells. Amongst these we were able to identify progressively differentiated cell populations. These profiles correlate with previously observed HDAC-inhibition and Apoptosis-related transcriptional signatures.

Conclusions: Understanding cell response heterogeneity to HDAC inhibitors will shed light on the variability of transcriptional response upon drug delivery to Neuroblastoma cells. Single cell resolution will allow to detect short-term rewiring and/or the insurgence of resistance mechanisms. This can help understanding how HDAC inhibitors can benefit from the combination with other drugs, in order to further guide the tumor's molecular machinery towards differentiation and apoptosis.

V333 SIOP19-0833 | New Germline ALK Mutation - A Potential Cause of Congenital Metastatic Neuroblastoma, Dysmorphism and Developmental Delay

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Background/Objectives: Anaplastic Lymphoma Kinase (ALK) is a transmembrane receptor tyrosine kinase that plays an important role in nervous system development. The ALK gene is located on chromosome 2p23. Germline ALK abnormalities predisposes to neuroblastic tumours and are the commonest cause of hereditary neuroblastoma. Within the ALK gene there are a number of mutational hotspots. F1174 is the 2nd commonest site of somatic mutation with only one previously reported case in the germline. This was specifically F1174V and the child had congenital neuroblastoma and fatal encephalopathy / brain stem abnormality¹.

Design/Methods: We report the case of a child (now 3 years old) with congenital neuroblastoma and developmental delay who was found to have a germline F1174L ALK mutation.

Results: A 3 year old boy presented at birth with blue-berry muffin spots and was found to have congenital Ms neuroblastoma with a right adrenal primary tumour and skin/subcutaneous tissue and liver metastases. Biopsy confirmed favourable histology neuroblastoma with no evidence of MYCN amplification or segmental chromosomal abnormalities. After an initial period of observation he required 2 cycles of chemotherapy due to disease progression. Since then his tumour has slowly and continuously regressed. Genetic testing revealed an F1174L ALK mutation in the tumour which was subsequently found to be present in the germline. The child has had other health problems since birth including feeding difficulty and poor growth, gross motor developmental delay, hypertonia and convergent squint.

Conclusions: Germline ALK mutations predispose to early onset neuroblastoma. This new variant F1174L mutation may also be responsible for the more extended phenotype of poor feeding, small stature and developmental delay. Future reports of germline F1174L mutations will confirm or refute this finding.

1. de Pontual L, Kettaneh D, Gordon CT, Oufadem M, Boddaert N, Lees M, et al. Germline gain-of-function mutations of ALK disrupt central nervous system development. Human mutation 2011;32 (3):272-6.

V334 SIOP19-0322 | Exosome Secreted from Dedifferentiated Fat Cells (DFAT) Induces the Differentiation of Neuroblastoma Cells

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Background/Objectives: Recent reports have demonstrated that mesenchymal stem cells (MSCs) have the ability to induce the differentiation of neuroblastoma. Furthermore, the function of exosomes isolated from the culture supernatants of MSCs has been actively studied. Dedifferentiated fat (DFAT) cells have properties similar to MSCs. They are also easier to prepare than MSCs or ASCs, and uniform cells can be obtained. In this study, we investigated whether DFAT cells and exosomes secreted from DFAT cells can induce the differentiation of neuroblastoma cells.

Design/Methods: SK-N-SH cells were co-cultured with DFAT alone (DFAT group) or with DFAT-derived exosomes (exosome group) for three days. A single culture group served as a control (control group). At least 15 random fields were photographed and 50 cells per frame were counted and scored for the length of neurites. The mRNA expression of neuronal specific markers (*Neurofilament: NF* and *Tubulin beta III: Tubβ3*) was assessed by a quantitative RT-PCR. Data were

compared using Student's *t*-tests or a one-way ANOVA using a Tukey test.

Results: The length of the neurites in the cells of the DFAT group were increased in comparison to the control group (40% vs. 8%, $p<0.01$) and the expression of *NF* (DFAT group/Control group CT=2.18, $p<0.01$) and *Tubβ3* (DFAT group/control group CT=2.32, $p=0.0322$) was upregulated. The length of neurites in the cells of the exosome group was also increased in comparison to the control group (36% vs. 6%, $p<0.01$). The expression of *NF* (exosome group/control group CT=1.80, $p<0.01$) and *Tubβ3* (exosome group/control group CT=2.19, $p<0.01$) was upregulated in the exosome group. The ability to induce differentiation with DFAT exosomes increased in a concentration-dependent manner.

Conclusions: This study suggests that exosomes secreted from DFAT induce the differentiation of neuroblastoma cells. DFAT-derived exosomes may offer new insight into therapy for neuroblastoma patients.

V335 SIOP19-0154 | Outcome and Prognostic Factors of High Risk Neuroblastoma in Low Income Countries in National Cancer Institute, Egypt: Single Center Experience

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Background/Objectives: Patients with metastatic neuroblastoma or poor biologic features have poor outcome, with estimated 5-year survival rates of 50% (1). The most important prognostic factors are the age, stage, MYC-N gene status, DNA ploidy, and histology

Objective: To ASSES IMPACT OF DIFFERENT PROGNOSTIC FACTORS ON (OS) and (EFS)

Design/Methods: Retrospective study at the National Cancer Institute, Egypt including 133 high risk Neuroblastoma patients recruited from 1/01/2008 to 31/12/2015.

Results: All patients received induction chemotherapy (VP16/CARBO alternating with CADO) (6 to 8 cycles),.3 years OS for (CR, VGPR& PR) group was (51.7%) compared with (19%) (NR& PD) group in correlation to induction therapy with ($P<0.001$). many of poor prognostic factors by Univariate analysis had significant negative impact on both OS, EFS as high ferritin level with p value ($P=0.033$, $P=0.029$, unfavorable histology ($P=0.027$, $P=0.038$), stage 4 disease ($P=0.040$, $P=0.003$), respectively while On multivariate analysis the only independent factor that had negative significant impact on OS was the unfavorable histology ($P=0.005$) while the maintenance treatment had significant positive impact on O.S ($P<0.001$), on the other

side the independent factors that affect EFS negatively were unfavorable histology ($P=0.013$), stage 4 disease ($P=0.030$), need to salvage therapy ($P=0.008$) while doing surgery ($P<0.001$), and receiving radiotherapy ($P=0.010$) and maintenance treatment ($P<0.001$) had significant positive impact on survival. Patients who received HSCT showed better 3 years overall survival (66.5%) than those who did not (24.4%) ($P<0.001$). Surgical resection regardless extent of resection, consolidation by HSCT and radiotherapy, maintenance by Cis Retinoic has significant positive impact on outcome. The cumulative OS, EFS at 24, 36 months was (48.8%,29.3%) and (39.7%, 22.7%) respectively

Conclusions: High risk Neuroblastoma still having poor outcome especially in low income countries with lack of facilities and financial support, more insights should be directed to tandem transplant and immune therapy to improve outcome.

V336 SIOP19-1115 | Stage 4S Neuroblastoma Experience with the TPOG Neuroblastoma Treatment Protocols 2003 and 2009; on Behalf of the Turkish Pediatric Oncology Group

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Background/Objectives: To evaluate treatment outcomes of infants with stage-4S NB enrolled in the TPOG-NB Protocols.

Design/Methods: Shimada classification, MYCN, 1p, 11q, 17q aberrations, DNA-ploidy were analyzed for risk stratification. **TPOG-NB-2003;** primary surgery was performed if possible; four courses chemotherapy (VCR+Cyclophosphamide) were given to symptomatic infants. **TPOG-NB-2009;** observation of asymptomatic infants; in presence of life-threatening symptoms two/four courses chemotherapy (VCR+Etoposide+Carboplatin) were given. Primary surgery was performed if possible. If necessary RT was performed. Refractory patients treated accordingly upper risk group schema.

Results: There was 89 stage-4S infants, 82 of them were eligible.

TPOG-NB-2003 (n:30):

Primary surgery was performed in 10cases. Response rate of chemotherapy was 53%. Three second-look, four delayed

surgery were performed. Radiotherapy was performed in three cases. Low-RG (n:25) Because of progression, risk group and treatment schema changed to Intermediate-RG in 6 infants. In Low-RG median follow-up time 12years (2days–16,4years), the 15-years EFS 56%, OS 76%.

TPOG-NB-2009 (n:52):

Low-RG (n:31): Six infants observed. Primary surgery was performed in 11 patients, chemotherapy was given two of them. Progression to systemic-NB occurred in two of 11 cases. Chemotherapy was given to 17 patients. Two cases died at NICU. Thirteen cases received two courses, 4 cases received four courses chemotherapy. Delayed surgery was performed in two cases. In Low-RG, median follow-up time 42 months (2days–13,6years). The 8-years EFS 59%, OS 90%.

Intermediate-RG (n:18) Primary surgery was performed in 7 cases. Induction response to chemotherapy was 89%. Progression of liver metastasis required radiotherapy (n:2). Median follow-up time 40months (7days–8years), the 8-years EFS 82%, OS 94%.

In High-RG (n:3) two cases just diagnosed, one infant alive.

Conclusions: For management of stage-4S neuroblastoma, “wait&see strategy”, avoiding early surgery, supportive treatments, if necessary performing radiotherapy are important. Treatment outcomes of stage-4S NB were found to be better in the TPOG-NB-2009 protocol. According to our findings platinum based chemotherapy is preferable rather than cyclophosphamide containing chemotherapy.

V337 SIOP19-1311 | Localized Neuroblastomas, Experience of the TPOG Neuroblastoma 2009 Protocol; On Behalf of the Turkish Pediatric Oncology Group

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Background/Objectives: To analyze clinical characteristics, treatment outcomes of patients diagnosed as localized NB, and treated according to the TPOG-NB-2009 protocol.

Design/Methods: Age, stage, Shimada classification, MYCN, 1p&11q&17q aberrations, DNA-ploidy were anal-

ized for risk stratification. There was 535 patients with localized NB, 429 patients were eligible.

Results: Low-RG (225): In stage1-NB (n:184) patients, Two primary relapses and two unrelated deaths occurred. Three of 41 patients with stage2-NB received A7-block chemotherapy after primary surgery. One died with progression. The median follow-up time 29months; 8-years OS and EFS 98%.

Intermediate-RG (n:124) Stage2-NB (n:21): Primary surgery was performed in 14cases. Induction chemotherapy (A8+A9) response was 20/20 (PR+CR). Delayed/second-look surgery was performed in 10cases. One primary relapse, One sepsis-related, one operation-related deaths occurred. Stage3-NB (n:103): Primary surgery was performed in 35 patients. Induction chemotherapy (A8+A9) response was 97%. Delayed/second-look surgery was performed in 62. Four cases received radiotherapy to primary tumor site. Six patients relapsed at median 8months (4–48mos). Two patients died with progression, one died related to operation. The median follow-up time 40mos; 8-years EFS 90%, OS 95%.

High-RG (n:80): Stage-3 (n:77). Primary surgery was performed in 14patients. Response to induction chemotherapy (A9+A11) was 83%. Delayed/second-look surgery was performed in 50patients. Thirty-two cases received radiotherapy to primary site. Sixty-one patients were in conventional chemotherapy (CCT), 19 in HighDoseCT+HSCT arm. Twenty-five patients died related to progression (n:17), infections (n:6), HDCT+HSCT-related (n:2), operation-related (n:1). The median follow-up time 2years. The 8-years EFS 51%, OS 57%. The EFS and OS rates were significantly different between patients who received RT (n:33) or not (n:41) ($p<0.05$), and between patients with amplified-MYCN (n:27) or not (n:19) ($p<0.05$). The EFS and OS rates were not found significantly different between CCT (n:61) and HDCT+HSCT (n:19) patients.

Conclusions: Treatment responses and survival rates of localized-NB were found successful. According to our findings radiotherapy is necessary for stage3 high-RG patients, and we thought that CCT can be preferred in localized high-RG NB.

V338 SIOP19-0119 | Mobilization of Multi-Functional Tumor Infiltrating Lymphocytes Following Co-Administration of Anti-PD-1/PD-L1 Antibodies in a Murine Neuroblastoma Model

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Background/Objectives: Majority of tumors which respond to the immunotherapy using the anti-PD-1/PD-L1 monoclonal antibodies (mAbs) express PD-L1 on the cell surface. However, the frequency of PD-L1 expression on neuroblastoma cells is reported very low. Herein we demonstrate that co-administration of anti-PD-1 and/or anti-PD-L1 mAbs promotes anti-tumor effects in mouse neuroblastoma cells that dimly express PD-L1 in vitro. We further addressed roles of tumor infiltrating lymphocytes (TILs) in a murine neuroblastoma model.

Design/Methods: Mouse neuroblastoma cells (Neuro-2a) that dimly expressed PD-L1 in vitro were inoculated into the subcutaneous space of A/J mice, followed by intra-peritoneal injection of anti-PD-1 and/or PD-L1 mAbs (250 µg/mouse) 3 times (at the day 5, 7 and 12 following the tumor cell inoculation). Tumor sizes were evaluated, and further tumor, stromal, and immune cells from tumor-burden mice were analyzed using a flow cytometer. Multi-functionality of CD8⁺ TILs were measured by intra-cellular staining for IFN γ , CD107a, and TNF α .

Results: Co-administration of anti-PD-1/PD-L1 mAbs significantly suppressed tumor growth, and moderate tumor suppression was also observed in mice that received the monotherapy with either anti-PD-1 or anti-PD-L1 mAbs compared with mice that were treated with isotype-matched control mAbs. CD8⁺ TILs were most infiltrated in the co-administration group of both anti-PD-1/PD-L1 mAbs. While levels of Tim-3 as an exhaustion marker of TILs were not altered among groups of mice, IFN γ ⁺CD107a⁺TNF α ⁺ TILs markedly increased in the co-treated group. Dimly PD-L1-positive tumor and stroma cells were depleted from the tumor environment in an anti-PD-L1 treatment manner. When Neuro-2a cells were inoculated into T-cell deficient athymic nude mice, those antibody-dependent tumor suppressions were cancelled nonetheless of depletion of PD-L1^{dim} tumor and stroma cells.

Conclusions: Co-administration of anti-PD-1/PD-L1 mAbs increased multifunctional CD8⁺ TILs and enhanced anti-tumor effects against Neuro-2a neuroblastoma cells. Depletion of PD-L1^{dim} cells may contribute to an efficient anti-tumor immunity by TIL.

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Background/Objectives: Population-based survival rates for infant neuroblastoma have not improved over the last decade in the UK. There is no national clinical registry and the last trial closed in 2004. To understand outcomes of current treatments and reasons for any international differences in survival, we initiated a European collaborative research project to enrich cancer registry data with clinically relevant data sourced from treatment centres. We describe the efforts required in England to obtain additional clinical data and provide a detailed description of patient/tumour demographics.

Design/Methods: Infants (aged 0-12months) with a diagnosis of neuroblastoma/ganglioneuroblastoma registered in the English population-based national cancer registry between 01/1999-12/2010 were included. The registry requested the 17 principal treatment centres in England to provide additional clinical data on their patients into a datasheet prefilled with existing registry data and standard coding for additional data fields. Datasheets were completed by local oncologists from hospital records and returned to the national registry under its statutory approvals for handling personally identifiable data.

Results: 317 patients were identified in the registry and additional clinical data were obtained on 309 (97%). INSS stage was obtained in 303 (96%): 13%-stage I, 12%-stage 2, 21%-stage 3, 23%-stage 4s, 32%-stage 4. *MYCN* status was available for 248 (78%) tumours, with 15.3% amplified. Cases were diagnosed prenatally 6%, incidentally 17% and with clinical symptoms 77%. Treatment: 87 patients were registered in clinical trials and 197 were reported as being treated according to a protocol. 37 patients had high dose therapy and 12 had radiotherapy as part of first line therapy. 40 (13%) patients died. Time required to retrieve data from hospital records averaged 80min/patient.

Conclusions: International benchmarking of clinically detailed event free and overall survival rates according to treatment received and tumour biology is feasible at a population level. Significant resources, goodwill and close working with clinical centres is required.

V339 SIOP19-0815 | Learning from Clinically-Linked Population-based Cancer Registry Data on Infant Neuroblastomas for Comparative Cancer Outcomes Research

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V340 SIOP19-0372 | Therapy Intensification in High-Risk Neuroblastoma Patients with Poor Response to Standard Induction

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Background/Objectives: Survival of high-risk neuroblastoma remains lower than 50% despite implementation of multimodal therapy. Response to the induction chemotherapy is one of the prognostic factors. The role of therapy intensification in patients with poor response is still unclear.

The aim of the study was to analyze the results of therapy of high-risk NB patients with poor response to standard induction who received second-line topotecan-based chemotherapy.

Design/Methods: Twelve high-risk NB patients with poor response to standard induction of the German NB2004 protocol (cycles N5, N6) were included in the analyses. Response was assessed after 6 cycles according to the international response criteria and Curie score. Poor response was defined as mixed response and stabilization. Patients with poor response received two additional cycles of TCE (topotecan, cyclophosphamide, etoposide). Response, toxicity profile, overall (OS) and event-free survival (EFS) were assessed.

Results: Median age was 41.6 months (range 8.9-169.6). Male:female ratio - 1:1. Adrenal gland was a primary location in 6 (50.0%). 4 (33.3%) tumors were MYCN amplified. 7 (58.3%) had 3 metastatic compartments, bone and bone marrow were involved in all patients. 10/12 (83.3%) achieved mixed response, 2/12 (16.7%) – stable disease. Total 24 cycles were provided. Dose reduction was required in 9/24 (37.5%) cycles, 7/9 - because of hematological toxicity. No toxic deaths were observed. Response after 2 TCE cycles was assessed as complete - 1/12 (8.3%), very good partial response - 1/12 (8.3%), partial - 3/12 (25%), mixed - 4/12 (33.4%), stable disease - 2/12 (16.7%) and progression - 1 (8.3%). Response was improved in 5/12 (41.6%). 11/12 (91.7%) patients received megatherapy. Median follow-up was 23.0 months (range 8.3-50.4). 3-year EFS was 16.7% (95% CI 0.0-37.8), 3-year OS – 50.0% (95% CI 21.7-78.3).

Conclusions: Our data showed that in patients with poor response to induction chemotherapy two additional cycles of TCE improved response in 41.6% cases, but this was not translated into improved survival.

V341 SIOP19-0491 | Epidural Compression in Infants Less than 6 Month Of Age with Neuroblastoma: Single-Center Experience in Russia

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Background/Objectives: Epidural compression (EC) is severe complication of neuroblastoma (NB) in infants which may result in permanent neurological deficit. The aim to assess clinical presentation and outcomes of EC in infants less than 6 months of age with NB.

Design/Methods: Thirteen patients for the period 01.2012 - 12.2018 (84 months) were included in the analyses. Patients were treated according to German NB2004 protocol. Neurological status was assessed at diagnosis and during follow-up.

Results: Median age at diagnosis – 3.9 months (range 0.5-6.0). Male:female ratio was – 1.2:1. Neurological symptoms were the first presentation in 7 (53.8%) patients. Median time from the first neurological symptoms to diagnosis was 1.9 months (range 0.3-2.7). Primary tumor localized most common in retroperitoneal region - 8 (62%). Stage distribution according to INSS: 2 - 2 (15%), 3 - 6 (47%), 4S - 2 (15%) and 4 - 3 (23%). Risk group distribution: observation group – 11 (84.6%), medium-risk group- 2 (15.4%). MYCN amplification, 1p and 11q deletions were not observed in all patients. The degree of spinal canal compression: 33-66% - 4 (31%), >66% - 2 (15%), total canal involvement - 7 (54%). Neurological status at the time of admission: motor deficit and pelvic organ disfunction (n=6, 47%), motor deficit (n=5, 38%), no symptoms (n=2, 15%). The extent of surgery was biopsy in 4 (31%), tumor resection in 8 (62%), including 1/8 (8%) complete resection. Five (38%) children underwent neurosurgical procedure within 2 months from diagnosis, 11 (84.6%) received chemotherapy. Median follow-up was 32.8 months (range 0.5-77.7). Outcome: 9 (69.2%) – alive, 3 (33%) – died because therapy complications. Tumor progression observed in 2 patients. Neurological complications: lower paraparesis - 3 (23%), plegia - 4 (37%), paraparesis with pelvic organ disfunction - 2 (15%), not assessed in 1 (8%). Orthopedic late effects were detected in 3 patients.

Conclusions: Most infants with NB and EC developed neurologic sequela. Common guidelines must be established to standardized therapy, follow-up and rehabilitation.

V343 SIOP19-1494 | Ganglioneuroma Experience of the TPOG Neuroblastoma 2003 and 2009 Treatment Protocols; On Behalf of the Turkish Pediatric Oncology Group

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Background/Objectives: To analyze patients who diagnosed as ganglioneuroma and reported to TPOG-NB-2003 and 2009 protocols.

Design/Methods: Demographic features, clinical characteristics and follow-up periods of these patients were evaluated.

Results: There were 124 patients. The median age of diagnosis was 6.7 years (20 months - 16 years), F/M ratio was 1.17. Tumor localization: 53/124 surrenal, 1/124 cervical paravertebral, 43/124 thoracic paravertebral, 10/124 abdominal paravertebral, 2/124 thoracoabdominal paravertebral, 8/124 pelvic, 4/124 dumpell, 3/124 abdomen (mid-line/retroperitoneal). Primary surgery was performed in 113 cases (100 complete, 13 incomplete tumor excision). For these 13 patients with residue: Three second look surgery were performed, two of them resulted in complete tumor excision. Other 10 cases followed up without resurgery. The diagnostic method was biopsy in only 11 cases (9%). Seven second look surgery were performed, six of them resulted in complete tumor excision, and one resulted in incomplete tumor resection. Other 4 patients were followed up without surgery because of morbidity risk. Tumor localization of patients with residual mass: paravertebral thoracic and dumpell Histopathologically: 65% mature ganglioneuroma (n: 81), 14% maturation ganglioneuroma (n: 17), 21% ganglioneuroma NOS (n: 26) cases. Molecular cytogenetics were studied in 17% of the cases (n: 21). There was no MYCN positivity; in 3 cases 1p positivity and in 3 cases 17q positivity were detected. Two remarkable events occurred: One case diagnosed as GN in maturation, after primary surgery with no residual tumor relapsed from the primary as neuroblastoma (NB). Other case was diagnosis as GN and had a recurrence as NB. The mean follow-up time was 4 years (1 month - 16 years).

Conclusions: As the patients reported to protocols with diagnosis of ganglioneuroma evaluated, more than half of them had paravertebral tumors. 9% of the patients were followed up with residual tumor after surgery. In addition, 3% of the patients were diagnosed as inoperable.

V344 SIOP19-0773 | "Salvage" -Therapy of Recurrent Extracranial Malignant Neoplasms in Children (One Centre Experience)

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Background/Objectives: The overall survival rate of children with first-line polychemotherapy resistance in the first-line polychemotherapy, without conduction of high-dose chemotherapy with autologous transplantation, is not more than 10-15% and is one of the main causes of mortality in children and adolescents.

Design/Methods: Fifty six children with relapse or progression of malignant solid extracranial non-epithelial tumor from 2009 to 2018 performed "salvage" - chemotherapy according to the scheme: irinotecan (20 mg/m²/day 1-5 and 8-12 days), temozolomide (orally 100 mg/m²/day in 1-5 days) and irinotecan (40 mg/m² /day in 4-8 days), temozolomide plus bevacizumab (15 mg / kg on day 1 and day 15).

Results: The average age was 5.3 years. In the group of patients with forty-seven patients who received "salvage" - chemotherapy treatment according to the irinotecan / temodal scheme, the annual rate of non-recurrent survival was 27.0% (95% confidence interval: 12.1-41.8%), median survival was 6.9 months; the overall 1-year survival rate for this group was 88.9%, Three years-56.6%, and the median survival rate was 39.5 months. In nine patients, the objective response to "salvage" - chemotherapy under the irinotecan/temozolomide plus bevacizumab scheme in the form of partial regression was recorded in three patients, stabilization of the disease - in three patients, progression of the disease - in three patients. Three patients died of progression of the disease. The average interval from the establishment of a relapse or progression of the disease according to this scheme of "salvage" - chemotherapy to the detection of disease progression or death of the patient, clinical remission was 8 months. One patient was introduced into a clinical remission.

Conclusions: The use of different schemes of salvage therapy with irinotecan, targeting drugs and other cytostatics is promising for reinduction of remission, given their low myelotoxicity, relatively good tolerability and the results of treatment, and needs further study.

V345 SIOP19-1616 | Neurologic Complications from Central Nervous System Neuroblastoma Metastases

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Background/Objectives: Neuroblastoma metastatic to the central nervous system (CNS-NB) is associated with significant mortality (median survival <6 months, <10% survival at 36 months). Significant neurologic compromise can occur at the onset of CNS disease or during treatment. We analyzed the incidence and type of neurologic complications occurring in patients with CNS NB treated at Memorial Sloan Kettering Cancer Center (MSK).

Design/Methods: We reviewed medical records of all patients with radiographically and/or pathologically confirmed diagnosis of CNS NB treated at MSK over a 30-year period including: disease evaluation, generally every 3-month MIBG, CT of primary disease, bone marrow evaluation, and brain CT+/-MR brain and spine. Patients were classified as having CNS-NB detected while being asymptomatic and during routine extent of disease evaluations or having symptoms that promoted further evaluation and imaging. The types of symptoms were noted.

Results: 171 patients with CNS-NB were evaluated and treated for CNS-NB. 51 patients (30%) were asymptomatic having disease detected by routine radiographic evaluation. The most common symptom prompting imaging was headache (N=52, 30%) +/- vomiting (N=37, 22%). New onset seizures occurred in 22 patients (13%). Altered mental status was observed in 21 patients (13%) who "felt funny" (N=1), had slurred speech (N=1), lethargy (N=4) or became acutely obtunded (N=8). Motor weakness occurred in 12 patients (7%), ataxia in 9 (5%), and cranial neuropathies (anisocoria, hearing deficit, facial palsy) in 13 (8%). Other uncommon symptoms included eye pain (N=1), aphasia (N=1) and opsoclonus myoclonus syndrome (N=1).

Conclusions: With the current radiographic evaluation guidelines, 30% of patients will have CNS metastases detected by routine neurologic imaging. 70% of patients are symptomatic at disease presentation with headache and vomiting being the most common sign. The most serious complication, acute obtundation, occurs in 5% of patients. Clinicians should be aware that even subtle neurologic changes can be a harbinger of CNS metastases.

V346 SIOP19-0261 | High-Dose Naxitamab Plus Stepped-up Dosing of Granulocyte-Macrophage Colony-Stimulating Factor for High-Risk Neuroblastoma: Efficacy Against Histologically-Evident Primary Refractory Metastases in Bone Marrow

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Background/Objectives: *Background:* Cure of high-risk neuroblastoma (HR-NB) often requires ablating bone marrow (BM) metastases that are chemoresistant and

survive ¹³¹I-metaiodobenzylguanidine (MIBG) therapy. BM is ideal for immunotherapy with anti-G_{D2} antibodies including naxitamab (humanized-3F8; granted FDA's breakthrough designation in 2018) because of excellent accessibility to antibody, complement, and effector cells. Granulocyte-macrophage colony-stimulating factor (GM-CSF) exerts a dose-response effect in antibody-dependent cellular cytotoxicity and significantly improves outcome with murine-3F8 (*JCO* 2012;30:426).

Design/Methods: *Methods:* We evaluated HR-NB patients with histologically-evident chemoresistant disease in BM, but no soft tissue or prior progressive disease, for response to naxitamab+GM-CSF on protocol (NCT01757626). Cycles comprised naxitamab infused intravenously (30 minutes) x3 (Mon-Wed-Fri) and subcutaneously-administered GM-CSF starting 5 days pre-naxitamab in priming doses of 250µg/m²/day, then stepped-up to 500µg/m²/day beginning with antibody. Naxitamab was dose-escalated in the phase I portion and 9mg/kg/cycle (~270mg/m²/cycle, i.e., >2.5x dosage of ch14.18) in the phase I/II expansion. BM was assessed post-cycle 2 in aspirates+biopsies from bilateral posterior and anterior iliac crests. Cycles were monthly but were deferred if human anti-human antibody (HAHA) developed.

Results: The 19 patients enrolled through 5/2018 were 5m-to-19m (median 7.5m) post-diagnosis and age 2y10m-to-10y1m (median 5y2m). Included were 5 phase I and 14 phase I/II patients. Histology showed primitive NB in 12 and ganglioneuromatous cells in 7 patients. All (100%) patients achieved complete response (CR) in BM. 16 patients also had NB in bone/BM by 123I-MIBG scan; the latter showed CR in 12 (75%). 11 patients remained progression-free 20+-to-54+ (median 27+) months from enrollment, including 10 treated with anti-NB vaccine. HAHA developed in 2 patients post-cycle 2. Toxicities were as expected (*JAMA Oncol* 2018;4:1729).

Conclusions: Naxitamab+GM-CSF is effective against chemoresistant NB in BM, supporting further development of naxitamab which is proceeding in a pivotal international trial (NCT03363373).

V347 SIOP19-0990 | High-Dose Naxitamab (Humanized-3F8) PLUS Stepped-up Dosing of Granulocyte-Macrophage Colony-Stimulating Factor for Neuroblastoma: Outpatient Treatment Low Immunogenicity, and Major Responses in a Phase II Trial

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Background/Objectives: In preclinical (*Oncol Immunol* 2012;1:477) and phase I studies (*Oncol Immunol*

2017;**6**:e1358331; *JAMA Oncol* 2018;**4**:1729), naxitamab displayed features promising for improving efficacy and quality of life compared to other anti-G_{D2} antibodies: more prolonged binding to G_{D2}; enhanced antibody-dependent cellular cytotoxicity (ADCC); substantial but less complement activation which efficiently lyses neuroblastoma yet causes pain; safe dosing >2.5x higher than standard dosages (100mg/m²/cycle) of dinutuximab and murine-3F8; low immunogenicity; major anti-neuroblastoma activity; and pharmacokinetics and manageable toxicity supporting 3 doses/cycle administered outpatient. Granulocyte-macrophage colony-stimulating factor (GM-CSF) is well-tolerated, exerts a dose-response effect on ADCC (*Blood* 1989;**73**:1936), and significantly improves outcome with murine-3F8 (*JCO* 2012;**30**:426).

Design/Methods: In a phase I/II expansion (NCT01757626, opened 6/2016), patients with primary refractory neuroblastoma (persistent but no prior progressive disease) in bones/bone marrow received naxitamab 9mg/kg/cycle (~270mg/m²/cycle) divided into 3 doses infused intravenously (30 minutes) Mon-Wed-Fri. Subcutaneously-administered GM-CSF started 5 days pre-naxitamab in priming doses of 250µg/m²/day, then stepped-up to 500µg/m²/day with the first dose of naxitamab. Response was scored post-cycle 2 and then every 12 weeks. Cycles were monthly through cycle #5, then every 1-2 months. Patients received 5 cycles after a major response, defined as complete or partial response by international criteria. Cycles were deferred if human anti-human antibody (HAHA) developed.

Results: At enrollment, the 23 patients (12 males, 11 females) evaluable for response were 2.0-to-10.4 (median 4.6) years old and 4.9-to-19 (median 6.0) months post-diagnosis. Prior therapy included intensive induction chemotherapy (all patients), 2nd-line chemotherapy (15 patients), 131I-metaiodobenzylguanadine (5 patients), and combined chemotherapy+anti-GD2 antibody (5 patients). Fifteen patients (65%) had Curie scores >10. Eighteen (78%) achieved major response; 24-month progression-free survival was 50% (95% confidence interval: 27%-to-73%). One patient became HAHA (+). Treatment was outpatient, without unexpected toxicities.

Conclusions: Modest toxicity, low immunogenicity, and substantial anti-neuroblastoma activity support further development of hu3F8 which is underway in a pivotal international trial (NCT02502786).

V348 SIOP19-1007 | High-Dose Naxitamab (Humanized-3F8) Plus Stepped-up Dosing of Granulocyte-Macrophage Colony-Stimulating Factor for Relapsed Neuroblastoma Resistant to Salvage Therapy: A Phase II Trial

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Background/Objectives: In preclinical (*Oncol Immunol* 2012;**1**:477) and phase I studies (*Oncol Immunol* 2017;**6**:e1358331; *JAMA Oncol* 2018;**4**:1729), naxitamab displayed features promising for improving efficacy and quality of life compared to other anti-G_{D2} antibodies: more prolonged binding to G_{D2}; enhanced antibody-dependent cellular cytotoxicity (ADCC); substantial but less complement activation which efficiently lyses neuroblastoma yet causes pain; safe dosing >2.5x higher than standard (100mg/m²/cycle) with dinutuximab and murine-3F8; low immunogenicity; major anti-neuroblastoma activity; and pharmacokinetics and manageable toxicity supporting 3 doses/cycle administered outpatient. Granulocyte-macrophage colony-stimulating factor (GM-CSF) is well-tolerated, exerts a dose-response effect on ADCC (*Blood* 1989;**73**:1936), and significantly improves outcome with murine-3F8 (*JCO* 2012;**30**:426).

Design/Methods: In a phase I/II expansion (NCT01757626, opened 06/2019), patients with secondary refractory disease (persistent neuroblastoma after treatment for progressive disease [PD]) received naxitamab 9mg/kg/cycle (~270mg/m²/cycle) divided into 3 doses infused intravenously (30 minutes) Mon-Wed-Fri. Subcutaneously-administered GM-CSF started 5 days pre-naxitamab in priming doses of 250µg/m²/day, then stepped-up to 500µg/m²/day with the first dose of naxitamab. Response was scored post-cycle 2 and then every 12 weeks. Cycles were monthly x5, then every 1-2 months. Patients received 5 cycles after a major response, defined as complete or partial response. Cycles were deferred if human anti-human antibody (HAHA) developed.

Results: At enrollment, the 35 patients (20 males, 15 females) were 2.5-to-32.9 (median 6.4) years old, 0.4-to-10.8 (median 2.5) years post-diagnosis, and status-post 1 (n=23) or ≥2 (n=13) episodes of PD. Thirty-two (89%) patients previously received >1 anti-GD2 antibodies (dinutuximab, murine-3F8, naxitamab), including at >2 time points (n=15). Four (11%) patients became HAHA (+). Treatment was outpatient, without unexpected toxicities. Of 30 patients evaluable for response, 11 (37%) achieved major responses; 24-month progression-free survival was 39% (95% confidence interval: 20%-to-59%).

Conclusions: Modest toxicity, low immunogenicity, and the encouraging outcomes of ultra-high-risk patients support further development of naxitamab which is proceeding in a pivotal international trial (NCT02502786).

V349 SIOP19-1015 | High-Dose Naxitamab (Humanized-3F8) Plus Stepped-up Dosing of Granulocyte-Macrophage Colony-Stimulating Factor for Consolidating ≥ 2 nd Complete Remission of High-Risk Neuroblastoma

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Background/Objectives: In preclinical (*Oncol Immunol* 2012;1:477) and phase I studies (*Oncol Immunol* 2017;6:e1358331; *JAMA Oncol* 2018;4:1729), naxitamab displayed features promising for improving efficacy and quality of life compared to other anti-GD2 antibodies: more prolonged binding to GD2; enhanced antibody-dependent cellular cytotoxicity (ADCC); substantial but less complement activation which efficiently lyses neuroblastoma (NB) yet causes pain; safe dosing $>2.5\times$ higher than standard dosages (100mg/m²/cycle) of dinutuximab and murine-3F8; low immunogenicity; major anti-NB activity; and pharmacokinetics and manageable toxicity supporting 3 doses/cycle administered outpatient. Granulocyte-macrophage colony-stimulating factor (GM-CSF) is well-tolerated, exerts a dose-response effect in ADCC (*Blood* 1989;73:1936), and significantly improves outcome with murine-3F8 (*JCO* 2012;30:426).

Design/Methods: In a phase I/II expansion (NCT01757626, opened 6/2016), high-risk neuroblastoma (HR-NB) patients in $\geq 2^{\text{nd}}$ complete remission (CR) received naxitamab 9mg/kg/cycle ($\sim 270\text{mg/m}^2/\text{cycle}$) divided into 3 doses infused intravenously (30 minutes) Mon-Wed-Fri. Subcutaneously-administered GM-CSF started 5 days pre-naxitamab in priming doses of 250 $\mu\text{g/m}^2/\text{day}$, then stepped-up to 500 $\mu\text{g/m}^2/\text{day}$ beginning with the first dose of naxitamab. Disease status was evaluated every 10-12weeks. Cycles continued monthly $\times 5$ but were deferred if human anti-human antibody (HAHA) developed.

Results: At enrollment, the 44 patients (33 males, 11 females) were 2.2-to-24.5 (median 5.5) years old, 0.9-to-17.8 (median 3.1) years post-diagnosis, and status-post 1 (n=29), 2 (n=7), or ≥ 3 (n=7) relapses. Prior treatment included anti-GD2 antibody (dinutuximab, murine-3F8, naxitamab) in 38 (88%) patients; 13 (30%) patients were previously treated $>2\times$ with anti-GD2 antibody. HAHA developed in 11 (25%) patients after cycle #1 or #2, including 10 prior-treated with antibody. Treatment was outpatient, without unexpected toxicities. Post-protocol, 20 patients received vaccine. Twenty-four month progression-free survival was 52% (95% confidence interval: 36%-to-67%).

Conclusions: Modest toxicity, low immunogenicity, and encouraging outcome in this ultra-high-risk group support

further development of naxitamab which is underway in a pivotal international trial (NCT02502786).

V350 SIOP19-0559 | MIBG Therapy with Chemotherapy as Conditioning for Megatherapy in Advanced Stage Neuroblastoma: Busulphan vs Non-Busulphan based, an Early Treatment Related Toxicity Study

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Background/Objectives: Background and Objectives: Treatment of stage 4 neuroblastoma includes megatherapy with autologous stem cell transplant (ASCT) as consolidation therapy. Our center also included MIBG therapy as part of the conditioning. From 2012, conditioning changed from carboplatin-etoposide-melphalan (CEM) to busulphan-melphalan (BU-M) based. The early toxicities of the two conditioning regimens were compared.

Design/Methods: I¹³¹ MIBG was given at 12 mCi/kg 1-4 weeks before CEM or BU-M. Doses of CEM: carboplatin 300 mg/m²/day and etoposide 160 mg/m²/day iv for 4 days, melphalan 210 mg/m² iv over 2 days; BU-M: busulphan 0.8-1.2mg/kg/dose iv (adjusted according to AUC) Q6H for 16 doses, melphalan 140 mg/m² iv 1 day. The early toxicity was compared, in particular engraftment, veno-occlusive disease of liver (VOD) in the first 90 days post-ASCT.

Results: A total of 25 patients were treated from 2003 to 2019. Initial chemotherapy mostly followed the modified N7 protocol, recent years some were given COJEC. Resection of primary tumour was performed after 5 courses of chemotherapy. Immunotherapy with anti-3F8 was given in 15 patients before ASCT. Fifteen patients received CEM and 10 patients received BU-M. Median time from MIBG treatment to ASCT was 17 days (range 6-37 days). The median age at ASCT was 3.7 years and engraftment was 13 days and there was no difference between the two groups. None of the patients had failed engraftment. VOD occurred in 3 patients in BU-M group (30%) and none in CEM group, 2 resolved after acetylcysteine+/- defibrotide. One had severe VOD with bilirubin 800 $\mu\text{mol/L}$ and died of intracranial haemorrhage at 5 months post-ASCT. There was no significant difference in rate of infection or other organ failure.

Conclusions: MIBG therapy in combination with chemotherapy conditioning before ASCT is feasible. Busulphan based conditioning appeared to have higher incidence of VOD but the relationship with MIBG treatment needs further study.

V351 SIOP19-0329 | Insights into the Gene Expression Landscape of Minimal Residual Disease in Neuroblastoma Through Label-Free Isolation of Neuroblastoma Circulating Tumor Cells

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Background/Objectives: Existing methods of MRD determination in neuroblastoma provide limited quantitative and biological information and are unable to enrich for the cells in question. We investigated the hypothesis that cell size-based separation could isolate circulating tumor cells (CTCs) from peripheral blood of neuroblastoma patients, and compared their gene expression profiles with disease characteristics and treatment responses.

Design/Methods: Using a spiral microfluidic chip (Clearbridge, Singapore), CTCs were isolated from blood and bone marrow samples of 19 patients at 4 timepoints throughout their treatment and assayed for PHOX2B and TH expression by RT-PCR. Expression of 740 cancer progression-related genes, 730 genes from cancer-associated pathways, and 11 neuroblastoma-specific genes were analyzed using nanoString and their expression compared with disease characteristics and corresponding urinary and marrow MRD markers.

Results: Single cells with high PHOX2B and TH expression were isolated from normal blood spiked with NLF cells, and from patient blood samples. Unsupervised non-hierarchical clustering segregated high-risk INSS stage 4 patients from low- and intermediate-risk cases and normal blood samples. The former demonstrated increased signalling in JAK-STAT, cGMP-PKG, cAMP, Notch and NODAL pathways, upregulation of all 13 cancer-associated canonical signaling pathways, and decreased signalling in gene signatures related to ECM-receptor interaction, actin cytoskeleton, tight junction, focal adhesion, proteoglycans, and cell adhesion molecules. Neuroblastoma-specific genes were significantly upregulated in CTCs of patients with lymphatic metastases at diagnosis (MYC, $P=0.05$) and after induction chemotherapy (DDC, $P=0.01$), and in patients with hematogenous

metastases after consolidation (PHOX2B, GD2 synthase, GAP43, CHD5, PTPN14). Post-induction resolution of marrow disease correlated with decreased CTC expression of MYC and DDC and increase in KIF1B.

Conclusions: CTCs isolated using label-free size-based separation expressed characteristic neuroblastoma markers. Distinct expression profiles of a broader panel of neuroblastoma-specific and cancer-related genes correlated with the sites of metastases and treatment response, providing a dynamic multi-dimensional picture of MRD in the blood compartment.

V352 SIOP19-0508 | The Use of Ultrasonic Dissectors for Neuroblastoma Resection

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Background/Objectives: The use of ultrasonic dissectors is well described in surgical oncology for adults. In pediatric surgery, only few reports have been published for brain tumors, hepatoblastoma or biliary atresia. The aim of our study is to describe our experience in the use of ultrasonic dissectors for neuroblastoma excision.

Design/Methods: Data of patients treated for neuroblastoma in a single institution from January 2000 to October 2018 were collected. Tumor characteristics, surgical technique, postoperative complications and oncological outcome were analysed.

Results: In the analysed period, 43 patients were admitted at our centre for high risk neuroblastoma. Among these, 26 were operated with technical support of ultrasonic dissectors. Median follow-up was 13.8 months (range 0.3-140.4). All tumors had abdominal localisation: 19 were adrenal and 7 were in the midline; 17 were metastatic (stage M) and 9 patients were stage L2, according to INRGSS classification. Half of the patients presented minimal residual disease at the end of the procedure. Only 6 patients presented surgical complications, but none of them required surgical intervention (< grade III Clavien-Dindo). We observed 11 cases of complete remission (5 were L2 and 6 M at diagnosis). 11 deaths were observed, 6 after local recurrence and 3 metastatic recurrence. 4 patients were lost to follow-up.

Conclusions: The use of ultrasonic dissectors was feasible and safe for the surgery of neuroblastoma, which remains an extensive and sometimes challenging procedure. Ultrasonic dissectors may help to achieve radical surgery, which can improve significantly the outcome in high-risk neuroblastoma.

V353 SIOP19-1544 | Role of ABCC3 Drug Transporter in Neuroblastoma Cell Invasion

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Background/Objectives: Neuroblastoma is one of the most common extra cranial solid cancers in childhood. The amplification of the MYCN oncogene, encoding for a Basic-Region/Helix–Loop–Helix/Leucine-Zipper transcription factor, is the most important marker of aggressive neuroblastomas. This subgroup of tumors often shows a multiple drug resistant phenotype and although many high-risk neuroblastoma tumors initially respond to the first cycles of intensive chemotherapy, they frequently become refractory to treatment as the disease progresses. Chemoresistance can be due to several mechanisms, including those related to altered activity of specific ATP-binding cassette (ABC) drug transporters. ABCs shuttle hydrophobic lipophilic compounds across cell membranes in an ATP-dependent manner. We have found that MYCN can coordinate transcription of a large set of ABCs in neuroblastoma. ABCC3 is one of the most de-regulated ABCs whose expression is strongly down-regulated in case of high MYCN levels.

Design/Methods: We have measured invasiveness of MYCN-amplified neuroblastoma cells over-expressing ABCC3 by transwell-matrigel assay. Transcriptomic analysis has been performed by a Nimblegen oligonucleotide microarray. QRT-PCR and luciferase gene reporter assays have been used to validate microarray data. Dichlorofluorescein-diacetate assays have been employed to measure intracellular oxidative stress.

Results: Cells over-expressing ABCC3 were found to be less invasive *in-vitro* when compared to controls. Pathway analysis of microarray data has revealed a strong down-regulation of genes promoting cell migration and invasion. Among them, MET is the most down-regulated gene. MET encodes for the Hepatocyte Growth Factor Receptor, whose expression has been largely proven to be strictly correlated to cell invasiveness and advanced stage of many tumor types.

Conclusions: High levels of MYCN expression in tumors may trigger an altered ABC transporter expression profile, hence contributing to the control of drug and physiological substrate efflux in cancer cells. Further investigation on the MYCN-ABCC3 axis could reveal key druggable pathways correlated with metastatic behavior of neuroblastoma cells.

V354 SIOP19-0800 | PRIMA-1^{MET}-Induced Neuroblastoma Cell Death is Modulated by P53 and MYCN Through Glutathione Level

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Background/Objectives: Neuroblastoma is the most common extracranial solid tumor in children, with limited effective treatment options for high-risk tumors. Previously, we demonstrated that PRIMA-1^{MET}, which is known to activate p53, could be a promising new therapeutic agent for neuroblastoma treatment. In our current research, we addressed the role of p53, MYCN, and the glutathione (GSH) pathways in PRIMA-1^{MET} activity.

Design/Methods: Proteomic analysis of 4 neuroblastoma cell lines at 1 h and 9 h post-treatment with PRIMA-1^{MET} looked for possible S-glutathionylation and the addition of PRIMA-1^{MET} to proteins. LA1-55N neuroblastoma cells, with and without stable p53 expression, were prepared. We measured intra-cellular levels of GSH, S-adenosyl-homocysteine, and cysteine, and investigated the impact of cysteine, homocysteine, methionine, N-acetyl-cysteine, and GSH co-treatments on PRIMA-1^{MET}'s efficacy. Finally, we investigated the influence of p53 and MYCN using JQ-1, on the level of GSH and on survival of LA1-55N after PRIMA-1^{MET} treatment.

Results: Proteomic analysis demonstrated that GSH and PRIMA-1^{MET} do not bind to cellular proteins, either 1 h or 9 h post initial exposure. Cysteine, homocysteine, N-acetyl-cysteine, and GSH are able to save neuroblastoma cells from PRIMA-1^{MET}-induced death, even at late stage. PRIMA-1^{MET} causes a profound decrease of GSH concentrations, irrespective of the status of p53 or MYCN, by inhibiting GSH synthesis, downstream of cysteine. Increases in p53 and MYCN expressions induce an increase in GSH levels and cell survival. Repression of p53 and MYCN results in a decrease in GSH and an increased susceptibility to PRIMA-1^{MET}.

Conclusions: Our results suggest that direct interaction between PRIMA-1^{MET} and p53 has a limited role in neuroblastoma treatment. Instead, we demonstrated that PRIMA-1^{MET} is detoxified by GSH, which is modulated by p53 and MYCN. We propose a new model of PRIMA-1^{MET}/p53 interaction where p53 plays an indirect role in preventing PRIMA-1^{MET}-induced cell death by increasing GSH levels.

V355 SIOP19-1396 | Importance of Drug Formulation on the Pharmacokinetics of 13-CIS-Retinoic Acid (Isotretinoin) in Children with High-Risk Neuroblastoma

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Background/Objectives: 13-cis-retinoic acid (13cisRA) has become an established component of the treatment of high-risk neuroblastoma as maintenance therapy since 1999.

This study aimed to establish a valuable pharmacokinetic model of 13cisRA, regardless of the course and day of treatment, and to determine covariates implicated in the previously observed wide inter-patient and inter-occasion variability in 13cisRA pharmacokinetics.

Design/Methods: Twenty-eight children were included in this study and received six courses of 160mg/m²/day 13cisRA, with each course consisting of 2 weeks of treatment, followed by a 2 week rest period.

Plasma samples were studied at 6 points on days 1 and 14 from 50 courses.

Several population pharmacokinetic models were fitted using NONMEM software.

Results: The best model for this paediatric population was a modified zero order bi-compartment model combined with lag time. Allometric scaling was used in terms of clearance (CL), central volume (V₂), intercompartmental clearance (Q) and peripheral volume (V₃).

Based on this PK model, we observed that the method of drug administration had a significant impact on inter-individual and inter-occasion variabilities. Indeed the model was upgraded by setting the absorption rate parameter *K_a*, the lag time LAG, the duration of the zero order input *D* and the bioavailability *F*₁, with method of drug administration included and by taking it into account with respect to the corresponding inter-occasion variabilities.

Conclusions: This study highlights that formulation and patient weight need to be taken account when dosing 13cisRA and shows that the bioavailability is lower and more variable when capsules are opened.

We suggest that consideration of the method of drug administration will provide an explanation for some of the variability of 13cisRA pharmacokinetics and ensure a more appropriate overall drug exposure.

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V356 SIOP19-0476 | Neuroblastoma Treatment in Southern Vietnam

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Background/Objectives: Neuroblastoma is the most common extra-cranial tumor in childhood and the second most common malignancy treated at Children's Hospital 2, Ho Chi Minh City, Vietnam. EFS in high-risk patients in HIC has been reported at 50% with low and intermediate risk patients exceeding 90%. In many countries like Vietnam, limitations in diagnostic and treatment options can severely reduce survival. This study describes the current status of neuroblastoma therapy at a major pediatric cancer center in southern Vietnam.

Design/Methods: With approval of our local ethics board neuroblastoma patients have been treated per SIOPEN Low-and-Intermediate risk protocol and OJEC/OPEC for HR patients since 2011. Chart review was performed on 110 patients from 1/ 2014 – 12/2017. Due to diagnostic limitations, stratification was limited to presence or absence of metastatic disease and age. MYCN amplification was only performed on 63 (57%) patients.

Results: There were 53 females (48%) and 57 males (52%) with a median age of 26 months (range 1m to 10y6m). Visceral or bone metastases was present in 61% of patients at diagnosis. Ten patients were identified as Ms due to age and extent of disease. Overall, 60 children are still alive with an estimated four-year overall survival of 43% (median follow up of 20 months). Using the limited stratification scheme our four-year survival of Metastasis, Non-metastasis and Ms stage patients were 12%, 90% and 80%, respectively. For patients able to obtain MYCN testing, MYCN amplified OS was 11% compared to 66% for patients without MYCN amplification.

Conclusions: Our results illustrate poor survival for HR patients in Vietnam compared to HIC but overall NBL survival remains comparable to other centers in limited resource settings. Non-availability of MYCN testing for some patients could have falsely down-staged them to IR from HR. Without cost-effective treatment options, diagnostic improvements may benefit similar non-HIC environments

V357 SIOP19-1060 | Clinical Impact of ALK Mutations in Neuroblastoma

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Background/Objectives: Somatic *ALK* mutations have been reported in 8-10% of neuroblastoma. The largest published paper on clinical correlates included 126 patients enrolled on COG protocol ANBL00B1 (Bresler et al. Cancer Cell, 2014) but few other such comprehensive reports exist.

Design/Methods: Information on patients with *ALK* mutations treated at Memorial Sloan Kettering Cancer Center for whom long-term follow-up was available was retrospectively

analyzed. *ALK* sequencing was performed either by whole genome sequencing (35x depth), targeted exome sequencing (>500x depth on MSK-IMPACT or Foundation One platforms), or hotspot *ALK* mutation profiling (Sequenom). Statistical analyses were performed using chi-square or Kaplan-Meier methods.

Results: Ninety-seven patients with a median age at diagnosis of 2.6 (birth to 67.8) years were identified. At diagnosis, 21 (22%), 7 (7%) and 69 (71%) patients had low, intermediate and high-risk disease respectively; 24% had locoregional and 76% stage M NB. *ALK* mutations included F1174 (49%), R1275 (30%), R1245 (10%) and others (11%). Coexisting *MYCN*-amplification was noted in 38% and *ATRX* aberrations in 36% of patients. F1174 mutations were more common in high-risk patients and coexistent with *MYCN*-amplification ($p < 0.05$ for both). 50% of patients with high-risk NB achieved complete remission after induction therapy. *ALK* mutation site was not prognostic for progression-free (PFS) or overall survival (OS) in the entire cohort nor the high-risk subgroup. Coexisting *ATRX* mutations did not impact survival ($p > 0.05$). Germline *ALK* mutations (G1128A and R1275Q) were detected in 3/51 patients tested. Thirty-one patients were treated with *ALK* inhibitors: objective (though < partial) response was detected in two (7%) patients.

Conclusions: Somatic *ALK* mutations were noted across all stages and risk groups of NB, but no specific mutation was prognostic for OS/PFS. F1174 mutations were more commonly observed in patients with *MYCN*-amplification and high-risk NB. Response to *ALK* inhibitors was rare.

V358 SIOP19-0852 | Inhibitors of Ribosome Biogenesis Repress the Growth of *MYCN*-Amplified Neuroblastoma

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Background/Objectives: Dysregulation of ribosome biogenesis has emerged as a hallmark in the majority of cancers. Ribosome hyperactivity can be induced by *MYC* transcription factors controlling the expression of ribosome components. Neuroblastoma (NB), a malignant childhood tumor of the sympathetic nervous system, is frequently characterized by *MYCN* amplification and high MycN and c-MYC expression. Quarfloxin and CX-5461 have previously been described as small molecule inhibitors of RNA polymerase I. The aim of the study is to characterize the effects of quarfloxin/CX-5461 in NB.

Design/Methods: Apoptosis was analyzed by immunoblotting and annexin V flow cytometry. Cell cycle distribution

was evaluated by PI flow cytometry. Induction of p53 signaling was assessed by immunoblotting and using a p53 responsive luciferase reporter assay. Knockdown of *MYCN/TP53* was done by siRNA transfection. Presence of DNA damage was determined by immunoblotting against γ H2A.X. Female NMRI nu/nu mice were used for xenograft models. SK-N-BE (2)-C or IMR-32 cells were injected subcutaneously, and CX-5461 was administered by oral gavage.

Results: We found a strong correlation between high-risk disease, *MYCN* expression, poor survival and ribosome biogenesis in NB. Additionally, *MYCN* knockdown in NB cell lines repressed genes involved in ribosome biogenesis. Treatment of *MYCN*-amplified NB cell lines with quarfloxin/CX-5461 induced DNA damage and impaired growth by apoptosis in wt-*TP53* cells and G2/M-arrest in mut-*TP53* cells. Also, MycN was downregulated after treatment with quarfloxin/CX-5461 in *MYCN*-amplified cell lines with wt-*TP53*, but not in mut-*TP53* cell lines. CX-5461 repressed growth of established *MYCN*-amplified NB xenograft tumors in mice.

Conclusions: Our studies show that quarfloxin and CX-5461 repress growth and induce DNA damage in *MYCN*-amplified NB, with most effect in wt-*TP53* tumors. High-risk NB often harbor *MYCN*-amplification, but *TP53*-mutations are rare. Our findings suggest that inhibition of ribosome biogenesis represent new therapeutic opportunities for children with high-risk NB expressing high c-MYC/MycN levels.

V359 SIOP19-0889 | The Role of Peritoneal Fluid Cytology in Pediatric Malignant Abdomino-Pelvic Solid Tumors

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Background/Objectives: The detection of neoplastic cells in the peritoneal fluid signifies subclinical intraperitoneal spread beyond the primary organ involved in an abdomino-pelvic malignancy; this is a recognized indicator of poor prognosis in ovarian tumors as well as in other types of malignancies, such as gastric cancer in adults. Peritoneal fluid (or washings) cytologic analysis is currently included in the Children's Oncology Group (COG) staging system for extragonadal extracranial germ cell tumors. The role of peritoneal fluid cytological examination in children with abdominopelvic solid malignancies is unknown and is not a part of the current staging and risk stratification systems. Positive cytological analysis for malignant cells may prompt tumor upgrading, with subsequent legitimate treatment upscaling to enhance chances for cure.

In this study, we sought to evaluate the utility of the peritoneal fluid cytology in the management of pediatric solid abdomino-pelvic tumors.

Design/Methods: After obtaining IRB approval, we retrospectively reviewed the medical records of all the pediatric patients (0-18 years old), between January 2008 and July 2018, with abdomino-pelvic malignant solid tumors, who underwent surgical excision or biopsy of the tumor with peritoneal fluid cytological analysis.

Results: We identified 23 pediatric patients (age 0-18 years) with solid abdomino-pelvic tumors in whom peritoneal fluid was sent for cytological analysis. Four patients had a positive cytology for malignant cells. As a result of the positive cytology, two patients with Wilms tumor were upgraded to stage III from stage I and II respectively, and hence they received additional doxorubicin and abdominal radiotherapy. The other two patients were stage IV (one Wilms tumor and another neuroblastoma).

Conclusions: We recommend sending peritoneal fluid for cytological analysis during laparotomies for solid abdomino-pelvic tumors in children on routine basis, to detect patients with potentially more aggressive pathology who may benefit from management upscaling.

V360 SIOP19-1263 | Tandem High-Dose Chemotherapy and Autologous Stem Cell Transplantation with TTC/MEC REGIMENS ± 131I-MIBG for High-Risk Neuroblastoma

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Background/Objectives: High dose chemotherapy (HDC) and autologous stem cell transplantation (ASCT) is used for consolidation therapy in high risk neuroblastoma (HRNBL). Optimal conditioning regimens for HRNBL are still controversial. We retrospectively evaluate the outcome of tandem HDC/ASCT with topotecan-thiotepa-carboplatin and melphalan-etoposide-carboplatin (TTC/MEC) regimens ± ¹³¹I-metaiodobenzylguanidine (¹³¹I-MIBG) in HRNBL.

Design/Methods: Thirty-four HRNBL patients underwent HDC/ASCT. A regimen for first ASCT consists of topotecan (10mg/m²), thiotepa (900mg/m²) and carboplatin (1500mg/m²). We administered 210mg/m² of melphalan, 800mg/m² of etoposide and 1400mg/m² of carboplatin for

second ASCT. Carboplatin dose was reduced in MIBG-combined group to 1200mg/m².

Results: The median age at diagnosis was 45-month-old (range 4-month to 13-year). The 131I-MIBG treatment was added to 14 of the 34 patients. Local radiation therapy was added in 28 patients. There were 2 treatment-related mortalities, renal failure and pulmonary complication after second HDC/ASCT. The 5-year overall survival (OS) and event-free survival (EFS) rates of all patients were 79.3% and 69.4%, respectively. Between 131I-MIBG treated group and the other, the OS rates were 79.6%/79.1% (*p*-value 0.896) and the EFS rates were 69.3%/70.0% (*p*-value 0.891), respectively. The OS rate of *MYCN*-positive/-negative patients was 55.6%/93.3% (*p*-value 0.040), and the EFS rate of *MYCN*-positive/-negative patients was 55.6%/76.9% (*p*-value 0.036), respectively.

Conclusions: Tandem HDC and ASCT with TTC/MEC regimens ± 131I-MIBG showed promising results, considering the current state that anti-ganglioside 2 antibody is rarely used in Asia due to its cost. Long term follow-up is needed to determine the effect of adding 131I-MIBG and further efforts are required to reduce treatment-related toxicities.

V361 SIOP19-1397 | Neuroblastoma in Children: Clinical and Therapeutic Characteristics in the Center of Tunisia About 67 Cases

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Background/Objectives: Neuroblastoma (NB) is characterized by extreme clinical variability, ranging from spontaneous regression to rapidly fatal progression despite multidisciplinary treatment. The aim of this study is to describe clinical characteristics of NB in our region.

Design/Methods: A retrospective study included 67NB patients treated in the medical oncology department of CHU Farhat Hached from January 1996 to December 2017. The group at risk of neuroblastoma has been defined according to the international system of neuroblastoma.

Results: The average age was 3.5 years [2 months- 15 years] of which 23% were younger than 18 months. Abdominal swelling and fever were the most common symptoms in 67% and 71% respectively. The adrenal glands were the primary site in 27% of cases. Metastatic forms were observed in 72% of cases. The amplification of the *N myc* gene was performed

in 36 patients. The SFOP protocol was used in the neoadjuvant chemotherapy in 32% of cases with objective response in 40% of cases. Surgery was performed in 18 patients (26%). Adjuvant chemotherapy was administered to 19 patients. The 5-year overall survival was 53% with respectively 80% and 30% for localized, metastatic NB. Poor prognostic factors retained in the univariate analysis were age > 18 months and metastatic forms with respectively $p = 0.005$, $p = 0.03$.

Conclusions: Neuroblastoma is an extremely heterogeneous disease. The challenge remains for the management of metastatic forms in limited resources countries which implies the need of an adapted national protocol.

V362 SIOP19-1062 | Treatment Outcomes in Children with Relapsed/Refractory Solid Tumors: A Single-Center Study

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Background/Objectives: Despite recent improvements in overall survival for pediatric cancers, relapsed or refractory disease remains a significant cause of mortality. The cumulative effect of multiple relapses and salvage regimens is unknown. Here we describe the disease trajectory in patients with relapsed/refractory solid tumors, from time of first relapse to death, stable disease for 24 months, or no evidence of disease for 24 months.

Design/Methods: We reviewed electronic medical records for patients with relapsed/ refractory solid tumors treated at Texas Children's Hospital from 2002-2016. Kaplan-Meier analysis was used to evaluate time to relapse and death, with Cox regression analysis for each variable described. Log-Rank p-values are reported. Analysis was performed with SPSS v24.

Results: Of 80 patients with relapsed/refractory solid tumors reviewed, 38.7% were alive at last contact. Fifty percent were diagnosed with neuroblastoma. Patients had a mean of 2.75 (SD=2.16) progressions and 500 (SD=577) days from first relapse to death. Prolonged survival after first relapse was associated with phase I or clinical trial enrollment and increased time between diagnosis and relapse ($p < 0.05$). In a multivariate analysis, number of progressions and time between first and second relapse were most significantly associated with increased time from first relapse to death ($p < 0.001$). Taking a break from cytotoxic therapy (defined as >21 days between time of relapse and initiation of salvage regimen) (473 vs 576 days, $p = 0.565$) and tumor type (range 273-1328 days, $p = 0.568$) had no significant effect on time between first relapse and death.

Conclusions: The prognosis for patients with relapsed/ refractory solid tumors is poor. Factors associated with prolonged survival include total number of progressions and increased time between first and second relapse. Delay of cytotoxic therapy after relapse does not appear to impact survival, implying that this option could be offered to patients to promote quality of life and explore goals of care between treatment regimens.

V363 SIOP19-0724 | 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 tumors: medulloblastoma, germ cell tumor, soft tissue sarcomas and high-risk neuroblastoma. Nevertheless effectiveness convincing results haven't been obtained.

Design/Methods: From 2012 to 2018 year in the Department of Pediatric Oncology at the National Cancer Institute have been carried out 30 tandem transplantations (TT) in children with high-risk of neuroblastoma. Patient's age was 1 - 14 years. 24 pts. with primary neuroblastoma got TT after chemotherapy on HR-NBL-1/ESIOP protocol, 6 pts. as a consolidation of relapse second-line therapy. The first part of tandem transplantation was BuMel in all patients. Twenty-seven 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 then 500/ μ L after first cycle on +9-12 day, PLT count recovered on +12-34 day after PBSC. In 2 patient was observed neurotoxicity like short clonic and tonic seizures after second high-dose cycle. WBC count recovered more then 500/ μ L after second cycle on +9-11 day, PLT count recovered on +12-22 day. Currently, 13 of 30 patients are in CR, 6 patients had early relapse and continue treatment, 11 died of PD. The follow-up period after accomplishment of TT is 2 - 83 months.

Conclusions: 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%.

V364 SIOP19-0608 | Feasibility and Efficacy of Treatment Strategy of Tandem High-Dose Chemotherapy and Autologous Stem Cell Transplantation with Incorporation of High-Dose ¹³¹I-MIBG Therapy for High-Risk Neuroblastoma

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Background/Objectives: This study was performed to evaluate the safety and efficacy of tandem high-dose chemotherapy and autologous stem cell transplantation (HDCT/ASCT) combined with targeted radiotherapy using ¹³¹I-MIBG for high-risk neuroblastoma (HR-NBL).

Design/Methods: Patients with HR-NBL were treated with 8 to 10 cycles of induction chemotherapy before tandem HDCT/ASCT. All patients received ¹³¹I-MIBG treatment before second HDCT/ASCT. Local radiotherapy, differentiation therapy, and immunotherapy were done after tandem HDCT/ASCT.

Results: Eighteen patients were enrolled. Twelve patients (67%) received BuMel (Busulfan + Melphalan) regimen during their first ASCT while 6 patients received MEC (Melphalan + Etoposide + Carboplatin) regimen. Median dose of ¹³¹I-MIBG was 17.2±1.7 mCi/kg for first 8 patients, while (>12 mCi/kg) while 12 patients in latter period of the study received reduced dose of 10.7±1.2 mCi/kg (≤12 mCi/kg). The 3-year overall survival and event-free survival rates were 83% and 62%, respectively. Six patients experienced disease relapse at median 31 months after diagnosis. Among them, 5 patients died of disease. TRM was not observed. Patients, received ASCT with BuMel regimen, had less severe acute toxicities than patients with MEC regimen. Ten patients (56%) had hypothyroidism, 6 patients (33%) had CKD, and 6 patients (33%) had growth failure. Regimen of first HDCT/ASCT (BuMel vs. MEC) and dose of ¹³¹I-MIBG (>12 mCi/kg vs. ≤12 mCi/kg) affected on long-term toxicities without deteriorating treatment outcomes.

Conclusions: Tandem HDCT/ASCT with incorporation of high-dose ¹³¹I-MIBG therapy could be feasible for patients with high risk NBL. However, further study is needed to verify our findings.

V365 SIOP19-0928 | Genes Involved in Neural Differentiation are Overexpressed in Spontaneously Regressing Neuroblastoma

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Background/Objectives: Spontaneous regression characterizes a group of patients with metastatic neuroblastoma (NB) -classically known as stage 4s. This behavior extends to other tumors in infants that may not fulfil the criteria of 4s.

Design/Methods: GSE49711 was identified as a suitable dataset for analysis and was downloaded through NCBI-GEO site on 3-Oct-2018. This dataset includes 498 patients with NB linked to expression values of 23416 genes. Alive patients with stage 4s who had no MYCN amplification were labeled as very low risk (VLR, N=39) while those with high risk disease who died were labeled as very high risk (VHR, N=84) patients. Subsequently, edgeR was used to analyze differential gene expression (DGE). Hierarchical clustering (HC) followed by principal component analysis (PCA) were utilized. Finally, genetClassifier was used to generate a gene-classifier and validate it.

Results: DGE analysis identified a subset of 15 samples with overexpression of liver genes, indicating possible hepatic tissue contamination. Repeat analysis excluding these samples identified differentially expressed genes that separated samples with high accuracy using HC and PCA. Genes overexpressed in VLR patients were mainly involved in neuron differentiation, neuron development and generation of axons. KEGG identified GnRH signaling (p=0.044) as a potential pathway. Gene expression was similar to cerebellar purkinje cells (p=0.015). When applied to all samples, DGE identified 3 groups of patients (low-molecular-risk, intermediate-molecular-risk, high-molecular-risk). When analyzed in a logistic-regression model including age (>18mo), MYCN-amplification and stage, high-molecular-risk category was associated with significantly worse outcome (HR, 2.74;p=0.0016). A classifier was then generated using a different methodology and identified an 84-gene classifier that was highly accurate.

Conclusions: A novel stratification and testing for contamination resulted in highly accurate set of genes that are associated with neuronal differentiation and defining patients with excellent outcome who may have stage 4s like behavior. A highly accurate classifier was suggested. Also, an interesting role of sex hormones/GnRH pathway was suggested.

V366 SIOP19-1169 | Gene Expression Profiles Analysis Identifies a Novel Two-Gene Signature to Predict Overall Survival in Neuroblastoma

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Background/Objectives: **Background:** Neuroblastoma is the most common extracranial solid tumor arising from the developing sympathetic nervous system in childhood. However, specific tumorigenesis genes and signaling pathways are yet to be deciphered. This study integrated two cohorts profile datasets to detect genes involved in tumor cell growth and survival in neuroblastoma.

Design/Methods: **Methods:** Differentially expressed genes (DEGs) were calculated by DESeq R based on gene expression profiles from GSE3960 and GSE54720. Overlapping DEGs were then evaluated for gene ontology (GO) and KEGG pathways enrichment. The protein-protein interaction (PPI) network was constructed using Cytoscape software and the hub genes were identified by the Molecular Complex Detection (MCODE) plugin. Then, the identified genes were verified by UCSC Xena browser and the R2 for survival analysis. Furthermore, the hub genes expression in neuroblastoma cells and tissues were determined by quantitative RT-PCR and western blot.

Results: Twenty-two upregulated and twenty-eight downregulated DEGs were identified. Six hub genes including GFAP, GATA3, PAX6, OLIG2, ISL1 and LHX2 were selected using the Molecular Complex Detection (MCODE). UCSC Xena browser and R2 validated that higher expression levels of ISL1 and GATA3 were related to lower overall survival in TARGET-NBL, GSE62564 and E-TABM-38 databases. A two-gene panel consisting of ISL1 and GATA3 had a better prognostic value compared to ISL1 or GATA3 alone in the TARGET-NBL cohort ($p=0.045$ and 0.037). We also observed ISL1 and GATA3 protein expression were highly expressed in neuroblastoma cells and tissues compared to the corresponding cord blood mononuclear cells and normal tissues. And the mRNA levels of ISL1 and GATA3 had the same varying tendency as protein levels.

Conclusions: The present study identified a set of novel genes that may play a significant role in the initiation and progression of neuroblastoma. In addition, ISL1 and GATA3 may be potential biomarkers and therapeutic targets for neuroblastoma.

V367 SIOP19-1141 | Prospective Immune Phenotyping of Neuroblastoma Children at Diagnosis Reveals Specific Immune Defects Related to the Aggressiveness of the Disease

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Background/Objectives: Neuroblastoma is the most common extracranial solid tumor in children. Patients with low- and intermediate-risk neuroblastoma (LIRNB) have favorable prognosis and an excellent five-year survival rate of more than 90%. However, in the case of high-risk neuroblastoma (HRNB; ~50% of cases), the prognosis of treatment remains unfavorable and the five-year survival rate remains under 40% despite aggressive multi modal therapy.

We wanted to know if there was a defect in immune surveillance that could explain part of the aggressive phenotype of HRNB.

Design/Methods: We performed a prospective multi-center study on thirty one new cases of neuroblastoma at all stages. We performed a wide phenotyping of immune cells by flow cytometry in fresh whole blood, and fresh whole bone marrow at diagnosis of children diagnosed for neuroblastoma. Cell counts were performed in order to be able to reason in absolute values (G/L) rather than only percentages.

Results: Blood and bone marrow from 18 LIRNB and 13 HRNB were prospectively analyzed. We found that specific subsets of circulating immune cells such as myeloid dendritic cells BDCA-1+, plasmacytoid dendritic cells, Teff/Treg CD4+ T-cells, were decreased in HRNB blood compared to LIRNB groups as opposed to other subsets (e.g iNKT, g9d2 T-cells,...). More surprisingly, these differences were not due to defects in cell production as there was no difference found for the same cell populations in the bone marrow between LIRNB and HRNB children.

Conclusions: Specific immune cell defects are found in the blood from High risk neuroblastoma children that are not present in the blood of low & intermediate risk neuroblastoma children. These defects are not due to bone marrow production impairment. These results suggest that high risk neuroblastoma disease generates an impairment in the immune homeostasis of children. Gene expression analysis of cytokine/chemokine from these neuroblastoma tumors is underway (NCT01295762).

V368 SIOP19-0763 | Outcome of Anti-GD2 Immunotherapy in Dutch Patients with High-Risk Neuroblastoma

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Background/Objectives: In high-risk neuroblastoma (HR-NBL), approximately 50% of the patients suffer from recurrent disease. Anti-GD2 immunotherapy has been shown to reduce the number of recurrences in the COG cohort. Here we evaluate the outcome of a Dutch HR-NBL cohort treated with maintenance anti-GD2 immunotherapy after GPOH04/DCOG04 or POG9640 induction treatment.

Design/Methods: We included Dutch HR-NBL patients treated with immunotherapy between 2009 and 2016 according to the ANBL0032 study (n=47). We used a historic control group (n=37) treated with identical induction therapy between 2000 and 2015 with single-agent isotretinoin maintenance therapy. We collected data of clinical and histological patient characteristics and response to treatment before autologous stem cell transplantation. Survival time was calculated from start of the maintenance therapy for both cohorts. A landmark analysis was performed at 11 months to better understand the long-term effect of immunotherapy on prevention of recurrences.

Results: The median age of the patients at diagnosis was 41 months (range 1-196). The study and control group were comparable for baseline characteristics. There was a non-significant 10% improved 5-yr overall survival (OS) in favor of the immunotherapy group (immunotherapy 59±8%; control 49±8%; p=0.26) and a 8% improved 5-yr event free survival (EFS) (49±8% vs. 41±8%; p=0.46). For patients ≥18 months, there was a non-significant 19% 5-yr OS benefit (58±9% vs. 39±9; p=0.07) and a 17% 5-yr EFS benefit for patients treated with immunotherapy (46±8% vs. 29±8%; p=0.16). Landmark analysis shows a significantly better 5-yr EFS in the immunotherapy group compared with the control group for patients ≥18 months (65±10% vs. 41±11; p=0.04), indicating the prevention of late relapses.

Conclusions: This study confirms in a cohort with a different induction treatment the results of the COG study ANBL0032 that anti-GD2 immunotherapy improves the OS with 10% for HR-NBL. We further demonstrated an immunotherapy induced reduction of late recurrences in patients ≥18 months.

V369 SIOP19-0820 | Neuroblastoma Between 1990-2014 in the Netherlands: Increased Incidence and Improved Survival of High-Risk Neuroblastoma

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Background/Objectives: The incidence of childhood cancer in the Netherlands is slowly increasing for several entities, however for neuroblastoma specific this has not been analyzed yet. Here we study the trends in incidence, treatment and survival of neuroblastoma in the Netherlands over a 25-year period since 1990.

Design/Methods: The Netherlands Cancer Registry (NCR) collects data from clinical records in all hospitals. The NCR provided data on all patients <18 years old diagnosed with a neuroblastoma between 1990 and 2014, regarding age, gender, stage, treatment modalities and survival. For time trends in incidence we calculated the average annual percentage change (AAPC).

Results: The NCR registered 592 newly-diagnosed neuroblastoma cases, 0-16 years old, 45% of them were <18 months old and 52% had stage 4 disease. The age-standardized incidence rate (ASR) increased for stage 4 disease for all ages from 2.8 to 4.3 per million children per year (AAPC + 2.4%, p=0.01). Within stage 4 patients, the incidence increased only in patients ≥18 months old (from 2.3 to 3.8; AAPC +2.9%, p=0.03) and not in patients <18 months (AAPC +1.8%, p=0.26). No increase or decrease was seen in other stage/age combinations, indicating that stage-migration could not explain the increase. No other explanations could be identified. Five-year overall survival (OS) for the whole cohort increased from 44 ±5% in 1990-1994 to 61 ±4% in 2010-2014 (p<0.01). For patients with stage 4 disease, the 5-yr OS increased from 19 ±6% to 44 ±6% (p<0.01). Multivariable analysis revealed that high-dose chemotherapy followed by autologous stem cell rescue contributed mostly to a better survival of stage 4 patients (HR 0.54, p<0.01).

Conclusions: We observed an increase in the incidence of stage 4 neuroblastoma between 1990-2014, exclusively in patients ≥18 months. The survival of patients with stage 4

disease improved mostly due to the introduction of high-dose chemotherapy with stem cell rescue.

V370 SIOP19-0469 | Outcome of Patients with MIBG-Positivity Following Multi-Modality Therapy for Metastatic Neuroblastoma

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Background/Objectives: Metaiodobenzylguanidine (MIBG) scans are used to detect neuroblastoma metastatic lesions at diagnosis and during post-treatment surveillance. MIBG-positivity following induction chemotherapy for high-risk NBL correlates with poor outcome. However, there are reports of patients with progression-free survival despite MIBG-positivity. Factors distinguishing these survivors from patients who experience progression or relapse remain unclear. Predicting which MIBG-positive lesions may remain quiescent could permit sparing of additional therapies. We hypothesized that PET scans may help specifically identify less “active”, potentially differentiated, MIBG-avid lesions. Understanding how to recognize these rare patients will allow tailoring of therapy and impact surveillance.

Design/Methods: We conducted a multi-center retrospective analysis of pediatric patients diagnosed with INSS stage-4 neuroblastoma between 2002-2018. We identified patients with persistent MIBG positivity on their end-of-therapy scans without evidence of progression during treatment. We recorded patient characteristics including age, histopathology, biomarkers, treatment, and disease response. The study was approved by the Institutional Review Boards at Hospital for Sick Children and McMaster University

Results: Eight patients (median age at diagnosis, 32 months) were included. All remain disease-free with a median time-off-therapy of six years. Six patients continued to show MIBG uptake up to 6.5 years following active therapy. All patients at diagnosis had MIBG-avid metastases and tumors that lacked *MYCN* amplification. Five patients had histologic evidence of marrow involvement. Five had undergone myeloablative chemotherapy with stem cell transplant. Five patients had at least one PET scan performed and 0/5 had SUVs consistent with active disease. One had biopsy confirmed differentiated neuroblastoma.

Conclusions: Our preliminary analysis suggests that persistent positive MIBG scans in a subset of high-risk patients in first response may not always lead to progression. Studies are needed to determine whether *MYCN* status together with other clinical or biological characteristics, and /or PET scans, may identify patients with residual “inactive” MIBG lesions that do not require further therapy.

V371 SIOP19-0466 | The Addition of Gemcitabine to ¹³¹I-MIBG Therapy in Pediatric Patients with Relapsed or Progressive Neuroblastoma: An International Multi-Centre Phase II Trial (MIBG-GEM)

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Background/Objectives: ¹³¹I-metaiodobenzylguanidine (MIBG) is a targeted radiopharmaceutical active in patients with relapsed or progressive neuroblastoma. Gemcitabine is a radiosensitizer with preclinical activity in neuroblastoma (Lawrence 1999). This phase II trial aimed to evaluate the efficacy and safety of adding gemcitabine as radiosensitizer to ¹³¹I-MIBG therapy (Trial NL2263).

Design/Methods: Patients < 18 years old with relapsed or progressive neuroblastoma and with MIBG-avid tumors were eligible. Adequate bone marrow function (platelets >100 x 10⁹/L; >75 if BM involved) and adequate renal and hepatic function were required. Gemcitabine was given on days 1 and 8 of a 28day cycle. ¹³¹I-MIBG was given on day 1 starting at 444 Mbq/kg, aiming at a whole-body dose of 4 Gy after 2 cycles. Response was assessed according the International Neuroblastoma Response Criteria after each cycle. Dose-limiting toxicities (DLT's) were assessed during the first cycle in the first 6 patients. Gemcitabine started at dose-level 1 (DL1) 375 mg/m² and dose could be escalated when <10/19 patients had severe toxicity. The trial was open from 2011 to 2018 (6 centers) and was closed prematurely due to slow recruitment.

Results: To date, 16 patients (median age 9.9 years; range 6.3-11.7 years) received 1 (n = 10), 2 (n = 3), or 3 (n = 3) cycles of therapy. Myelosuppression was the most common toxicity. At DL1 1 pat experienced DLT with prolonged grade 4 thrombocytopenia >14 days. Objective responses occurred in 3 of 12 evaluable patients. Grade 3-4 events were seen in 15 patients, mainly thrombocytopenia. Eleven patients went off protocol because of toxicity (prolonged thrombocytopenia), four patients went off protocol with progressive

disease. One-year overall survival rate was 31% (95%CI 15%- 65%).

Conclusions: In the treatment of relapsed neuroblastoma patients, the addition of gemcitabine to 131I-MIBG therapy is tolerable, but no clinical activity was observed.

V372 SIOP19-0999 | A Safety Study of Administering Induction Chemotherapy for High Risk Neuroblastoma Without the Use of Prophylactic Myeloid Growth Factors

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Background/Objectives: Standard supportive care practice for induction therapy for high risk neuroblastoma (HRNB) includes adjuvant granulocyte colony stimulating factor (G-CSF) to limit chemotherapy related neutropenia, reduce infection risk, and minimize delays in treatment. Recent data from preclinical models suggest that G-CSF promotes the maintenance of neuroblastoma cancer stem cells and may reduce the efficacy of chemotherapy. The objective of this study was to determine the safety and feasibility of administering induction chemotherapy without routine use of prophylactic G-CSF.

Design/Methods: Children with newly diagnosed HRNB were treated with a six-cycle induction chemotherapy regimen, omitting prophylactic G-CSF. G-CSF was administered to all patients after cycle 3 for stem cell mobilization, and granulocyte-monocyte colony stimulating factor (GM-CSF) was administered after cycle 5 prior to surgical resection of primary disease. The primary outcome measure was the incidence of grade 3 or higher infection per CTCAE v4 after six cycles of therapy. We hypothesized that the infection rate would be comparable to our institutional baseline rate of 58% infection for patients receiving induction chemotherapy with prophylactic growth factor support. The trial used an Ahern single stage design.

Results: Twelve patients with HRNB were evaluable for the study end point. Three patients completed the entire 6 cycle regimen with no infections. Nine patients experienced grade 3 infections (Bacteremia 4, Skin/soft tissue infection 3, urinary tract infection 2). No patients experienced grade 4 infections, required intensive care treatment or died from infection. In total, patients completed 57 cycles of chemotherapy on study. Eight of these cycles were affected by a delay in chemotherapy administration due to neutropenia.

Conclusions: Greater than expected number of serious bacterial infections were observed with administration of

induction chemotherapy for HRNB without the use of prophylactic myeloid growth factors.

V373 SIOP19-0793 | PRP19 Promote Cell Proliferation and Invasion by Regulating Hippo Signaling Pathway in Neuroblastoma

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Background/Objectives: Neuroblastoma (NB) is the most common extracranial solid tumor in children. Given the prognosis of high-risk NB remains rather poor with the conventional treatment, there is an urgent need to discover new therapeutic strategies by revealing the molecular mechanism behind the malignant biological behavior of high-risk tumors and achieving targeted therapy.

Design/Methods: The correlation between clinical characteristics, survival and Prp19 expression were assessed using a neuroblastic tumor tissue microarray, and then validated in two independent RNA datasets. The roles of Prp19 in NB cell proliferation and invasion were studied by using siRNA and shRNA in vitro and vivo. RNA sequencing and bioinformatics analysis uncovered the underlying mechanisms. RIP and qPCR were used to exam the physical interaction of mRNA and its turnover time.

Results: Neuroblastic tumor tissue arrays and two independent validation datasets indicated that Prp19 was associated with high-risk markers and served as a prognostic marker for worse clinical outcome in NB. Knockdown of Prp19 inhibited proliferation and invasion ability of NB cell lines. In vivo experiments also showed that down-regulation of Prp19 can attenuate the tumorigenic capacity of NB cells. RNA-seq analysis showed that the expression of YAP, a key member of the Hippo-YAP pathway, and its downstream genes was significantly inhibited after Prp19 knocking down. To verify that YAP is the downstream of Prp19, we examined changes in partial cell phenotype such as proliferation and invasive ability after silencing YAP. Indeed, same as Prp19, cell proliferation and invasion were impaired after YAP was silenced. Further molecular study suggested that interruption of Prp19 could reduce mRNA half-time of YAP and consequently downregulated the expression of YAP.

Conclusions: Prp19 is associated with high-risk markers and poor prognosis and plays key role in NB proliferation and invasion with the underlying mechanism of regulating Hippo-YAP pathway.

V374 SIOP19-0810 | Neuroblastoma and Opsomyoclonus Syndrome: Experience of 6 Cases at a Single Center

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Background/Objectives: Opsomyoclonus and ataxia syndrome is a rare and severe clinical condition which is characterised by irritability, behaviour changes, dancing eye movements, myoclonus and ataxia. In this study we aimed to evaluate clinical and neurological features and follow up of these patients.

Design/Methods: Between 2007-2018 there were 91 symptomatic nervous system tumors. Retrospective evaluation revealed 6 cases of OMAS besides neuroblastomas. Age, gender, time to diagnosis, tumor location, stage, pathological features, treatment of tumor and neurological condition and immunotherapy were noted.

Results: All of the patients were detected during neurological evaluation. Time to diagnosis ranged from 3 days to 4 months. Age range was 4 months to 23 months, and male to female ratio was 1. Three of the tumors were located at thoracic paravertebral region; whereas other 3 were at adrenal region. Five patients had stage 2; one patient had stage 1 disease. Three patients underwent primary surgery. Five patients were treated with low risk treatment regimen; radiotherapy had been applied to tumor region in two patients. In 5 patients, neurological treatment consisted of both steroid and IVIG. In one patient, only IVIG had been applied. Treatment duration of neurological disease ranged between 4 months to 18 months. One of patients was still under treatment. In other five patients there were no recurrence of primary and neurological disease. In one patient, behaviour problems occurred as a late effect. In another patient special education was necessary for fine motor and speech skills. These two patients were the patients in whom second look surgery was performed. In patients with primary surgery, immunotherapy was ended at 1, 4 and 7 months respectively.

Conclusions: In patients with primary surgery neurological treatment was brief as expected. Opsomyoclonus syndrome associated with neuroblastoma should be detected and treated early for the prevention of late neurological sequelae.

V375 SIOP19-1332 | Predictors of Survival in Patients with High-Risk Neuroblastoma who Failed Tandem High-Dose Chemotherapy and Autologous Stem Cell Transplantation

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Background/Objectives: The aim of this study was to explore the prognostic factors in patients with high-risk neuroblastoma who failed tandem high-dose chemotherapy and autologous stem cell transplantation (HDCT/auto-SCT).

Design/Methods: Survival outcomes were compared according to characteristics at initial diagnosis, at relapse/progression, and after relapse/progression in patients who experienced relapse/progression after tandem HDCT/auto-SCT from 2006 to 2018.

Results: From 2006 to 2018, 43 patients who experienced relapse/progression after tandem HDCT/auto-SCT received salvage treatment. Thirty patients underwent allogeneic SCT (allo-SCT) after reinduction treatment. Thirteen of 43 patients remain alive, and the 2-year probabilities of event-free survival (EFS) and overall survival (OS) from initial relapse/progression were $21.2 \pm 6.6\%$ and $43.6 \pm 7.9\%$, respectively. A higher neuron-specific enolase (NSE) level (> 24 ng/mL) at relapse/progression was an independent worse prognostic factor for OS. Nine of 30 patients who underwent allo-SCT remain alive, and the 2-year probabilities of EFS and OS from allo-SCT were $18.3 \pm 7.7\%$ and $23.3 \pm 8.6\%$, respectively. A higher NSE level and no incorporation of ¹³¹I-metaiodobenzylguanidine (MIBG) treatment into allo-SCT were independent worse prognostic factors for OS after allo-SCT.

Conclusions: The results suggest that a higher serum NSE level at relapse/progression is a marker for worse prognosis in patients who failed tandem HDCT/auto-SCT, and that incorporation of ¹³¹I-MIBG treatment into allo-SCT may improve the outcome.

V376 SIOP19-1219 | Single-Cell RNA-SEQ Identifies that Adrenergic Neuroblasts Possess a BI-FATE Differentiation Potential in Peripheral Neuroblastictumors

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Background/Objectives: The aim of this study was to investigate the heterogeneity of the primary tumors in children with peripheral neuroblastic tumors (PNTs) as well as to identify sub-populations of tumor cells that could explain the mechanism of metastasis.

Design/Methods: We analyzed 5,309 single cells from 7 primary PNTs with a variety of clinical and therapeutic

backgrounds, including 3 neuroblastomas, 3 ganglioneuroblastomas, and 1 ganglioneuroma. Single cells were sorted by flow cytometry and scRNA-seq profiles were performed by using SMART-seq2 approach.

Results: Malignant and non-malignant cell sub-populations were identified based on the presence of tumor-associated copy number variation or by distinct lineage-specific expressed genes. Our data revealed a high heterogeneity of cells in which we identified 15 clusters that correspond to 4 adrenergic neuroblastoma and 3 mesenchymal neuroblastoma, 8 non-malignant cell clusters. Firstly, neuroblastomas are characterized by low immune cells infiltration compared with ganglioneuroblastoma and ganglioneuroma. Notably, the lack of cytotoxic T cells infiltration and the prevalence of macrophages/monocytes may play an important role in the progression of advanced stage MYCN-not-amplified neuroblastoma. Secondly, using the Monocle v2 algorithm to project cell trajectories as a function of pseudotime, we identified that adrenergic neuroblasts (ADRN-high) possess a bi-fate differentiation trajectory toward adrenergic neurons (ADRN-low) or mesenchymal neuroblasts. Metastatic neuroblastoma harbored more ADRN-lowneuroblasts. Finally, advanced stage neuroblastomas are characterized by heterogeneous tumors with multiple differentiation states compared with early stage tumors.

Conclusions: Single cell analysis provides an unparalleled insight into both the malignant and microenvironmental heterogeneity of peripheral neuroblastic tumors and might be a useful substrate to identify targets for novel therapy.

V377 SIOP19-0268 | 11Q23 Deletion Display A Poor Prognosis for Patients with Nonamplified MYCN in Bone Marrow Metastatic Neuroblastoma

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Background/Objectives: Interphase fluorescence in situ hybridization (FISH) of bone marrow cells has been confirmed to be a direct and valid method to assess MYCN amplification for BM metastatic neuroblastoma (NB). But MYCN amplification alone is incomplete. 11q23 deletion has recently been included in risk classification of NB.

Design/Methods: We analysed MYCN and 11q23 status of 101 BM metastatic NB using interphase FISH of BM cells. And specifically compared the biological characteristics and prognostic impacts of both aberrations.

Results: MYCN amplification and 11q23 deletion were seen in 11.9% and 39.6% of patients with metastases. The two markers were negatively related. We found MYCN amplification mainly occurred in older children, high LDH and high

NSE levels group ($P=0.041$, $P<0.001$, $P<0.001$), and more patients had events occurred ($P=0.004$). 11q23 deletion was only associated with age ($P=0.001$). The outcome of patients with MYCN amplification was obviously lower than those with MYCN normal (3-year EFS $8.3\pm 8.0\%$ vs. $43.8\pm 8.5\%$, $P<0.001$). 11q23 deletion displayed a poor prognosis only for those patients who lack MYCN amplification (3-years EFS $34.3\pm 9.5\%$ vs. $53.4\pm 10.3\%$, $P=0.037$). The patients with MYCN amplification and 11q23 deletion had the worst outcome ($P<0.001$).

Conclusions: The present findings indicate that interphase FISH is very helpful for BM metastatic NB in identifying the genetic aberrations. Combined assessment of MYCN and 11q23 status are more accurate in recognizing the patients at high-risk of disease progression.

Solid Non Brain Tumours - Rare Tumours and Histiocytosis

V378 SIOP19-0576 | Colorectal Cancer in Children and Adolescents: Single Institutional Experience from Pakistan

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Background/Objectives: Colorectal cancer is very rare in children and young adolescents with a worse prognosis in pediatric age group. The Oncology Department of the Children's hospital Lahore is the biggest public sector referral center providing cancer treatment free of cost. We performed an analysis of all CRC cases treated from January 2017 to January 2019 with an unusually high number of cases over the duration of two years.

Design/Methods: Retrospective review of all patients less than 18 years of age with histological proven colorectal carcinoma registered during two years. Spss20 was used to analyze the data of age, gender, staging, histopathology, modes of treatment, place of residence and outcome. They were treated with FLOFOX

Results: Total of 15 patients with mean age of 13 years (11-18 years) were included with M: F ratio of 2:1. Majority of them 13/15 87% resided in rural areas. Rectosigmoid was the most common site 10/15 66% followed by rectum 13% and one case each from jejunum, transverse colon and caecum. Signet ring adenocarcinoma was the most common histopathology 8/15 53% followed by mucinous and NOS types. Only one case was localized, 9/15 (60%) regional metastases, and 5/15 (30%) distant metastases. Biopsy was done using colonoscopy in 40%, true cut biopsy in 20% and via laparotomy in 6/15 40% cases done for acute intestinal obstruction. Palliation was done in 20% of cases at diagnosis, and given after poor response in

6/15 40% cases, during the course of treatment. Three patients (20%) have completed treatment and are well with around one year follow up. Two patients relapsed after complete treatment and put on palliation and two patients abandoned treatment

Conclusions: Colorectal cancer has a fatal outcome as majority of them are diagnosed late. Better awareness and early referral to tertiary centers with strong multidisciplinary team management survival can be increased

V379 SIOP19-1464 | Adrenocortical Tumors in Children

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Background/Objectives: Pediatric adrenocortical tumors (ACTs) are poorly understood due to limited number of cases. This study is designed to determine outcome, demographic and clinical characteristics of ACTs in children.

Design/Methods: Nineteen children who underwent surgery for ACTs between 2000 and 2017 were included. The medical records were reviewed retrospectively and age, sex, clinical characteristics, diagnostic methods, stage of disease, surgical finding, treatment, pathologic findings, and outcome were evaluated.

Results: Female to male ratio was 13:6. Mean age of patients were 7 ± 5.8 years (52day-16year). Thirteen patients had adrenocortical carcinoma (ACC), five had adrenocortical adenoma (ACA) and one had neuroendocrine differentiation of adrenocortical tumor. Endocrine dysfunction was noted in 78% of the patients and virilization (n=9) was the most common presentation followed by Cushing's syndrome (n=6). Twelve patients presented with palpable abdominal mass. Ultrasound scan, computerized tomography and magnetic resonance imaging were used for the diagnosis. Six patients had tru-cut biopsy suggesting adrenocortical carcinoma in all. All patients with ACA had localized disease, whereas 70% of the patients with ACC had regional invasion or metastatic disease. Three patients had distant metastases one of which were detected preoperatively. Excision of tumor without disruption of capsule and tumor spillage was achieved in all but 5 patients. All patients who had tumor rupture (n=5) had recurrent tumors. Three of these patients were died and two were lost to follow-up. The mean follow-up time of 19 patients was 58 months (4-170). Mortality was 30% in ACC and associated with metastatic disease and tumor rupture.

Conclusions: ACTs are rare in childhood and more than half of them is malignant. The most important aspect of therapy for ACTs is early diagnosis and total excision without tumor rup-

ture. Tumor rupture and advanced-stage disease are the major determinants of poor outcome in adrenocortical carcinoma.

V380 SIOP19-1472 | Pheochromocytoma in Children

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Background/Objectives: Pheochromocytoma, a catecholamine-secreting tumor arising from chromaffin cells, is most commonly found in the adrenal medulla. Pediatric pheochromocytoma are rare. This study aimed to determine outcome, demographic and clinical characteristics of pheochromocytoma.

Design/Methods: Ten children who underwent surgery for pheochromocytoma between 2000 and 2017 were included. The medical records were evaluated and age, sex, symptoms and physical findings at presentation, results of biochemical tests, details of surgery, pathologic findings, and postoperative course were noted.

Results: Female to male ratio was 5:5. Mean age at time of diagnosis were 13.4 years (6-17) months. The most presenting symptom were headache (n=5) and sweating (n=4). The most frequent physical examination finding was hypertension (n=7). Eight patients were sporadic while 2 patients had von Hippel-Lindau disease. The mean time from initial symptoms to diagnosis was 20 months (2-60). The tumors were left sided in 4 patients, right sided in 3 patients and bilateral in 3 patients. Preoperative medical therapy was done in all patients by preoperative intravenous fluid and/or various drugs including phenoxybenzamine, metyrosine, prazosin, doxazosin, labetalol, calcium channel blockers and ACE inhibitors. The diagnosis of pheochromocytoma was made by laboratory and radiologic studies. Ultrasound scan, computerized tomography, magnetic resonance imaging, and MIBG scintigraphy were used for the diagnosis. Total excision was achieved in all patients. The mean follow-up time of 8 patients was 52 months (2-144). Two patients were lost to follow up. There was no mortality or recurrence.

Conclusions: Pheochromocytoma are rare in childhood. Medical management is as important as the surgical procedure. The most important aspects of therapy for pheochromocytoma are early diagnosis, surgical excision and multidisciplinary approach.

V381 SIOP19-0784 | Identification of Gardner Syndrome Among Paediatric Fibroblastic and Myofibroblastic Tumours: A Study of 7 Cases

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Background/Objectives: Gardner syndrome (GS) is an autosomal dominant disease due to germline alteration in the *Adenomatous Polyposis Coli (APC)* gene with different phenotypes, multiple colorectal adenomatous polyps and other neoplasias. Gardner fibromas and fibromatosis diagnosed at paediatric age with a family history of colorectal polyps or neoplasia are associated with GS, but familial history is absent in many cases. Objective: to study of *APC* gene in paediatric patients diagnosed with fibroma or fibromatosis.

Design/Methods: Retrospective analysis of the clinical and genetic data of paediatric patients diagnosed with fibroma or fibromatosis.

Results: Ten patients were diagnosed in the last 25 years: 4 fibromas and 6 fibromatosis. Seven cases were studied: 5 fibromatosis and 2 Gardner fibromas. Median age: 5.1 years-old (range:15 days-12 years). Three patients had family history of polyposis or neoplasia. Two patients were genetically GD confirmed. One patient with nuchal Gardner fibroma and pilomatricoma had the *de novo* germline deletion c.4611delA. Other patient had cervical fibromatosis at the age of 12 years, received chemotherapy but suffered several abdominal desmoids tumours 22 years later when the germline deletion c.5826_5829del was identified. GD is probable in 2 cases with familial polyposis, but the genetic results are pending, as well as in 3 more patients (neonatal onset, aggressive abdominal presentation and late digestive haemorrhage). Clinical management was difficult when total surgical removal was not achieved (3 cases).

Conclusions: Suspicion of cancer predisposition syndromes is important in some soft-tissue tumours. Inherited gastrointestinal cancer predisposition syndromes like Gardner syndrome in childhood can present with a tumoral phenotype, like fibromas and fibromatosis. Familial history should be evaluated but *de novo* mutations can be detected. Review of paediatric cases is necessary to identify GD for an adequate genetic counselling. Detection of *APC* mutations is important for cancer screening and surveillance recommendations since childhood.

V382 SIOP19-1638 | Adrenal Cortical Tumors in Children: A Retrospective French Study about Technical Surgical Aspects

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Background/Objectives: Recently a pathological review emphasized that the surgical stage for adrenal cortical tumors (ACT) was one of the major prognosis factors. We report here a retrospective multicentric French descriptive study concerning ACT.

The objective is to describe the surgical strategies and stage results, especially regarding the use of laparoscopy, and the need for further surgeries in case of evolutive/relapsing tumors.

Design/Methods: Pediatric patients with histologically proven ACT and complete surgical reports operated between 2000 and 2018 in 18 French oncology centers were included.

Results: 54 patients were operated, 15 cases (28%) had mini invasive surgery (MIS), 13 by laparoscopy and 2 by retroperitoneoscopy. 39 cases had open surgery (OS). In MIS cases, the tumor size was less than 5 cm in 11 cases (12 cases in OS), the tumor's size was between 5 and 10 cm in 4 cases (22 cases in OS). Despite 2 tumoral ruptures and the absence of post-operative treatment no recurrence were observed after MIS. Only 6 of those 15 MIS patients were older than 5 year old.

Among OS cases, 5 tumor's sizes were bigger than 10 cm, 22 were between 5 and 10 cm. 5 tumoral rupture occurred in OS cases.

For 2 patient with local relapse, redux surgery were done. They were alive 5 years later, with 5 years of complete remission for one of them.

Conclusions: With those results we can say that laparoscopic surgery is safe and feasible; there is no more effraction in open vs mini invasive surgery and no major events in patients treated with MIS during followup. Age and size of the tumor don't seems to be a limit for MIS. The few cases of relapse/progressive disease were treated in open surgery,

with some encouraging cases in favor of the pursuit of curative treatment.

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V383 SIOP19-1018 | Experience of Pediatric Tuberous Sclerosis Complex

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Background/Objectives: To evaluate our patients with tuberous sclerosis complex (TSC) retrospectively.

Design/Methods: Medical records of patients with TSC between 1987 and 2018 were evaluated retrospectively.

Results: Seventeen patients with TSC were evaluated. The median age of diagnosis was 7 years (1month-16years). The patients of 62% convulsion, 12% prenatal intracardiac rhabdomyoma, 12% murmur, 7% prolonged jaundice, 7% due to skin rash were diagnosed as TSC.87% of the patients had skin involvement in the diagnosis; 93% of these patients hypomelanotic macules, 28% adenosebaceum, 14% schgreen patch, 14% cafe au lait revealed. Clinically and radiologically, all patients had CNS involvement, 62% had convulsion, 25% had mental retardation revealed and 13% had no clinical findings. According to the radiological findings, cortical tuber in 50% of the patients, subependymal nodule in 68%, corticosubcortical hamartoma in 44%, periventricular calcification in 13%, periventricular hyperintensity in 6% had revealed. In two of the patients with intracardiac rhabdomyoma in 44%, intracardiac rhabdomyoma was detected in fetal prenatal period. Spontaneous regression was observed in three patients in control ECO and lesions were observed in three patients. 62% of the patients had renal involvement at the time of diagnosis; 90% of these patients had angiomyolipoma, 10% had polycystic kidney disease. In one of the patients with angiomyolipoma, the lesion was progressive in another center and partial nephrectomy was performed with the aim of tissue diagnosis.

Conclusions: The clinical data of our patients with TSC were consistent with the literature, but none of them had eye and lung involvement and no malignant disease was detected. Everolimus treatment was recommended to our patient who had progressive growing bilateral renal angiomyolipoma and underwent partial nephrectomy, but treatment was refused by the family. It should be kept in mind that multidisciplinary approach is necessary in the follow-up and treatment of patients with TSC and physicians should be sensitive in determining the patients who need treatment in terms of current targeted treatments.

V384 SIOP19-1042 | Langerhans Cell Histiocytosis: A Single Center Experience

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Background/Objectives: To evaluate patients with langerhans cell histiocytosis (LCH) who were diagnosed and treated at our center.

Design/Methods: The medical records of patients with LCH were reviewed. The clinical characteristics, treatment details and responses were analyzed retrospectively.

Results: 48 patients treated with LCH were analyzed. The median age of diagnosis was 5years (3months-16years), Male/Female:1. 58% of the patients presented with a mass, 42% with back-extremity pain, 23% with skin rash, 8% with imbalance in walking, 4% with polyuria-polydipsia.75% of the patients had single system, 25% had multisystem involvement and 17% had risky organ involvement.88% of the patients had bone involvement;76% had single bone, 24% had multiple bone involvement. Systemic chemotherapy (CT) was given to 77% of the patients; Seventeen of these patients received LHC-III protocol, 13 of them had LCH-IV protocol, seven of them were given CT according to DALHX-83/90 protocol. Local surgery for 52% of patients;radiotherapy (RT) was applied to 15% of the patients. Six of 10 patients who developed relapse developed relapses once in six, twice in three patients and three times in one. Relapsed/refractory disease as a treatment for the treatment of chemotherapy in three patients with cisplatin and interferon KT was cured in three, three patients developed a relapse/refractory disease and one died due to disease progression. Three of these patients developed relapse/refractory disease and were treated with clarofarabine;again, a patient was given a first relapse of clarofarabine. One patient died due to meningococemia and one due to disease progression. The median follow-up period was 5years (1month-18years). Overall survival rate was (OS) 98% in 1 year;5 and 15 years was 96%. Event-free survival rate (EFS) was 83% at 1 year, 5% at 15 years was 73%.

Conclusions: 3/4 of the patients with LCH had single system involvement. The survival and overall survival rates of all patients with single system and multiple system involvement were consistent with the literature. The combination of

clarofarabine or cisplatin and interferon alone was effective in relapse/refractory LCH patients.

V385 SIOP19-1524 | Juvenile Xanthogranuloma: A Single Center Experience

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Background/Objectives: To evaluate patients with juvenile xanthogranuloma (JXG) who were diagnosed and followed up in our center.

Design/Methods: The medical records of the patients were evaluated retrospectively. Clinical characteristics of patients, laboratory tests (hemogram, liver and kidney function tests, lipid profile), eye examination, abdominal and transfontanel ultrasonography in terms of organ involvement were analyzed.

Results: Nine patients with JXG were evaluated. Eight patients diagnosed <12 months and one patient diagnosed at the age of 14 years. M/F:3.5. Of the patients, 33% had focal and 66% had multifocal involvement. Lesion regions: 66% (n: 6) skin, 22% (n: 2) subcutaneous soft tissue, 11% (n: 1) eyelid. In one of the two patients with subcutaneous soft tissue involvement, the lesion was located on the right scrotum and the other on the right side of the neck. None of the patients had systemic involvement. 55% of the patients underwent diagnostic surgery and the lesions were completely resected. None of the patients were directly applied to the oncology department, after the histopathologic examination they referred to our department.

Conclusions: JXG is a rare non-Langerhans cell histiocytosis in infants and children and the etiology is unknown. Skin involvement is the most frequent and may form one or more papules or nodules. The most common eye involvement is non-skin involvement. Systemic involvement occurs in 4% of patients and mortality is between 5% and 10%. In addition, JXG can develop on the basis of neurofibromatosis type-1, which increases the risk of juvenile myelomonocytic leukemia in patients. The prognosis is good and the lesions are mostly spontaneous recovery. Surgical or systemic treatment is received to selected cases. Patients with JXG should be evaluated at regular intervals in terms of systemic involvement and should be followed by pediatric oncology department.

V386 SIOP19-1649 | Long Term Follow-up of Pediatric Nasopharyngeal Carcinoma in Israel

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Background/Objectives: Nasopharyngeal carcinoma (NPC) is a rare childhood cancer. Information regarding the clinical characteristics, biology and long term follow up of childhood NPC is scarce. We present our data on very late follow up on NPC in children.

Design/Methods: Retrospective data was collected from medical files and electronic data. This study was approved by local IRB committees.

Results: Between 1989-2018, 43 children with NPC were treated in 5 Pediatric Hematology-Oncology centers in Israel. Thirty four patients (79%) were males. Median age at diagnosis was 14 years (6-18 years). Sixty three percent (22 of 35) of the children were Jewish, 34% (12 patients) were Arabs. Four patients (11%) were diagnosed with stage 2 disease, 23 patients (64%) were diagnosed with stage 3 disease. None of the children had distant metastases at presentation. All patients received radiotherapy at an average dose of 65.6 Gy (60.0-74 Gy). All children were treated with cisplatin-based chemotherapy according to the regimens used during these years. Median time of follow-up was 12.6 years (5.2 months to 26 years). During long term follow up, ten children (23%) had an event. Five patients had local (1 child) and distant (4 patients) disease recurrence. Median time to recurrence was 44 months (4-48 months). Four children developed secondary malignancy. Median time to secondary malignancy diagnosis was 105 months (53-163 months). One child developed intracranial bleeding from a cavernoma in the radiation field margins. Median time to first event was 57.5 months (4-163 months). Six children died during follow-up. Four children succumbed to their disease, and 2 children died from secondary malignancy. Twenty five year overall survival and event free survival were 86.8 ±5.5% and 84.3±5.9% respectively

Conclusions: Nasopharyngeal carcinoma is rare in children. Continued long term follow up is necessary in order to consider novel treatment approaches for this highly curable neoplasm

V387 SIOP19-0108 | Rare Histiocytoses – Experiences in the German Registry and Consultation Cases

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Background/Objectives: Rare or Non-Langerhans cell histiocytoses (non-LCH) include many malignant and benign, localized or diffuse diseases. In pediatrics, the most frequent are Rosai-Dorfman disease (RDD) and (juvenile) xanthogranulomatosis (JXG), followed by Erdheim-Chester disease (ECD), and malignant histiocytoses. Frequently, the precise histological diagnosis is undefined. Recently, molecular genetic alterations, particularly in the ras-raf kinase pathway, were identified.

Design/Methods: In 2012, the German registry and consultation study for non-LCH - part of the International Rare Histiocytic Disease Registry - was initiated.

Results: Fifty-nine patients were reported (26/29 female/male, 4 unknown; aged 0-4 years:25; 5-9:9; 10-14:6; 15-19:8; 20-39:3; >39:7). Thirty-five patients are in observation (0-6 years), 6 patients died (aged: 1, 10, 42, 42, 51, 54 years); 18 lost to follow-up (lfu). Among 11 RDD patients (all survivors or lfu), 6 only had cervical lymphadenopathy (1 received steroids), 5 had extended disease (2 meningeal, 1 mediastinal/tracheal compression, 1 bone, 1 liver/lungs; 5 received steroids/polychemotherapy). Among 18 JXG patients (all survivors or lfu), 2 had localized, 4 generalized skin involvement, 2 bone, 3 CNS, 1 eye, 3 deep soft tissue, 2 skin/liver involvement, 2 mediastinal/tracheal compression. 5 patients received steroids/polychemotherapy. Two ECD patients were lfu. Three had histiocytic sarcoma (2 died despite polychemotherapy; one survived after polychemotherapy/BMT). One patient had Langerhans cell sarcoma (survivor after polychemotherapy), 1 had H syndrome. Non-LCH was undefined in 22 (4 deaths after different treatment attempts). One patient with ALK positive undefined non-LCH received Alectinib. Complete genetic workup was only performed in 9 patients; BRAF mutations were found in 3 patients (1 ECD, 1 XG, 1 undefined non-LCH); KRAS in 2 (1 RDD, 1 JXG); ALK in 2 (1 RDD, 1 undefined non-LCH).

Conclusions: Rare histiocytoses represent a very heterogeneous disease spectrum. Appropriate consultation depends on international prospective data collection, which should be further propagated.

V388 SIOP19-0242 | Functional Analysis of Young Patients with Desmoid-Type Fibromatosis: Initial Surveillance Does Not Jeopardize Long Term Quality of Life

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Background/Objectives: With recent conservative strategies, prognosis of patients with desmoid-type fibromatosis (DTF) is about function preservation. We analyzed the long-term quality of life (QoL) of pediatric patients with DTF to help physicians decide the best strategy.

Design/Methods: All French patients (<18years) treated for a DTF between 2005-2016 in the EpSSG NRSTS-05 study were analyzed. A first wait-and-see strategy was recommended. Patients' QoL was analyzed with the internationally validated Child Health Questionnaire (CHQ), including a parent±child form, or an adult form. We focused on the most relevant subscales scores: physical functioning (PF), role social limitations physical (RP), bodily pain (BP), general health perception (GH) and physical (phS) and psychosocial (psS) summary measures.

Results: Overall, 52 families (parents n=29 with 22 corresponding answers of children/patients now adults n=23, median age at diagnosis=11.5years) answered the CHQ (median delay since diagnosis=6.2years; min2.2-max13.3years). Primary site: head/neck (27%), limbs (52%), or trunk (21%). As initial management, 30 patients were first observed (57%), 13 had immediate surgery (25%) and 9 received chemotherapy (18%). Total burden of therapy was surgery (23pts/44%), chemotherapy (33pts/63%), radiotherapy (2pts/4%), surgery+chemotherapy (14pts/27%), chemotherapy+radiotherapy, surgery+chemotherapy+radiotherapy (1 each). Five year-PFS was 39.1% (95%IC: 27.7-50.5%).

Regarding the parent forms, patients have significant lower PF (86vs.96.1; p=0.03), RP (82vs.93.6; p=0.04), GH (60vs.73; p<0.005) and PhS (46.2vs.53; p=0.02) scores compared to healthy population. Comparison of QoL subscales scores according to initial strategy (wait-and-see vs. surgery/chemotherapy) did not reveal any difference (PF=87.3vs.84.9; p=0.80/RP=83.4vs. 78.7; p=0.72/BP=78.9vs.78.2; p=0.95/GH=59.7vs.60; p=0.97).

Patients with exclusive medical strategy have a similar QoL comparing to the ones operated at least once: PF=86.9vs.5.7; $p=0.89$ /RP=81.4vs.81.9; $p=0.97$ /BP=77.1vs.80.8; $p=0.72$ /GH=61.4vs.57.5; $p=0.57$). Similar results were found using child forms and for patients who had become adults.

Conclusions: Initial wait-and-see strategy does not affect long term functional impairment. This study helps to propose first observation for non-threatening DFT.

Acknowledgments: SOS-Desmoid association

V389 SIOP19-0585 | A Retrospective Analysis of Langerhans Cell Histiocytosis Carried BRAFV600E Mutation in Children

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Background/Objectives: To investigate the clinical features of patients with Langerhans cell histiocytosis (LCH), and analyze associations between BRAFV600E mutation status and clinical features.

Design/Methods: A retrospective analysis was performed for the clinical data of 57 patients with diagnosed LCH. Real-time fluorescence quantitative was used to detect BRAFV600E mutation in paraffin-embedded tissue samples, and peripheral blood and/or bone marrow were tested by high-throughput sequencing.

Results: Of the 57 patients (41 males and 16 females), 28 were aged ≤ 2 years and 29 were aged >2 years (mean age, 4.17 ± 0.48 years; age range, 2.0 months-12.0 years). 20 patients in the SS group and 37 in the MS group. Chemotherapy response rate was obviously lower in the MS group (25.0% vs 64.7%, $P=0.008$) and the patients age ≤ 2 years (56.5% vs 23.1%, $P=0.017$). Patients with risk organ involvement (83.8%, $P=0.003$) and low age (89.3%, $P=0.000$) were concentrated in the MS group. 36 patients were successfully determined BRAFV600E status, in which the positive rate of BRAFV600E in paraffin-embedded tissue samples reached 69.4% (25/36). However, the positive rate of BRAFV600E was not associated with early treatment response, age, sex, affected organ and clinical classification ($P>0.05$). 4 patients were simultaneously detected for peripheral blood and/or bone marrow. Only 1 case was positive with BRAFV600E in peripheral blood. The child with liver and spleen involvement had progressive disease after initial treatment, and had to be given the treatment of Cladribine combined with Cytarabine. This child was evaluated to be AD-stable after 4 sessions chemotherapy and is awaiting stem cell transplantation.

Conclusions: Age ≤ 2 years and multisystem involvement are unfavourable prognostic factors of LCH which may be related

to the low age, risk organ involvement and the poor tolerance of chemotherapy. BRAFV600E mutation was not linked with treatment response, age, sex, affected organ and clinical classification. Further research and analysis need to expand the sample size.

V390 SIOP19-1378 | Nasopharyngeal Cancer Among Children: Clinical Features, Outcomes and Prognostic Factors

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Background/Objectives: To describe epidemiology, clinical features and treatment. To evaluate survival and prognostic factors of nasopharyngeal cancer on children.

Design/Methods: Retrospective study of 46 children with nasopharyngeal cancer recruited in two radiation therapy institutions in Tunisian center between 1995 et 2017.

Results: The median age was 14 years. The sex ratio was 1.55. The mean pre-consultation interval was 3 months. The main presenting symptom was the cervical mass (85%). Three patients had a paraneoplastic syndrome. Histological examination revealed UCNT (96%), non-hodgkin lymphoma (2%) and rhabdomyosarcoma (2%). One patient had bone metastases at presentation. Thirty nine patients received upfront chemotherapy followed by radiotherapy (RT). Six patients received concurrent chemo-radiotherapy. The patient with bone metastases received chemotherapy followed by RT to the tumor and metastases. The mean dose of RT delivered to the tumor was 70Gy (68-74Gy). Bone metastases received 30Gy in 10 fractions. After a median follow up of 103 months, local recurrence and metastatic bone relapse occurred in 4 and 7 cases. At the last follow up, 28 patients were in complete remission, 15 had died and 3 were lost. Neuroendocrine toxicities were observed in 8 patients. The overall (OS) and disease free survival (DFS) at 5 and 10 years was respectively 73.9%, 65.7% and 80%, 71.1%. In the univariate analysis, The T stage and the complete remission after RT were significant factors impacting both OS ($p<0.0001$; $p=0.004$) and DFS ($p=0.001$; $p=0.005$). In the multivariate analysis, the complete remission after RT was an independent factor impacting significantly OS ($p=0.02$) et DFS ($p=0.04$). The T stage was an independent factor impacting only OS ($p=0.035$).

Conclusions: Pediatric nasopharyngeal tumors are relatively frequent in the north of Africa. Metastatic relapse constitutes the main cause of death. The improvement of radiation therapy techniques and chemotherapy has achieved a satisfying outcome with acceptable toxicities.

V391 SIOP19-0099 | Outcome of Liver Involvement in Pediatric Langerhans Cell Histiocytosis: Report from Children Cancer Hospital-Egypt

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Background/Objectives: **Background:** Liver involvement in pediatric Langerhans' cell histiocytosis (LCH) usually presents as a part of a disseminated disease, its frequency is known to be high and is associated with adverse outcomes.

Objectives: To assess the frequency and outcome of liver involvement in pediatric LCH

Design/Methods: A Retrospective study included 52 pediatric LCH patients with liver involvement. All patients treated at the Children's Cancer Hospital-Egypt during the 10 years period 2007 - 2017.

Liver involvement was determined by the following: unexplained liver enlargement more than 3 cm below the costal margin and/or dysfunction (Hypoalbuminemia, hyperbilirubinemia, hypoprothrombinemia and/or increased liver enzymes).

Results: Of 117 children with multisystem LCH, 52 (44.4%) had liver involvement. The median follow-up of patients with liver involvement was 44 months (range, 2 to 131). Of 52 studied patients, 30 (57.6) patients had hepatomegaly without disturbed liver function, 21 (40.4%) patients had hepatomegaly with liver dysfunction, and one patient (2%) had average-sized liver with disturbed function. The 5-year overall survival (OS) and event free survival (EFS) of all patients with liver involvement was 65% and 38.5% respectively.

For patients with liver dysfunction (n=22), the 1-year OS and EFS was 63.3% and 35.8% respectively compared to 96.7% and 86.7% respectively for those with hepatomegaly (n=30). (P<.001, and P=.001 respectively). At end of induction, disease progression was seen in 13/22 patients (59%) with liver dysfunction, of them 10/13 patients (77%) died, and in 4/30 patients (13%) with hepatomegaly, of them only one patient (25%) died.

Conclusions: Though Liver is considered as a high risk organ in management of LCH, patients with disturbed liver functions tend to have a refractory disease and dismal outcome compared to those with hepatomegaly alone. Further studies are recommended to confirm this poor outcome and hence,

this group of patients might benefit from upfront different therapeutic planning.

V392 SIOP19-0803 | Adrenocortical Carcinoma in the Pediatric Population; a Single Institution Experience from a Developing Country

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Background/Objectives: Childhood adrenocortical carcinoma (ACC) is a rare neoplasm. Pediatric experience is gained from its more frequent adult counterpart. Endocrine disorders attract the attention for early intervention. Virilization and Cushing's syndrome are the most common abnormalities in functional tumors. Surgical resection remains the cornerstone of treatment. The aim of this study is to assess the clinical features and survival outcome of patients with ACC.

Design/Methods: Retrospective data for eighteen patients treated at Children's Cancer Hospital-Egypt (CCHE), below 18 years, were collected between July 2007 and November 2016 and followed up till November 2018. Modified Children's Oncology Group (COG) staging system and COG-ARAR0332 protocol were adopted for management of cases.

Results: Data included seven males and 11 females; median age was 48.5 months. Six patients had been diagnosed with stage I disease; four with stage II; 3 with stage III and five with stage IV. Sixteen patients had presented with functioning tumors. The most common isolated endocrine abnormality in females was primary hypercortisolism (n=3) followed by virilization (n=2). All male patients but for one, presented with precocious puberty in the form of hirsutism. Also, two of them had premature penile enlargement. All males had elevated testosterone levels. Complete excisions were achieved in 11 cases; another three ended with partial excisions. Patients with stage III and IV (n=8), received chemotherapy plus mitotane. By the end of this study, ten patients had survived; five-year

overall survival of 66.3%. Surviving patients were all of stage I or II diseases. Seven patients who did not survive died out of tumor progression, while one died from chemotherapy toxicity.

Conclusions: The prognosis of ACC is essentially dependent on the complete resection of the tumor as well as the initial tumor stage. The mitotane and chemotherapeutic agents (cisplatin, doxorubicin and etoposide) may control tumor growth in advanced stages for only short periods.

V393 SIOP19-0832 | Favourable Outcomes in Children and Adolescents with Sex Cord Stromal Tumours (1990-2015): A First Report by the South African Children's Cancer Study Group

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Background/Objectives: Paediatric sex cord stromal tumours (SCSTs) are extremely rare and there is no data on outcomes reported from Africa. We sought to evaluate outcomes of children and adolescents with biopsy-proven SCSTs in preparation for the introduction of a national protocol.

Design/Methods: Retrospective data was collated from nine South African paediatric oncology units. Kaplan-Meier analysis with Cox regression was performed to determine 5 year overall survival (OS).

Results: From January 1990 to December 2015, 24 patients were diagnosed with SCSTs, 4 males (median age 100.52

months) and 20 females (median age 78,18 months). Histologies included: 1 thecoma, 12 Sertoli-Leydig cell tumours and 11 juvenile granulosa cell tumours. Only stage impacted overall survival (OS): Stage 1, 100%; Stage 2, 0%, Stage 3, 80% and Stage 4, 50%. Twenty one patients underwent primary surgery and the remaining 3 following neo-adjuvant chemotherapy. Patients assigned FIGO stage 1C disease and above received chemotherapy, except 1 with FIGO stage 3A disease who is a survivor. One patient with FIGO stage 1A disease received chemotherapy for rising markers and survived. Twelve patients received chemotherapy: 6 JEB (carboplatin, etoposide, bleomycin), 4 BEP (bleomycin, etoposide, cisplatin) and 2 others. One patient who received JEB was changed to PEB (cisplatin, etoposide, bleomycin) after 2 courses. Two patients developed hearing impairment: 1 received BEP and the other PEB. Only 3 patients had audiograms and only 2 glomerular filtration rate (GFR) testing prior to chemotherapy. Three patients died of disease. There were no treatment-related deaths.

Conclusions: Although the numbers in this cohort are small, this study represents a relatively large cohort and the OS of 82.6% is encouraging. It is essential that the management of rare tumours such as SCSTs be standardised to ensure the best possible OS and to limit long-term sequelae. Based on these results, a standardised management protocol has been designed.

V394 SIOP19-1362 | Breast Masses in Children and Adolescents

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Background/Objectives: Breast lesions in children and adolescents are usually of benign nature. Fibroadenoma is the most commonly reported lesion in this age group. These lesions can be difficult to be distinguished from malignant tumors. Large size, rapid growth, lobulation and heterogeneity make malignancy more likely

Design/Methods: Files of all children and adolescents (<18 years) with breast masses who presented to King Hussein Cancer Center (KHCC) from 2003 till 2018 were retrospectively reviewed. Demographic data as well as radiology reports, pathology reports and outcomes were recorded.

Results: Twenty female patients presented with breast masses during the study period. Age ranged from 11.6 to 18 years (Median, 16.3 years). Ultrasound studies were done for 19 patients and MRI for one patient. Masses were reported in the left, Right, or both breasts in 11, 6 and 3 patients, respectively. Biopsy was done for 14 patients for suspicion of malignancy, 3 of these had subsequent resections. Pathology reports

showed fibroadenoma (N=11), papilloma (N=1), sarcoma phylloides (N=1) and alveolar rhabdomyosarcoma (N=1). Surgery was done for the patients with rhabdomyosarcoma, intraductal papilloma and for two patients with fibroadenoma (total 4 patients). The patient with phylloides tumor was lost to follow-up before surgery. For the 6 patients who had no biopsy, fibroadenomas were diagnosed based on ultrasound characteristic findings. These patients had no further events reported.

Conclusions: The majority of our patients had fibroadenoma diagnosed based on pathologic or radiographic findings. Approximately, 10% had malignant lesions and required further treatment. Triaging of these patients by expert radiologists is necessary not to miss malignancy.

V395 SIOP19-1422 | High Burden of Deep-Seated Plexiform Neurofibromas (PN) in Children with Neurofibromatosis 1 (NF1): Image-Defined Risk Factors

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Background/Objectives: PN may cause significant morbidity in children with NF1. We sought to describe image-defined risk factors of adverse outcomes in deep-seated PN.

Design/Methods: Retrospective analysis of consecutive patients with NF1 in a pediatric hematology and oncology center, with central review of imaging studies.

Results: Twenty-six children, of male/female ratio 1.1 and median age 5.8 years with NF1 were evaluated for NF1-related oncological manifestations. Nine, 20 and 6 patients had neurofibroma (s), optic pathway glioma (OPG) or both, respectively. Three of 6 patients with high burden of deep-seated PN, had significant morbidity with need of major surgery +/- radiotherapy. They were boys aged 13, 8 and 4 yo with paraspinal/intraspinal PN with intra-foraminal localization and dumb-bell shape (N=2), atypical localizations i.e. in tonsils, brainstem medulla and fifth, seventh, eighth and twelfth cranial nerves and orbit (N=1), and cervical PN with intracranial extension occupying the pterygoid fossa, occipital bone erosion, cervical neurovascular bundle displacement and airway compression (N=1). Progression to malignant peripheral nerve sheath tumor (MPNST) seven years after diagnosis in a previously resected cervical PN with modest size increments between 6-monthly imaging studies occurred in 1 patient. Treatment included low-grade chemotherapy for OPG with no effect on PN (N=1), spinal surgery for severe plexo-and radiculopathy (N=2), spher-

noidal radiation for severe exophthalmos (N=1), and intensive chemotherapy for MPNST without response (N=1). Three patients with stable disease had high burden PN of intra-abdominal and paraspinal localization (N=2) and in skull base (N=1). In comparison with patients with stable disease, patients with symptomatic progression of PN had more often intra-foraminal localization, bone erosion or even mild size increases on serial imaging.

Conclusions: Image-defined risk factors on initial and serial imaging of deep-seated PN might identify patients with NF1 at high risk of short- and long-term complications or evolution, including MPNST.

V396 SIOP19-0794 | Metronomic Chemotherapy and Liposomal Doxorubicin Among Children with Kasabach-Merritt Syndrome

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Background/Objectives: Kasabach-Merritt syndrome (KMS) is a rare constellation of consumptive coagulopathy and thrombocytopenia in patients with Kaposiform hemangioendothelioma or tufted angioma. KMS is associated with up to 30% mortality risk, due to hemorrhage and vital organ invasion. Conventional therapy includes corticosteroids, vincristine, interferon-alpha and is largely ineffective.

Design/Methods: Fifteen patients, 10 male/5 female, median age 4 months, with KMS were treated at our center between 2013 and 2017. In 80% of the cases vascular tumor was detected at birth and among 50% KMS was accompanied by either severe hemorrhage or bone destruction. In all cases previous conventional therapy was not effective. Therapy included three (consecutively applied) approaches 1) propranolol at 2-3 mg/kg/day; 2) metronomic chemotherapy: cyclophosphamide at 50 mg/m²/day, days 1-14, and vinblastine 1mg/m² at day 1; these courses were administered every 14 days; the number of courses ranged from 6 to 12; response was evaluated after 3 courses; 3) liposomal doxorubicin at 1 mg/kg, 2 to 10 injections at 28-day interval; response was evaluated after 2 courses.

Results: Fifteen patients received propranolol therapy. Complete response was achieved in 4 cases and partial response in 1 case. Median time to complete recovery of blood counts was 53 days, 50% reduction of the tumor volume at 90 days. Eleven patients received metronomic chemotherapy, 1 case had complete response, 1 - partial response, 7 - stable disease. Ten patients received liposomal doxorubicin. All achieved complete response, after a median of 6 courses. At 3-year

follow-up 14 patients (93%) are alive and disease free at last follow-up.

Conclusions: Among patients with KMS and localized vascular mass propranolol monotherapy can be effective and offered as first line. Metronomic therapy may induce stable disease in the majority of patients, although complete responses are rare. Liposomal doxorubicin was effective in all cases with complete durable responses.

V398 SIOP19-1431 | Biallelic Mismatch Repair Deficiency in Pediatric Colorectal Carcinoma Patients at KHCC, the Major Cancer Center in Jordan

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Background/Objectives: Biallelic Mismatch Repair Deficiency (BMMRD) is a devastating cancer predisposition syndrome that presents with brain, gastrointestinal and hematological malignancies. A previous report from our center showed high prevalence of BMMRD among children with high grade glioma. High rates of consanguinity may be a contributing factor.

Design/Methods: We conducted a retrospective analysis of pediatric patients (<18-years) who were diagnosed with biopsy proven CRC from Jun2006 until feb2019. Data collected included the presence of café-au-lait macules (CALMs) and/or other signs of NF1, consanguineous parents, family history of Lynch syndrome-associated tumors, second malignancies and siblings with cancer. Tumor blocks were reviewed and additionally stained for MMRD by immunohistochemistry (IHC) of the corresponding proteins.

Results: Overall 9 patients were studied (5 females). The age at diagnosis ranged from 5-18 years with a median age of 13.4 years. Four patients had consanguineous parents. Two had CALMs. Five had family history of associated malignancies. Except for the 5-year-old patient who had medullary carcinoma, all others (N=8) had the more common and less aggressive adenocarcinoma histopathology; 4 of them showed the unfavorable mucinous adenocarcinoma subtype. MMRD stains were positive in 4 patients, all of them had one or more clinical suggestive feature; two patients had biallelic loss of MSH6, one patient biallelic loss of PMS2, and the youngest of our group (5-years-old) had heterozygous loss of MLH1 which goes with acquired Lynch Syndrome. Four died after a median follow up of 15.5months (range 14-35 months) and 3 moved out of the country and were subsequently lost to follow-up.

Conclusions: In our study, one-third of studied patients had BMMRD as proven by IHC. Despite small numbers, our data

suggests that diagnosis of CRC in a child should lead to testing for BMMRD and proper genetic counseling.

V399 SIOP19-1480 | Clinical Characteristics and Outcome of Eleven MRT Patients Treated in a Single Institution

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Background/Objectives: Non-CNS Malignant rhabdoid tumors (MRT) are rare and highly aggressive pediatric cancer. Standard therapy has not established yet. To know the clinical characteristics and outcome of MRT, we reviewed clinical courses of MRT patients treated in our institution between Apr 2005 and Mar 2019

Design/Methods: This is a retrospective analysis of patients' medical records.

Results: Among twenty-four consecutive Rhabdoid tumor patients, eleven extracranial MRT patients (46%) were identified (0y0m-12y10m, median 1y5m). There were four boys and seven girls. All were pathologically diagnosed as MRT. Their primary site was kidney (MRTK) (n=3), neck/upper mediastinal (n=3), liver (n=3), retroperitoneum (n=1) and unknown (n=1). Seven patients had metastasis at their diagnosis (63%). A patient had synchronous tumors. A neonate with unknown primary site had multiple metastasis in liver, kidney, lung, brain and bone, and showed massive bleeding. Primary resection was only possible in two patients with local MRTK. Initial emergency debulking surgery was required in two patients with neck/upper mediastinal MRT because of their airway/vascular or spinal cord compression. Four of eleven patients start their chemotherapy under respiratory support. Most of the patients were treated with VDC/ICE regimen. Three non-MRTK patients were also treated with HD-Chemotherapy (HiMEC 1, TEPA/MEL 2). Radiotherapy was given to six patients except three patients who introduced palliative therapy for tumor progression soon after their diagnosis. Mean observational period of all 11 patients was 3.7 years. The 3-year overall survival was 27±15%. Mean survival period was 625 days. Two MRTK girls, one in 2nd CR, are long-term survivors. Also, a stage 4 neck MRT boy who received 59.6Gy local irradiation, HD-Chemotherapy and WT1 peptide vaccine survive in CR more than 3 years without primary tumor resection.

Conclusions: Although most of MRT showed dismal prognosis, chemo/rad-sensitive patients might have chance to survive with aggressive therapy.

V400 SIOP19-0652 | Pediatric Adrenocortical Tumors Associated with a Beckwith-Wiedemann Syndrome: Morphological and Immunohistochemical Profile

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Background/Objectives: Pediatric adrenocortical tumors (ACTs) are very rare tumors frequently associated to cancer predisposition syndrome. Histological features of tumors arising in the setting of Beckwith Wiedemann syndrome (BWS) are poorly described. The aim of this study was to review the morphological and immunohistochemical features of BWS associated pediatric ACT.

Design/Methods: Among 95 cases of histologically reviewed pediatric ACT treated between 2000 and 2018 and registered in the French database, 5 cases with sufficient outcome-related information available were included. Clinical and histological data were collected. Ki67 and p57 immunostaining were performed.

Results: Mean age at diagnosis was 3 years (range: 1–6) vs. 5 (range: 0–17) for the whole cohort. There were 4 female and 1 male. In all cases but one, ACT revealed the diagnosis of BWS. Molecular subtypes (performed on blood-leucocyte DNA) included segmental paternal uniparental isodisomy of 11p15.5 (n=3) and loss of methylation of IC2 (n=1) (missing data for 1). Three patients had clinical features of systemic overgrowth syndrome at birth including macroglossia and hemihyperplasia (missing data for 2). Initial clinical symptoms related to hormonal overproduction were virilization (n=5), Cushing syndrome (n=3) and hypertension (n=1). Median weight and size of tumors were 19.5g (3–30) and 4.5cm (2.0–5.5) respectively. All tumors were localized at diagnosis (stage COG I) and had histological favorable criteria. Ki67 was under 10% and p57, performed in 2 cases, was not expressed. All patients were cured by complete surgery alone. Events were characterized by metachronous tumor in 2 cases (nephroblastoma and contralateral ACT). All patients were alive with no evidence of disease after a median follow-up of 92 months (ranges: 30 – 155).

Conclusions: Pediatric ACT arising in the setting of BWS are exceptional, occur in young patients and are characterized by favorable histological features and outcome.

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V401 SIOP19-1543 | The French Fracture Database: An Efficient Way to Improve Knowledge on Very Rare Malignant Pediatric Tumors

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Background/Objectives: Since 2012, the French very rare pediatric group, called FRACTURE, registered all very rare malignant pediatric tumors (VRT), defined by an incidence <2/million inhabitants in a specific database. The study proposes the first analysis of this database.

Design/Methods: Data recorded between 2012 and 2018 are analyzed.

Results: Overall 675 patients were registered in 34 centers and concerned 130 different histotypes. Most frequent tumors were neuroendocrine tumors of the appendix (8.1%; 55 patients), undifferentiated nasopharyngeal carcinoma (NPC, 6.3%; 43 patients), pheochromocytoma/paraganglioma (5.0%; 34 patients), solid pseudo-papillary tumor of the pancreas (SPP, 4.7%; 32 patients), salivary gland tumors (4.4%; 30 patients), pleuropulmonary blastoma (PPB, 3.6%; 24 patients) and cutaneous melanoma (3.4%; 23 patients). In the same time, Fracture group settled up national guidelines on NPC, adrenocortical carcinoma, SPP, sialoblastoma and melanoma. In addition, the group took part in specific European guidelines on thymic tumors and PPB. National and international retrospective analyses on VRT have been presented in 35 scientific congresses and published in 14 peer reviewed journals.

Conclusions: Development of national pediatric VRT database succeeds to register a considerable number of patients and is an efficient way to improve knowledge and collaborative studies in such exceptional tumors. A collaboration with the French national pediatric tumor

registry is currently under planning. National and international collaborations allow harmonious therapeutics recommendations even in VRT in order to treat such rare diseases in a uniform way and to analyze them prospectively.

V402 SIOP19-1122 | Colorectal Carcinoma in Children and Adolescents, Experience at a Single Argentinian Institution

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Background/Objectives: Colorectal carcinoma (CRC) is the third most common malignancy in adults. However, these tumors are extremely rare among children, particularly before puberty.

It usually begins with nonspecific signs and symptoms, so the index of suspicion is low, consequently, the diagnosis may be delayed.

Reports in the literature indicate that poor prognostic factors are more common in children than in adults, resulting in worse outcome.

Our objective is to report clinical profile, treatment and prognosis of CCR in children and adolescents in our institution.

Design/Methods: We retrospectively analyzed 15 patients younger than 20 years-old with CCR referred to Hospital de Pediatría Dr. J.P. Garrahan, Buenos Aires, Argentina between 1987 and 2018.

Results: Fifteen patients <20 years (11-19) were admitted during the study period. Male/Female was 10/5. The median time of delay in diagnosis was 2.37 months (8days-5months). The most common symptoms were abdominal pain and weight loss; 5 patients presented with acute surgical abdomen. Two patients had been previously treated for a high grade glioma, one of them with Neurofibromatosis type 1. Other two patients had increased risk factor for developing CCR: One with Crohn's disease and one with ulcerative colitis. Unfavorable histotypes were more frequent: mucinous adenocarcinoma was observed in 9 patients, 5 being signet ring cell carcinoma. Poorly differentiated and un-differentiated tumors (grades III and IV,) were 6/15. Rectosigmoid was the most common primary site (8 patients). Fourteen patients presented with advanced stage of disease (stage III-IV); more than half (9/15) had distant metastases. Only 2 patients were alive. Thirteen patients died because of the disease. The 1-year progression-free survival was 28,5%. Median of mortality was 9.8 months.

Conclusions: CCR in children represents a rare tumor, and it is characterized by aggressive behavior and delayed diagnosis, resulting in a worse prognosis than in adults.

V403 SIOP19-0385 | Clinicopathological Features and Outcomes of Pediatric Differentiated Thyroid Carcinoma: Experience from a Tertiary Cancer Centre in India

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Background/Objectives: Thyroid carcinoma is an extremely rare disease and contributes to 1.5-3% of childhood carcinoma. The purpose of this study is to assess the detailed clinicopathological features and outcomes of differentiated thyroid carcinoma (DTC).

Design/Methods: Medical records of children aged ≤14 years, pathologically diagnosed as DTC at a tertiary cancer institute between 1st January 1998 and 31st December 2015 were retrospectively analyzed. Survival outcomes were evaluated using the Kaplan–Meier method.

Results: One hundred and twenty five children with DTC were treated with a male:female ratio of 1:2.9. Median age at presentation was 12 years (2-14 years). Thyroid swelling was the most common presentation (60.4%) followed by thyroid nodule (21.1%). Histological examination revealed Papillary Thyroid Carcinoma (PTC) in 98.4% cases. Among the variants of PTC, classical was predominant (72%) followed by follicular variant (17.6%). The extrathyroidal extension was seen in 32 children (25.6%). Sixty nine patients (55%) had metastases at presentation (63- lymph nodes only and 6- lymph node and lungs). Relapse was noted in 13 children including nine nodal recurrences, three local recurrences and one case of nodal recurrence with concurrent bone metastasis. These patients were salvaged with nodal dissection and radioiodine therapy. The median follow up period was 99 months (13-243 months). 5 year Overall Survival was 100% and 5 year Relapse Free Survival was 94.8%. Univariate analysis did not show any significant association between the clinicopathological features and the disease outcomes.

Conclusions: Pediatric DTC had an aggressive behavior characterized by a high rate of extrathyroidal extension, nodal and pulmonary metastasis. Our study reaffirmed favorable prognosis despite aggressive behavior and even after a relapse.

V404 SIOP19-1280 | Clinical Outcomes of Langerhans Cell Histiocytosis Single Institute Experience

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Background/Objectives: Langerhans cell histiocytosis (LCH) is a relatively rare disease, characterized by the abnormal proliferation of the Langerhans cells. Its incidence is rare; with an annual incidence of 3 to 9 cases per million in children. This study is conducted to assess the clinical features, course and treatment outcomes of children and adolescents diagnosed with LCH in resource limited country.

Design/Methods: Retrospective study was carried out between 2005 till 2015; Children up to 18 years with LCH that presented to Shaikat Khanum Memorial Cancer hospital were included after the IRB approval.

Results: Twenty-nine patients were diagnosed, with median age 3 years (range 06 months-18years). Single system LCH was diagnosed in 12 patients (41.4%), out of which unifocal bone was involved in 3 patients (10.3%), multifocal bone in 3 patients (10.3%). Lymph nodes were involved in 5 patients (17.2%), whereas perianal muscles in 1 patient (3.4%). Multi-system LCH was present in 17 patients (58.6%), out of which 6 patients (20.7%) were risk organ positive. Bone marrow was involved in 03 patients (10.3%), liver in 03 (10.3%). Hypothalamic pituitary was involved in 4 patients (13.8%). After initial treatment complete remission was achieved in 21 patients (71.4%), 01 patient (3.4%) died during treatment. Disease progression was in 2 patients (6.9%), who later died due to treatment and disease related complications. Relapse was present in 6 patients (20.7%). Mortality was 50% with MS-LCH risk organ. Over all 3-year survival was 89.7%, whereas EFS was 72.4%.

Conclusions: Most of our patients that presented had multisystem involvement, risk organ positive patients had poor outcomes, despite being treated on the recommended treatment guidelines. In resource poor settings we need to look at BRAF and other mutations at time of diagnosis and other factors associated with poor outcomes.

Key Words: LCH, Risk organ, outcomes.

V405 SIOP19-0659 | Langerhans Cell Histiocytosis (LCH) in Children: Clinical Presentation, Management and Outcome of a Clonal Myeloid Neoplasia

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Background/Objectives: LCH is an inflammatory myeloid neoplasia. We present clinical characteristics, management and outcome of single-center cohort.

Design/Methods: Sixty-three patients (63.5% males) with histologically-proven LCH, diagnosed between 1974-2019,

with median age 3.7 years, treated with HS-LCH protocols are presented. A) Single-system unifocal 38/63 patients: A1) *Single-bone-lesion*: 34/38 biopsied/curettage; 26/34: follow-up (4/26 with CNS-risk-lesion); 8/34 VBL/PDN for 6-12 months, due to special symptoms/site (femoral-head:2, vertebrae:2, mandible:2, other:2). A2) *Pituitary-lesion*: 1/34, Ara-C/iv-IgG for 12 months (possible neurodegeneration). A3) *Skin single-lesion*: 3/34, follow-up. B) Single-system multifocal: 5/63 patients. All bone (3/5 with CNS-risk+lesion). Four (4/5) received 12-months VBL/PDN (one patient <2 years-old), one is still on treatment. C) Multi-system: 20/63 patients, (median age: 0.14 years, 14/20 <2 years-old) while 14/20 had risk-organ (RO+) involvement (lung-3, liver and/or spleen-3, lung/liver-1, liver/spleen/BM-4, liver/spleen/BM/lung-1, BM-1, lung/liver/spleen-1). All patients were treated according to HS-LCH-protocols. Diabetes insipidus was present in 6/63; 3/6: with CNS-risk bone lesions. Of ten patients checked for BRAF-V600E-mutation five were positive.

Results: Twenty-eight/34 patients with single-bone lesion remain in CR1, while 6/34 patients relapsed: 5/6 bone-only disease, 1/6 Multi-System disease (all alive, in CR2=3, CR3=2, CR4=1). Five patients with multifocal-bone disease are in: CR1=3, CR2=1, 1 on-treatment. Six patients with RO (-) multisystem disease: CR1=5, CR2=1. Ten, 10/14 RO (+) patients are in: CR1=8, CR2=1, CR4=1; 4/14 are deceased (age<2years-old, diagnosed before 1983). Of 5 BRAF-V600E(+) patients 3 single-bone disease are in CR1 without treatment; 1/5 patient with refractory disease in CR1 after third-line treatment; 1/5 in CR2. Sixteen, 16/22 patients diagnosed younger than 2 years-old are in CR1, CR2:1 and deceased:4 (1: lost follow-up). In total, 47/63 patients remain in CR1 (EFS: 74.6%); OS 93.7%. 1

Conclusions: Continuous effort in understanding the molecular biology of LCH, careful staging, and appropriate treatment stratification, remains the cornerstone for optimal outcome, for this newly recognized as clonal myeloid neoplasia of childhood.

V406 SIOP19-0137 | Exploring Heterogeneity of COG Stage III Disease in Pediatric Adrenal Cortical Tumors: The French Pediatric Rare Tumor Group (FRACTURE) Experience

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Background/Objectives: Stage III COG pediatric adrenal cortical tumors (ACT) is a heterogeneous condition comprising retroperitoneal lymph node involvement and unresectable tumors, associated with a poor prognosis, and microscopic residual disease, whose prognosis is less clear. Objective is to describe clinical characteristics and outcome of COG stage III patients with primary localized operable ruptured tumors.

Design/Methods: Patients with histologically reviewed pediatric ACT were investigated (n=95) from the French pediatric rare tumor database (FRACTURE).

Results: Among 18 stage III, 12 patients had microscopic residue due to initial biopsy (n=5, 4 percutaneous and 1 open), intraoperative rupture (n=8) or R1 surgery (n=1) (2 patients with 2 conditions). Median age was 6.2years (0.5-17). Seven tumor weights were >200g (median 350g (range: 71-1270)). Initial tumor resection was performed for all patients. First line therapy included mitotane (n=8) and chemotherapy (n=6). After a median follow-up of 96 months (25-119), 4 early progressions and 2 relapses occurred. A total of 7 patients died, including 5 of disease. Among the 2 patients alive currently under therapy, 1 has no evidence of disease (NED) and 1 has evolutive disease. The 3 patients alive with NED were <2 years-old at diagnosis with tumor <200g. Only 1/5 patient that underwent initial biopsy was alive with NED. Microscopic residual disease correlated significantly with worse prognosis: 5y-PFS 44%; 95IC:22-87% vs. 87%; 95IC:80-96), p<0.0001) for the whole cohort.

Conclusions: Stage III diseases by microscopic residual tumor appears to have a dismal prognosis, pleading for the systematic use of adjuvant therapy, especially when associated with risk factors such as age and tumor weight. Extreme caution regarding initial clinical and radiological presentation should be taken before considering any biopsy of an adrenal mass in children given its strong prognostic value in case of ACT.

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V407 SIOP19-0606 | Clinical and Biopathology Analysis of Inflammatory Myofibroblastic Tumors in Children and Adolescents: A Report from 5 Pediatric Tertiary Oncology Centers

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Background/Objectives: Inflammatory myofibroblastic tumors (IMT) are rare and intermediate malignancy diseases with frequent somatic molecular rearrangement. In the Era of targeted therapy, guidelines on optimal IMT management are lacking as well as coherent series with biopathology analysis.

Design/Methods: For this retrospective study, we reviewed all patients with IMT treated in 5 tertiary pediatric centers between 2000 and 2017. Central pathology review as well as additional molecular analysis were planned.

Results: Thirty-two cases were identified. Median age at diagnosis was 7.5 years (range: 3m-16y). Tumor location included thorax (n=12), abdomen (n=10), head and neck (n=8) and limbs (n=2). One patient had metastatic disease. Thirteen cases (40%) are ALK-positive. Among 17 ALK-negative IMT, 3 are ROS1-positive and 2 are ETV6-NTRK3-positive. Primary surgery was performed for 22 (69%) patients while 10 patients had various medical therapies followed by delayed surgery in 5 cases. Medical therapy consisted of steroids (n=10, 3 responses), targeted therapy (n=3: 1 ALK, 1ROS1 and 1 NTRK-positive IMT, 3 responses), and MTX-vinblastine (n=1; 0 response). One patient had mutilating surgery. Seven recurrences occurred (6 loco-regional, 1 metastatic): 6/22 in the surgery first group and 1/10 in the group of surgery with adjuvant therapy. After a median follow-up of 2.8 years (range: 5m to 9.3y), 3-years event-free and overall survivals were respectively 75% (95% CI, 61-94%) and 97% (95% CI, 87-100%). Quality of resection (R0 vs R1/R2) was not associated with higher tumor failure (p=0.48) but tumor location influenced outcome with thoracic tumors

having highest risk of recurrence ($p=0.02$). Three years EFS was not statistically different between IMT cases with or without somatic molecular abnormalities (65% vs. 82%; $p=0.45$).

Conclusions: Surgery is effective in most pediatric IMT. If needed, neo adjuvant therapy including targeted therapy should be proposed to allow adequate and non-mutilating surgery. The role of other medical therapies should be better evaluated.

V408 SIOP19-1757 | Differential Expression Of microRNAs in Plasma of Langerhans Cell Histiocytosis (LCH) Patients and Correlation with T Cell Exhaustion

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Purpose: LCH lesions are mainly comprised of pathologic CD207+ DCs and infiltrating immune cells, the majority of which are T lymphocytes. The mechanisms responsible for recruiting activated and exhausted T cells to LCH lesions and contributions of these T cells to pathogenesis are not known. In the past decade, non-coding microRNAs (miRNAs) have been identified as crucial regulators of immune modulation for tumor immune escape. Therefore, we investigated role of miRNAs in T cell function modulation in LCH. **Method:** Circulating microRNA profiling was performed on plasma samples from LCH and healthy controls ($n=10$ each) using NanoString platform. **Results:** Twenty-one miRNAs were differentially expressed in LCH samples. Putative messenger RNA (mRNA) targets of these miRNAs were predicted in situ. hsa-miR-93-5p, which targets PDCD1LG2 and CD69, was downregulated in LCH patients. PDCD1LG2 encodes programmed cell death 1 ligand 2, the ligand for PD-1 receptor, whose expression is high in both progenitor and terminal progeny sub-types of exhausted CD8+ effector T cells. This indicates miR-93-5p downregulation as a possible contributor to T cell exhaustion in LCH. Another factor that is over-expressed in the terminal progeny exhausted CD8+ T effector cells is EOMES (encoding eomesodermin). Two of the 21 differentially expressed miRNAs in LCH, hsa-miR-182-5p and hsa-miR-25-3p, were predicted to target EOMES. Although hsa-miR-182-5p was not downregulated in LCH patient samples, hsa-miR-25-3p is significantly downregulated indicating pleiotropic effect of miRNAs in rendering T cell exhaustion in LCH patients. **Conclusion:** These data indicate a potential role for miRNAs in regulating the exhausted and dysfunctional status of lesional T cells. miRNA may represent a novel class of diagnostic and therapeutic targets for patients with LCH.

V409 SIOP19-0591 | Pediatric Cancer Studies Triggered by the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) Aim at Labels, Not at Improved Treatment

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Background/Objectives: Both FDA and EMA reward/demand pediatric cancer studies. Do these studies advance pediatric cancer care?

Design/Methods: Publications of FDA representatives, FDA-triggered pediatric oncology studies (published and/or listed in www.clinicaltrials.gov), and FDA/EMA pediatric reports were analyzed.

Results: FDA representatives express two assumptions: (1) children, defined as $<17y$, need separate proof of efficacy; (2) with the exception of chronic myelogenous leukemia (CML), the biology of pediatric cancer is different from adult cancer. From 1997 on, FDA-rewarded studies investigated individual cytotoxics in heavily pretreated young patients. But standard-of-care was already combination treatment with many cytotoxics. Another round of chemotherapy with a single cytotoxic did not help patients, but rewarded companies with patent extension, researchers with publications, and the FDA with improved standing in medical care. The EU expanded the definition of children to $<18y$ and demands "pediatric investigation plans" (PIPs) also for rare diseases. One FDA-rewarded study package requested ipilimumab "pediatric" melanoma studies; 13 EMA PIPs demand "pediatric" studies in solid tumors including melanoma; two "pediatric" monotherapy studies with ipilimumab and vemurafenib, respectively, were terminated in 2016; many other PIP-studies continue recruiting.

Conclusions: FDA/EMA-requested/demanded "pediatric" oncology studies focus on labels in administratively defined "children". FDA/EMA age limits are not physiological. FDA-expressed assumptions about different biology of "pediatric" malignancies are wrong. FDA/EMA reports list regulatory, not therapeutic achievements. Some EU researchers perform predominantly PIP-demanded oncology studies. In close collaboration with researchers, the EMA demands "pediatric" studies and threatens non-approval of innovative drugs. Researchers and EMA representatives co-author lauding reports.

Publications by FDA representatives express the flawed "therapeutic orphans" concept, enriched by additional wrong assumptions about the biology of "pediatric" malignancies. The EMA further expanded the "pediatric imperative". PIPs do not advance treatment. Ethics committees should be alerted, should re-analyze ongoing "pediatric" studies,

suspend questionable ones, and reject new ones. US+EU pediatric laws need revision.

V410 SIOP19-0453 | Underexpression of MIR-150 is Associated with Poor Prognosis in Stage II/III of Pediatric Adrenocortical Tumors

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Background/Objectives: Although adrenocortical tumors (ACT) are rare in children, in Brazil its incidence is 10-15x higher than the worldwide. Except to metastatic tumors, the differentiation of malignant and benign forms in childhood is difficult and to date, there are no histological or molecular markers that can reliably distinguish them. Aiming to find potential biomarkers of ACT prognosis, we validated the expression of miR-34a, miR-142, miR-150, miR-214 and miR-708 that was found differentially expressed in a microarray-based microRNA profiling, conducted previously by our group

Design/Methods: The microRNA expression levels were analyzed by quantitative real-time PCR in 68 consecutive tumor samples obtained at diagnosis from children with diagnosis of ACT and in 16 pediatric non-neoplastic adrenal samples. Association with clinical/biological features and survival were done using Mann-Whitney test and Kaplan-Meier curves. Knockdown of miR-150, using lentiviral vectors in the ACT cell lines H295A was done and the gene expression of WNT/B-catenin, NOTCH and TGFB pathways were compared between control and knockdown cell line

Results: It was observed a lower expression of miR-214 and higher expression of miR-34a and miR-142 in children with ACT when compared with non-neoplastic adrenal controls ($P < 0.05$). Tumors with weight > 200 g had lower expression of miR-150, miR-214, miR-142 and miR-708. In the 18 patients classified as intermediate clinical stages (II and III), lower expression of miR-150 (using the median as cut-off) was associated with significant higher risk of unfavorable event and/or death and lower 5-years event free-survival (45% vs 100%, $P = 0.019$). Knockdown of miR-150 in H295A cell lines showed a decreased of *NOTCH1/2*, *GSK3B*, *AXIN2* and *CTNBN1* and increased of the *DKK3* expression when compared with control

Conclusions: The present data suggests that miR-150 expression could be a potential prognostic marker in patients with

intermediate stages of the disease and it can regulate its action by controlling WNT/B-catenin and NOTCH pathways. (Grant FAPESP-14/20341-0)

V411 SIOP19-0971 | The Role of MIR-630 in Pediatric Adrenocortical Tumors

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Background/Objectives: In children, adrenocortical tumors (ACT) are rare, with advanced tumors presenting very poor prognosis. In Brazil its incidence is 10-15x higher than the worldwide. Its biology is not completely understood and except to metastatic tumors, the differentiation of malignant and benign forms in childhood is difficult and to date there are no histological or molecular markers that can reliably distinguish them. Aiming to understanding better the tumor biology, we analyzed by *in vitro* studies the effect of the overexpression of miR-630, which was underexpressed ($-4.4x$) in samples from 37 children with ACT compared to 9 non-neoplastic pediatric adrenal samples in a previous miRNAs microarray study performed by our group.

Design/Methods: Using a lentiviral vector, miR-630 expression was induced in the H295A adrenocortical tumor cell line and cell proliferation was measured using ATP levels and Resazurin colorimetric assays at 24h, 48h, 72h, and 96h times. The gene expression of *PTCH1*, *SUFU*, *GLI1* and *SMO* was investigated after miR-630 induction by quantitative real-time PCR.

Results: Although after induction of miR-630 expression, the increased cell proliferation observed was not significantly different from control, this induction promoted an increasing in the expression of the genes belonging to the Shh signaling pathway: *PTCH1* (+1.88-fold), *SUFU* (+2.07-fold), *GLI1* (+2.53-fold) and *SMO* (+3.17-fold).

Conclusions: The present results suggest an involvement of miR-630 in pediatric ACT by controlling the Shh signaling pathway. (Grant FAPESP-14/20341-0)

V412 SIOP19-1523 | Plasma Protein and Cytotoxic T-Cell Gene Expression Profiles Distinguish Hemophagocytic Lymphohistiocytosis from Other Hyper-Inflammatory Diseases

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Background/Objectives: Hemophagocytic Lymphohistiocytosis (HLH) is a life-threatening disorder that shares many overlapping clinical features with other hyper-inflammatory diseases including sepsis and systemic inflammatory response syndrome (SIRS). This study evaluates the plasma protein profiles of HLH, sepsis, and SIRS and the gene expression profiles of cytotoxic T-cells (CTLs) and monocyte/macrophages (Mono/Mac) in HLH compared to sepsis.

Design/Methods: The Luminex platform measured 135 analytes in 41 patients with HLH to 47 patients with severe sepsis or SIRS in discovery and validation cohorts. Disease status comparisons and 3-Nearest Neighbors Prediction classifier were developed. CD3+8+ CTLs and CD3-68+ Mono/Mac were isolated from peripheral blood of 12 patients with HLH, 10 with severe sepsis, and 4 healthy controls. Gene expression data was analyzed using Gene Set Enrichment Analysis (GSEA).

Results: Seventeen analytes were significantly different between HLH and sepsis/SIRS. A prediction classifier using ten analytes differentiate HLH from SIRS/sepsis with sensitivity 0.857 and specificity 0.833, and GSEA of HLH CD8+ T cells was enriched for the IFN- γ signature. Elevated CCL20 was associated with risk of death in the HLH cohort.

Conclusions: This evaluation of plasma proteins demonstrated that HLH has a distinct inflammatory profile compared to severe sepsis and SIRS and the IFN- γ response elements, CXCL9, CXCL10, and CXCL11, are all upregulated in HLH. GSEA also demonstrates that CD8+ IFN- γ signaling is more significant in patients with HLH compared to sepsis. The "HLH classifier" could be a clinically useful tool to assist with diagnosis of critically ill children with hyper-inflammatory syndromes that require distinct clinical approaches. Additionally, the results from this study support rationale for therapeutic strategies to target IFN- γ to control pathologic inflammation for HLH patients with HLH.

V413 SIOP19-0292 | Multicystic and Diffuse Malignant Peritoneal Mesothelioma in Children

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Background/Objectives: Malignant and multicystic peritoneal mesothelioma are tumor developing from the mesothelial cells, extremely rare in children. No specific guidelines are available at this age.

Design/Methods: We performed a retrospective analysis of all identified children (under 18 years-old) treated in France from 1987 to 2017 for a diffuse malignant peritoneal mesothelioma (DMPM) or a multicystic peritoneal mesothelioma (MCPM)

Results: Fourteen patients (5 males and 9 females), aged 2.2 to 17.5 years were selected. The most frequent revealing symptoms were abdominal pain, ascitis and alteration in general condition. Eight patients had epithelioid mesothelioma, 3 biphasic mesothelioma and 3 MCPM. Eight patients with DMPM diagnosis received cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (HIPEC). Among them, 6 patients had neoadjuvant systemic chemotherapy, 1 patient, post-operative chemotherapy and 1 patient CRS and HIPEC only. Three patients received exclusive systemic chemotherapy. All patients with MCPM had exclusive surgery. After a median follow-up of 7 years (2-24), 4 patients (4/11; 1 death) with DMPM and 2 patients (2/3) with MCPM had a local and distant recurrences.

Conclusions: Peritoneal mesothelioma tumors in children is a rare condition with difficult with high risk of recurrence. Worldwide interdisciplinary collaboration and networking are mandatory to help diagnosis and provide harmonious treatment guidelines.

V414 SIOP19-1305 | Decreased Expression of TGFBR2 Predicts Poor Prognosis in Pediatric Patients with Adrenocortical Tumors

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Background/Objectives: Childhood adrenocortical tumors (ACT) are rare neoplasms with significant incidence in the South and Southeast of Brazil. Although metastatic stages of these tumors characterize aggressive behavior and unfavorable prognosis, there is no reliable biomarkers to discriminate

between malignant and benign tumors or to predict prognosis in earlier stages. Thus, based on recent evidences from our research group that suggest a dysregulation of TGF- β pathway in these tumors, we aimed to investigate the predictive potential of TGF- β -related genes as prognostic markers of pediatric ACT.

Design/Methods: The expression of TGFB1, SMAD3, TGFBR1 and TGFBR2 genes were analyzed by quantitative real-time PCR in 66 pediatric ACT and in 18 pediatric non-neoplastic adrenal samples. Association between gene expression profiles with clinical/biological features and survival were done using Mann-Whitney test and Kaplan-Meier curves.

Results: Our results showed a decreased expression of SMAD3 and TGFBR2 in pediatric ACT when compared with non-neoplastic adrenal controls ($P < 0.01$). Although no association between SMAD3 and clinical/biological features was found, the lower expression of TGFBR2 was significantly associated with higher tumor volume ($> 200 \text{ cm}^3$; $P = 0.02$), presence of metastasis ($P = 0.002$), recurrence ($P < 0.001$), higher risk of unfavorable event and/or death and lower 5-years event free-survival (56% versus 97%, $P < 0.001$) and overall survival (69% versus 97%, $P = 0.004$).

Conclusions: The present data suggest that TGF- β signaling pathway is downregulated in pediatric ACT and that TGFBR2 expression could be a potential prognostic marker in patients with these tumors. (Grant FAPESP-14/20341-0)

V415 SIOP19-1309 | Underexpression of MSI2 is Associated with Clinical Features of Unfavorable Prognosis in Pediatric Adrenocortical Tumors

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Background/Objectives: Musashi (MSI) 1 and 2 are RNA-binding proteins that regulate several cellular functions and recently have emerged as regulators of cancer development. However, their role in adrenocortical tumors (ACT) remain unknown. ACT are rare in children, but its incidence is particularly higher in Brazil. Currently, there are no reliable biomarkers to predict prognosis and/or to discriminate benign and malignant ACT. Thus, aiming to find potential biomarkers of ACT prognosis, we investigated the gene expression profile of MSI1 and MSI2 in tumor samples of pediatric patients with ACT.

Design/Methods: The gene expression of MSI1 and MSI2 was analyzed by quantitative real-time PCR in 28 tumor samples obtained at diagnosis from children with diagnosis of ACT and in 16 pediatric non-neoplastic adrenal samples. Association between gene expression profiles with clinical/biological features and survival were done using Mann-Whitney test and Kaplan-Meier curves.

Results: It was observed a lower expression of MSI1 and MSI2 in pediatric ACT when compared with non-neoplastic adrenal controls ($P < 0.01$). However, only the expression of MSI2 was associated with clinical features of unfavorable prognosis. Lower expression of MSI2 was observed in tumor samples from patients who underwent recurrence and its expression was associated with significant higher risk of unfavorable event and/or death ($P < 0.05$).

Conclusions: Taken together, our data suggest that MSI2 may be involved in ACT development and that its lower expression may indicate unfavorable prognosis in pediatric ACT. (Grant FAPESP-14/20341-0)

V416 SIOP19-0067 | Clinicopathological Analysis of BRAF V600E Mutation in Pediatric Langerhans Cell Histiocytosis

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Background/Objectives: To investigate the relationship between BRAF V600E mutation and clinicopathological features in children with langerhans cell histiocytosis (LCH).

Design/Methods: Forty-one cases of children with LCH diagnosed in department of pathology, Xinhua hospital, School of Medicine, Shanghai Jiao Tong University from January 2017 to July 2018 were collected. BRAF V600E mutation was detected by immunohistochemistry (Ventana, clone VE1) and amplification refractory mutation system (ARMS) fluorescence PCR, respectively. The consistency of the two methods was compared, and the relationship between BRAF V600E mutation and clinicopathological characteristics was analyzed.

Results: The positive rates of BRAF V600E mutation detected by immunohistochemistry and ARMS fluorescence PCR were 51.2% (21/41) and 53.7% (22/41), respectively. The agreement of the two methods was quite good (97.6% concordance, $\kappa = 0.951$, $P < 0.001$). Only the tan granular staining of cytoplasm in tumor cells was identified as positive rather than nonspecific staining of inflammatory cells in the background (false positive). BRAF V600E mutation rates in males and females were 57.9% and 50%, respectively. The mutation rate shows an increasing trend in patients under 3 years old than that aged 3 years and above (59.1% vs. 47.4%), and in skin lesions than that in bone lesions (66.7% vs. 51.4%),

but there were no statistical significances ($P > 0.05$). The mutation rate was 53.6% for single lesion and 53.8% for multiple lesions.

Conclusions: The agreement between the immunohistochemistry and ARMS fluorescence PCR methods for detecting the mutation of BRAF V600E gene in LCH was quite good. False negative or false positive should be noted in immunohistochemical analysis. The BRAF V600E mutation has increasing trends in children under 3 years old or in lesions involving the skin, but it still needs to expand the sample for further study.

V417 SIOP19-0489 | Clinico-Pathological Features and Outcome of Wilms Tumor (King Fahad Medical City, Saudi Arabia)

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Background/Objectives: Wilms Tumor (nephroblastoma) is the most common pediatric renal malignancy. This study sought to describe the clinical and pathological characteristics of Wilms tumors and evaluate the clinical outcome in children treated at King Fahad Medical City.

Design/Methods: We retrospectively identified all patients with a confirmed histopathological diagnosis of Wilms tumor between 2006 and 2016. Demographic data as well as clinical and pathological characteristics were collected. The survival trends (overall survival and event-free survival) were assessed.

Results: Thirty-eight (38) children with Wilms tumor were reviewed. There was slight female predominance with 26 females (68.4%), and 12 males (31.6%). The mean age at diagnosis was 49.7 months, with a standard deviation of 27.8 months. There were 20 tumors on the left side, 15 tumors on the right side and three were bilateral. There was pulmonary metastasis in 16 patients (42.1%). The majority of patients had favorable histology (92.1%), while diffuse anaplasia and focal anaplasia represented 8.9% and 2.6%, respectively. There were 5 patients with stage I, 4 patients with stage II, 13 patients with stage III, 10 patients with stage IV and 3 patients with stage V. Upfront surgery was offered to 17 patients while delayed surgery after chemotherapy was performed in 21 patients. Radiotherapy was given to 24 patients. The overall survival rate was 92.1%, and the event-free survival rate was 84.2%.

Conclusions: The clinicopathological features and the excellent outcome of our patients are comparable to similar international studies using either SIOP (International Society of Pediatric Oncology) or COG (Children Oncology Group)

treatment protocols. Limitations to our study include small sample size and lack of cytogenetic risk stratification.

Solid Non Brain Tumours - Renal Tumours

V418 SIOP19-1521 | Epidemiology and Treatment Outcomes of Pediatric Cancer in the Center of Tunisia

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Background/Objectives: Pediatric cancer incidence is increasing in the last twenty years. It is the leading cause of death among children with 300 000 deaths per year. This study aims to describe the epidemiology of pediatric cancer and treatment outcomes in the center of Tunisia.

Design/Methods: A retrospective study about patients aged under 16 years treated for an histologically proven cancer between 2013 and 2017 in the department of medical oncology of Farhat Hached University hospital, Sousse (Tunisia).

Results: One hundred and eleven patients were studied. Median of age was 48 months with a sex ratio of 0.98. The distribution of cancer in this study was Nephroblastoma (18.9%), Neuroblastoma (17.1%), mesenchymatous tumor (17.1%), bone cancer (10.8%), Burkitt lymphoma (9%), brain tumors (9%), germ cell tumor (7.3%), nasopharyngeal tumor (4.5%), retinoblastoma (4.5%) and hepatoblastoma (1.8%). The most common types of cancer in patients aged under 2 years were: Neuroblastoma (31%), nephroblastoma (7%) and germ cell tumors (13.8%), in patients aged between 2 and 5 years: Neuroblastoma (25%), Nephroblastoma (17.5%) and Rhabdomyosarcoma (RMS) (17.5%), in patients aged between 5 and 10 years: Nephroblastoma (17.9%), RMS, Ewing sarcoma and Burkitt lymphoma 14.3% each, in patient aged more than 10 years: nasopharyngeal carcinoma (28.6%), osteosarcoma (14.3%) and germ cell tumors (14.3%). Cancer was localized, locally advanced or metastatic in respectively 18.9%, 55.9% and 25.2%. In bone tumors, neoadjuvant chemotherapy allowed a conservative surgery with clear margins in 3 cases. Median overall survival (OS) in this study was 22 months and median disease free survival was 11 months. Median OS in non metastatic and metastatic patients was respectively 24 and 19 months. Germ cell tumors had the best OS (42 months).

Conclusions: Pediatric cancer management is still a burden in our country especially in the metastatic disease. Access to

intensive chemotherapy is limited which had negative repercussion on survival rates.

V419 SIOP19-0989 | Nephron Sparing Surgery in the Treatment of Nephroblastomatosis: How Far Is It Safe ?

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Background/Objectives: Purpose: Nephroblastomatosis (NBis) is associated with a high risk of developing Wilms tumor (WT). The option of nephron sparing surgery (NSS) has been debated in the recent literature. This procedure is being used increasingly to preserve kidney tissue and function. However, NSS is feasible only for selected cases. This retrospective study evaluates the role of NSS in improving survival of children with NBis.

Design/Methods: This retrospective, observational and descriptive study includes 13 children presenting with NBis cared for in the unit of pediatric oncology and department of pediatric surgery B in children's hospital of Tunis from 2004 to 2018. Data on clinical, imaging and histological features were collected.

Results: Median age was 18,3 months (ranges 2m-39m). NBis was bilateral in 9 cases. Chemotherapy CT was given in all children. All children were operated on, 8 on both kidneys and 5 on one. Operative procedure consisted on NSS for 13 kidneys and total nephrectomy for 8 kidneys. In these children who had NSS, 4 had bilateral WT, 2 had unilateral WT associated with bilateral NBis, and a suspected mass associated with bilateral NBis was notified in 2 cases. After histological review, all children had NBis and WT was associated in all cases. For these 17 WT, 1 was low risk tumor, 14 were intermediate and 2 were high. With a median follow-up of 33,2 months, 11 children are alive with no recurrence and a normal renal function. In one case, relapse was notified after NSS and the child had secondary total nephrectomy. He is alive and still has a normal renal function. One child had progressive tumor and died. He had otherwise WT associated with NBis on a horseshoe kidney. One child died after recurrence.

Conclusions: In children with WT, NSS seems not to impair the outcome and has advantage on renal function over total nephrectomy

V420 SIOP19-0371 | Management and Outcome of Stage IV Nephroblastoma in Children: A Report from the International Society of Pediatric Oncology (SIOP) 2001 Trial in France

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Background/Objectives: Wilms tumor (WT) is the most common renal tumor in children. About 15% of the patients present with stage IV disease at diagnosis. We analyzed epidemiology, management and outcome of children with stage IV nephroblastoma treated in France according to the SIOP 2001 recommendations.

Design/Methods: The SIOP 2001 study is an international, multicenter study for children with renal tumors aged between 6 months and 18 years. Records of patients identified in France with stage IV WT were retrospectively reviewed from the national SIOP database. Patients were treated with 6 weeks preoperative chemotherapy including Vincristine, Actinomycin and Doxorubicin (VAD). Patients in complete remission (CR) remained on 3-drugs VAD. Patients with remaining metastases had 4-drugs chemotherapy (Cyclophosphamide/Doxorubicin and VP16/Carboplatin) with radiotherapy to the persisting and/or high-risk metastases. We analyzed epidemiological data, histological characteristics, pre- and postoperative chemotherapy, surgery of metastases, modalities of radiotherapy if required, response to treatment, event-free and overall survival.

Results: Between 2001 and 2016, 123 patients were treated in France for metastatic WT. The sex ratio was 0,8 (54M/67F). Median age at diagnosis was 55,7 months (4,6 years). Metastases were predominantly (92%) located in the lungs: lung only in 67% and lung and liver in 12%. Local stage distribution was 17/22/61% respectively for stages I/II/III. Histological risk distribution was 6/80/14% respectively for low/intermediate/high risk. After pre-operative chemotherapy, 39% of the patients remained with inoperable metastasis. Fifty-three percent of the patients received flank or abdominal radiotherapy. Sixteen percent received lung radiotherapy. Twenty-one patients (17%) relapsed, 90% of them in the lungs. With a median follow-up of 61 months, 73% of the patients were event-free and 85% were alive.

Conclusions: A minority of patients needed lung radiotherapy. These results are concordant with the analysis of the international cohort.

V421 SIOP19-1536 | Impact of Central Pathology Review in France for the Treatment of Children with Kidney Tumour Included in the SIOP2001 Trial

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Background/Objectives: The main objective of the International Society of Paediatric Oncology (SIOP) Renal Tumour Study Group (RTSG) is to increase survival and reduce treatment toxicity in children with kidney tumours. A standardized diagnostic procedure and risk stratification are mandatory to adjust treatment recommendations for kidney tumours. Central pathology review (CPR), introduced in France in 2002, was established to monitor and give appropriate feedback to local pathologists. In order to analyse the impact of CPR in France for patients included in SIOP2001, we compared diagnoses, histological risk groups and local stage data from local, national and international pathologists' panels.

Design/Methods: We reviewed pathological data of patients from 33 SFCE centers submitted for CPR from May 2002 to December 2015 during the SIOP 2001 study. Pathological data from local, national and international review SIOP/RTSG Pathology Panel were compared focusing on histological risk group and local stage.

Results: 1690 children with kidney tumour were submitted for CPR. Among them, 1265 were included in the SIOP2001 study, whereas 425 (25%) were not included (benign or low risk cystic tumours, non-WT, and adult WT). No significant differences were seen between local and national

pathologists in 81% of cases, whereas clinically relevant discrepancies related to stage and risk group were observed in 11% and 4%. No significant differences were observed between national and international panel in 96%, whereas discrepancies related to local stage were observed in 4%.

Conclusions: The main discrepancy, related to the local stage assessment, confirms that CPR is mandatory to assign the proper risk group and local stage of kidney tumours in order to identify children requiring less or more intensive treatment and to prevent toxicity and relapses. However, in the future, the use of more parameters in the setting of UMBRELLA protocol, including absolute chemoresistant blastemal volume and biomarkers, might help to more better stratify patients.

V422 SIOP19-1009 | Aniridia in a Large Paediatric Cohort - The Sickkids Experience

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Background/Objectives: Aniridia, congenital absence of the iris (complete or partial), may occur in isolation or as part of anterior segment dysgenesis disorders, with varying phenotypes and genotypes. *PAX6* pathogenic variants in the absence of a contiguous deletion involving the neighbouring *WT1* gene are reassuring in patients with aniridia as it is believed to negate the need for Wilms tumor (WT) surveillance, often found in the context of 11p deletion syndrome. Clinical descriptions of paediatric patients with aniridia are limited.

Design/Methods: This retrospective review describes clinical and genetic findings in paediatric patients (age <18 years) with aniridia at The Hospital for Sick Children (SickKids), Toronto (1993-2018).

Results: Aniridia occurred in 78 patients (44 male, 34 female). Sixty-seven patients had genetic testing performed (clinical, n=60; research, n=7). 40/67 had genetic findings: *PAX6* pathogenic variant (n=27, including 1 child with co-existing Klinefelter syndrome), *PAX6*-related disorder (n=2), 11p deletion syndrome (n=8), *CHD7* mutation (n=1), complex chromosomal arrangement (n=1), balanced chromosomal inversion (n=1). Four additional patients had a known *PAX6* familial mutation.

Eight patients had 11p deletion syndrome, of whom four required surgery for renal lesions. Three patients had a confirmed WT. 3/8 patients developed proteinuria and hypertension by early adulthood, 2 of whom had prior unilateral/bilateral surgical intervention for WT. As anticipated,

several patients had additional anomalies associated with this syndrome.

20/33 patients with *PAX6*-related disorders / *PAX6* variants had documentation of renal imaging. Seventeen had a normal renal ultrasound. Three had renal findings: nephromegaly (n=1), duplex collecting system (n=1), ectopic pelvic cystic dysplastic kidney (n=1), 1 of whom had additional anomalies possibly unrelated to this mutation.

Conclusions: This case series reports renal findings in several patients with *PAX6*-related disorders without apparent *WT1* involvement. We recommend performing a baseline renal ultrasound on all patients with aniridia and consideration of comprehensive sequencing technologies in future cohorts.

V423 SIOP19-0890 | Chemotherapy in Preserving Renal Units and Preventing Wilms Tumor Development in Children with DHPLN. A Report from the Children's Oncology Group Study AREN0534

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Background/Objectives: Diffuse hyperplastic perilobar nephroblastomatosis (DHPLN) represents a distinct clinical phenotype of diffuse nephrogenic rests throughout the kidney parenchyma. Wilms Tumors (WT) develops in 100% of untreated patients and between 32-52% of those treated. Treatment has ranged from observation to multiple regimens of chemotherapy. Renal preservation rates have not been reported. An aim of Children's Oncology Group (COG) study AREN0534 was to prospectively evaluate the efficacy of chemotherapy in preserving renal units and preventing WT development in DHPLN.

Design/Methods: Patients were enrolled through COG protocol AREN03B2 with central radiological review. DHPLN was defined as the cortical surface being composed of hyperplastic rests, with the nephrogenic zone involved with a rind capping all of one or both kidneys. Treatment was with vincristine and dactinomycin (EE4A) with imaging at weeks 6 and 12. If stable or decreasing disease, treatment was

continued for 19 weeks. Renal preservation, WT development rates and demographics are reported.

Results: Nine patients enrolled; 5 females and 4 males. Median age at diagnosis was 13.26 (2.9-22.0) months. 8/9 started chemotherapy without biopsy. One had an upfront partial nephrectomy and was found to have WT within the DHPLN specimen. All patients remained alive with the median follow-up of 3 (1.9-6.1) years. No patient is anephric; 16 of 18 kidneys are functioning (89%). Three patients had no surgery while on treatment, two had nephrectomies, 3 partial nephrectomies and one had enucleation. One had WT at diagnosis, of the remaining 8, three never developed WT while 2 developed WT on therapy; 3 developed WT off therapy (at 6, 12 and 60 months). All had FHWT with one patient on a second relapse having focal anaplasia

Conclusions: Regimen EE4A is associated with successful preservation of renal units and excellent OS, although the majority of DHPLN patients developed WT. The ideal type and duration of chemotherapy to prevent WT remains elusive.

V424 SIOP19-0462 | Management of Wilms Tumor Associated with Malignant Inferior Vena Cava Thrombus; Single-Center Experience

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Background/Objectives: Around 4-10% of Wilms tumor (WT) can be associated with an inferior vena cava (IVC) thrombus.

Design/Methods: Data were retrospectively reviewed for 51 pediatric patients with WT associated with IVC thrombus treated at Children Cancer Hospital Egypt-57357 between July 2007 and December 2016.

Results: Median age was 4.4 years and 23 cases (45%) were males. Forty-seven cases (92.2%) had favorable histology WT. Four patients (7.8%) had bilateral WT and 25 patients (49%) were stage IV. Initial thrombus level was determined radiologically as infra-hepatic, retro-hepatic, supra-hepatic and intra-cardiac in 33, 9, 6 and 3 patients respectively. All

except one patient started neoadjuvant chemotherapy (CTH) and no thrombus progression was observed after 6 weeks of CTH with complete thrombus resolution seen in 33.3% of cases. The mean cranio-caudal diameter (CCD) of IVC thrombi was 6.5 cm at initial presentation, and 3.6 cm after 6 weeks of CTH. One patient had stationary intra-cardiac thrombus after neoadjuvant CTH, while remaining patients had partial thrombus regression and underwent en-bloc thrombectomy during nephrectomy. None of the included patients suffered from major surgical complications. There was no significant correlation between viability of malignant thrombi and their initial anatomical level (P value = 1.0) nor their level after neoadjuvant CTH (P value = 1.0) nor the percentage change in CCD of thrombi (P value = 0.319). The 5-year OS and EFS were 75.9% and 71.1%, respectively. Neither OS nor EFS correlated significantly with initial anatomical levels of IVC thrombi.

Conclusions: patients with WT and IVC tumor thrombus can be successfully managed by neoadjuvant chemotherapy followed by surgery and radiotherapy. Radical nephrectomy with en-bloc thrombectomy after initial tumor and thrombus regression seems a successful approach for local control in this group of patients. Measuring the cranio-caudal dimension of thrombus and its response to treatment can help in the surgical plan.

V425 SIOP19-0070 | Bilateral Synchronous Wilm's Tumor Sixteen Years Single Tunisian Center Experience Following SIOP Strategy

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Background/Objectives: **Background:** Wilm's tumor is the most common pediatric renal malignancy. Synchronous bilateral occurrence accounts for 5-7%. The treatment is challenging based on chemotherapy and nephron sparing surgery.

Objective: Analyze clinical and pathological features and evaluate the outcome of patients with synchronous bilateral Wilm's tumor (SBWT) diagnosed and treated in our unit.

Design/Methods: This retrospective study reports the care of 14 patients diagnosed with SBWT between September 2002 and September 2018 and treated according to SIOP 2001 recommendations. We reviewed clinical findings, treatment and outcome data.

Results: The sex ratio was 1,8. The average age was 20 months. The most common disclosure mode was the discovery of an abdominal mass (8 cases). The extension assessment showed pulmonary metastases in 2 cases and liver metastases in 1 case. All patients had pre resection chemotherapy based essentially on Vincristine and Actinomycine. The surgery consisted on complete unilateral nephrectomy in 3 cases,

complete unilateral nephrectomy associated with contralateral partial nephrectomies in 10 cases and bilateral tumorectomies in 1 case. The surgery was complicated by acute renal failure in one case. The histo-prognostic classification concluded to 4 high-risk nephroblastomas and 15 intermediate-risk nephroblastomas. We recorded 4 stage I, 5 stage II and 2 stage III. Nephroblastomatosis was noted in 9 cases. Adjuvant chemotherapy was given in all cases according to the local stage and histological prognostic factors. A postoperative radiotherapy was performed in one case. 12 patients are in complete remission with normal renal function, 2 carriers of Metastatic disease died by tumor progression.

Conclusions: SBWT impose 2 conflicting issues: achieving a high cure rate while maintaining an adequate renal function. Prolonged preoperative chemotherapy followed by conservative surgery can achieve these goals in an important proportion of patients. The prognosis is conditioned by an early diagnosis and multidisciplinary management.

V426 SIOP19-0975 | Pediatric Renal Masses: Wilms' Tumors But What Else

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Background/Objectives: Renal tumors other than Wilms' tumors are rare in childhood. Non Wilms' tumors account for less than 1% of childhood cancers. The diagnosis is mainly assessed by history, clinical presentation, laboratory findings, imaging and pathological examination. The objective of this study is to distinguish differences between non-Wilms tumors.

Design/Methods: A retrospective study was conducted in the oncologic unit of the Children's Hospital of Tunis concerning the cases of non-Wilms' tumors during the last decade.

Results: We collected 19 cases of renal masses (12 boys and 7 girls): 5 clear cell sarcoma of the kidney (CCSK), 3 rhabdoid tumors (RT), 3 clear cell renal cell carcinoma (RCC) including a case related to XP11.2 translocation, 1 papillary carcinoma, 5 intrarenal neuroblastoma and 2 pseudotumors (focal pyelonephritis). The average age was 42.7 months (range: 0-13 years). The main disclosures were abdominal mass (6) and macroscopic haematuria (5). Hypercalcaemia had been noted in 2 cases. In imaging, the tumor was well limited in 17/19 cases with an average size of 81 mm*76 mm*70 mm. Calcifications were noted in 10/19 cases (4 neuroblastoma /5). Necrosis was found in 10/19 (3/5 neuroblastoma, 3/4 ccsk). Vessel displacing was described in 7/19 cases (4/5 neuroblastoma) and vascular thrombosis was reported in 3/19 cases (3 neuroblastoma). Extension assessment had shown metastases in 3 cases (2 RT, 1 CCSK). A needle biopsy was realized in 10 cases. 4 patients had a primary surgery considering the age. 12 patients had been treated primarily as Wilms' tumor. An

unilateral radical nephrectomy was performed in 17 children. 12/17 patients with malignant tumors are currently in complete remission. Death occurred in 5 cases (2 RT, 2 CCSK, 1 N-MYC amplified neuroblastoma). 1 patient is still treated.

Conclusions: Needle biopsy of renal masses is recommended in case of atypical clinical, radiological features or non response to neo-adjuvant chemotherapy.

V427 SIOP19-1037 | Chemotherapy and Nephroblastomatosis a Call Alert for Oncologists and Surgeons

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Background/Objectives: Nephroblastomatosis (NBM) being premalignant is actively treated to decrease the risk of Wilms tumor (WT).

Design/Methods: We conducted retrospective record search for children with NBM treated between January 2005 and December 2018. Demographic, radiologic, treatment modalities and pathology were reviewed. Management was multi disciplinary. Dactinomycin (0.045 mg/kg) and vincristine (1.5 mg/m²) were given monthly for 12 months or till resolution or surgery. Data analyzed for NBM evolution, development of Wilms, indications and types of surgery.

Results: Eleven children, predominantly females (8) were identified. Median age 17.5 months (range 8m-15y).

Bilateral perilobar NBM was the most common type (N 8).

Six had other problems; congenital pelviureteric junction stenosis (PUJ) (N 3), hemihypertrophy (N 2) and hypertension (N 1).

WT was documented in 4 children at presentation, 3 of whom had bilateral NBM, including one child with bilateral WT.

WT was treated for stage according to SIOP-2001 protocol. NBM regressed, all remain alive and tumor free.

NBM in the remaining 7 was treated with 2-drug regimen: lesions regressed in 3 while 4 developed multi focal WT in one kidney 12-24 months post start of therapy while NBM regressed in the other kidney.

In children with WT (N 8), stage I prevailed without anaplastic histology.

Kidney relapse occurred in 2: one suffered multiple relapses during therapy with disease progression, spontaneous tumor rupture and death.

Nephrectomy was performed in 5 with different combinations of PUJ, NBM, WT while nephron sparing surgery (NSS) was more common and successful for Wilms in bilateral NBM.

With median follow up of 32 months 10 children remain alive and tumor free.

Conclusions: The development of WT while on the recommended chemotherapy protocol for NBM or shortly afterwards in our cohort calls for more effective approach to prevent the development of WT.

With sufficient parenchyma, NSS is an effective modality for local control.

V428 SIOP19-0492 | Long-Term Outcomes of Bilateral Wilms Tumour

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Background/Objectives: Bilateral Wilms tumour (BWT) is rare, accounting for only 4-7% of all Wilms tumours. The treatment is challenging with the attempt to achieve a high cure rate with minimal long-term complications. The aim of this study was to evaluate the OS and late-effects of children with BWT treated in Finland during 1986-2006.

Design/Methods: A total of 20 patients with BWT were identified. The mean age at diagnosis was 1.8 years (0.25 – 4.57 years). Four patients (20%) had underlying abnormalities (hemihypertrophy, Denys-Drash syndrome, chromosome 11 rearrangement), and two were identical twins. 15 (75%) had biopsy and 5 (25%) went to upfront operation. Two (10%) had unfavourable histology. Five patients (25%) had metastatic disease at diagnosis, one patient died before operation. None of the patients had bilateral nephrectomy, 17 (85%) had nephron-sparing surgery and two were only biopsied. Five patients received 10-20 Gy radiotherapy and three received high-dose melphalan and autologous stem cell transplant. 5/19 patients (26%) had recidive.

Results: The mean follow-up time was 13.5 years (0.3 – 26.6 years). One patient had died and 19 were alive (OS 95%). Five patients had a recurrence but all were cured (EFS 70%). Two patients had received renal transplant, one had mild renal insufficiency and two had proteinuria with hypertension. 13/19 had GFR measured at the last follow-up visit (51Cr-EDTA or estimated GFR). Four patients (31%) had GFR <90 ml/min, and 3 patients (23%) had GFR >170 ml/min/1.73m² as an indicator of hyperfiltration. Long-term complications at the last follow-up visit were: Psychiatric diagnosis (16%), delayed puberty (5%), scoliosis (5%), obesity (10%), peripheral neuropathy (5%), and second malignancy (5%). Seven patients (37%) had no long-term complications.

Conclusions: The OS of children with BWT is good, but they need close follow-up for recurrence and late

complications. Kidney-sparing surgery is essential for maintaining renal function.

V429 SIOP19-1542 | Establishing and Conducting a National Renal Tumour Advisory Panel to Aid Decision Making for Patients with Complex Renal Tumours

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Background/Objectives: The bi-monthly UK National Renal Tumour Advisory Panel (NRAP), established in March 2017 provides a forum for discussion of complex cases. The expert multi-disciplinary panel aims to optimise patient management. We present the experience of the panel, from the perspective of the panel and referring clinicians.

Design/Methods: A retrospective review of cases was undertaken. Disciplines represented on the panel included medical and radiation oncology, surgery, radiology, and reference histopathology. Feedback was sought from referring clinicians.

Results: Ninety discussions took place for 80 patients, from 19 UK centres, between June 2017 and February 2019. The average number of cases discussed was 3 (1-5) and meetings lasted between 30 and 75 minutes. The most common reason for referral (27%) was for relapsed tumours, followed by metastatic disease (25%). Other reasons included management of nephroblastomatosis, other histologies, bilateral Wilms, adult Wilms and advice regarding nephron sparing surgery (3 cases), significant caval thrombus and suspected tumour rupture. The majority of discussions required input of all disciplines. The case was presented by the treating team and imaging was reviewed via live link. The case was discussed and advice given, documented and circulated. The panel chair spent around 4 hours per panel meeting. The referring clinicians expressed the positive impact of the discussion at the NRAP meeting and support around their decision making and discussion with families. Some had issues with ability to use webex in their hospitals and could only dial in for discussion without benefit of seeing live imaging review.

Conclusions: The UK National Renal Tumour Advisory Panel, has proved to be a viable and valuable resource for

patient management decision making. The sustainability of this project should be considered, as the time cost to involved individuals is significant and does not form part of their NHS job plans.

V430 SIOP19-0374 | Wilms Tumors and Their Precursors: Radiologic Diagnosis Versus Histopathology

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Background/Objectives: Despite typical imaging features described for Wilms tumors (WT), nephroblastomatosis and nephrogenic rests (NR), the radiologic assessment is not always congruent with the final histology. The aim of this study was to compare the imaging features of renal nodules with their final histology and identify radiological factors that would better differentiate WT from NR.

Design/Methods: Patients with bilateral or multifocal unilateral renal tumors with histologically confirmed NR or nephroblastomatosis were included. A senior radiologist blinded to histology reviewed CT images at diagnosis and after neoadjuvant chemotherapy.

Results: Among 205 nodules identified in 48 patients (mean 4.3 nodules/patient) at diagnosis, 175 were resected after a median of five courses of chemotherapy for the first side and 13 courses for the second side. The radiology/pathology correlation showed 118 (74,6%) nodules adequately classified, 20 (11,3%) false positive for WT (9 patients) and 20 (11,3%) false negative (9 patients). WTs were significantly bigger at diagnosis and preoperative assessment and their size decreased quicker than other tumor types ($p < 0.0001$). WT and NR had a similar homogeneity rate. 5% of nodules thought NR that were finally WT were heterogeneous while 17% of nodules initially diagnosed as WT that were finally NR were homogeneous.

Conclusions: Radiological misdiagnosis occurred in 25% of kidney nodules. The size of nodules at diagnosis and their decrease under neoadjuvant chemotherapy may be an interesting factor to help recognizing WT from NR before surgery. Other criteria like homogeneity did not seem key features and lost value in small lesions.

V431 SIOP19-0158 | The SIOP Africa / PODC - Collaborative Wilms Tumour Project

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Background/Objectives: The Collaborative Wilms Tumour (WT) Africa Project has implemented an adapted WT treatment guideline in seven centres in sub-Saharan Africa as a multi-centre prospective clinical trial since 2014. A retrospective file study as a baseline evaluation done before starting the collaborative project documented end of treatment survival without evidence of disease, death during treatment and abandonment of treatment (incomplete treatment).

Design/Methods: Children below 15 years diagnosed with a unilateral Wilms tumour were included over 4 years between 2014 and 2018. Funding was distributed to all participating centres and used to cover treatment, travel and other associated costs for patients. Patient characteristics, co-morbidities, tumour characteristics and events were documented.

Results: We included 260 patients. Median age was 3.5 years, 57% of patients were girls. History of complaints was more than two months in 51% of patients. Two percent of patients were HIV positive. At diagnosis, 35% of patients had documented metastatic disease, and 42% had a tumour larger than 15 cm on imaging. Five percent of patients had documented neutropenia ($< 0.5 \times 10.9/L$) during treatment. Compared to the baseline evaluation, end of treatment survival without evidence of disease increased from 52% to 70% ($p=0.001$). Abandonment of treatment decreased from 23% to 12% ($p=0.01$). Death during treatment decreased from 21% to 16% (N.S.). Relapse of disease occurred in 20% of patients. Two – year event free survival is 47% with a median follow up of 27 months (range 1-57 months).

Conclusions: This collaboration, using relatively simple and low-cost interventions, led to a significant decrease in treatment abandonment and increase in survival at the end of treatment. Improved supportive care is needed to reduce death during treatment. Nurses will be key to achieving this. Late presentation and lack of radiotherapy contribute to a high relapse rate.

V432 SIOP19-1414 | Wilms' Tumor Revisited

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Background/Objectives: We present outcome analysis of Wilms' tumors for patients treated over last two decades in a resource challenged setting.

Design/Methods: A retrospective study was conducted on 52 pediatric patients with WT managed in one of the two units of the Department between 1998 and 2018. Those who died within hours of admission, or who are still receiving post-operative treatment have been excluded from the study. Data regarding 12 earlier patients was completely lost, so evaluable data was available for only 40 patients.

Results: Forty patients with a median age of 3 years had M:F ratio of 2.3:1. Upfront nephrectomy was performed in 13 patients (1999-2007; group I), while 27 patients received upfront chemotherapy (2008-2018; group II). Group I included 4 (30.8%), 3 (23.1%), 6 (46.1%) patients in stages I, II and III respectively, while Group II included, 7 (25.9%), 10 (37%), 8 (29.6%) and 2 (7.4%) patients in stages I, II, III and V respectively. Intra-operative tumor spillage occurred in 38.5% and 11.1% in Groups I and II respectively. Febrile neutropenia was commonly associated with chemotherapy. Rates of early abandonment for the group I and II were 30.8% and 11.1% respectively. The median follow-ups for those who completed therapy were 5.54 and 4.49 years in group I and II respectively. Four (30.8%) patients in Group I were lost to follow-up, 3 (23.1%) died and 3 (23.1%) had tumor recurrence (all of them were stage III initially). Group II had 2 (7.4%) mortality, and 1 (3.7%) recurrence; 2 (7.4%) patients lost to follow-up. Four-year EFS were 67.1%, 42.3%, 29.1% for stages I, II and III respectively in (group I), while in group II, 4-year EFS were 83.4%, 71.2%, 41.9% and 50% for stages I, II, III and V respectively.

Conclusions: The patients undergoing upfront surgery had higher rates of intra-operative spillage, staging, mortality, tumor recurrence and lower EFS, when compared to those having upfront chemotherapy.

V433 SIOP19-0356 | Agreement Between Clinico-Radiological Signs at Diagnosis and Radio-Histological Analysis After Neoadjuvant Chemotherapy of Suspected Wilms Tumor Rupture: Consequences on Therapeutic Choices

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Background/Objectives: According to SIOP criteria, every patient presenting with preoperative Wilms tumor (WT) rupture must receive abdominal radiotherapy. Neoadjuvant chemotherapy reduces tumor volume and is responsible for the development of peritumoral capsule formation which can mask tumor rupture on histological analysis, while it was clinically or radiologically obvious at diagnosis. Yet, there are no protocol recommendations for this particular presentation.

Objectives: Study the agreement between clinico-radiological signs and histological confirmation after neoadjuvant chemotherapy of suspected WT rupture and describe the therapeutic choices arising in consequence.

Design/Methods: We performed a descriptive retrospective study on a monocentric series of patients with WT between June 1991 and August 2017.

Results: Out of 71 patients, 28 presented with suspected tumor rupture. We observed good agreement between clinical and radiological signs of suspected rupture (κ coefficient: 0.67). However, we assessed poor agreement between these signs and histological conclusions after neoadjuvant chemotherapy (κ coefficient: 0.27). Only 5 patients with clinico-radiological signs were over-treated with radiotherapy while tumor rupture had been refuted after histological review. The notion of abdominal trauma and the presence of intra peritoneal effusion seemed to guide collegial decision to over-treat these patients. No statistical difference in survival between patients with and without suspicion of tumor rupture at diagnosis was observed.

Conclusions: This study highlights the need for recommendations in case of discrepancy between radiological and histological signs of rupture at diagnosis and after neoadjuvant chemotherapy. A study with stronger statistical power is necessary to define criteria which would lead to optimize the treatment in this context.

V434 SIOP19-0611 | Impact and Evolution of Hypertension at Diagnosis in Wilms Tumour Patients- Results of a Retrospective Study

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Background/Objectives: Hypertension associated with renal tumours is mainly related to renin-angiotensin mechanism, but could be multifactorial.

Design/Methods: We retrospectively reviewed case notes of 60 patients with Wilms tumours. Hypertension was defined

as systolic and/or diastolic blood pressure (BP) over 95th centile (adjusted for age, sex, height). Incidence of hypertension, potentially contributing factors, use of medications before, during, and after nephrectomy and impact on relapse free survival (RFS) and overall survival (OS) were studied. Patients were treated as per SIOP WT-2001 protocol.

Results: From January 2009 to December 2014, sixty children (25 males, 35 females), median age 3.8 years (range 1-11 years), were treated. Fifty-five had a unilateral tumour, 5 bilateral; 18/60 had metastatic disease. Tumour volumes calculated from cross-sectional imaging (predominantly CT) ranged from 78 ml to 1,903 ml; mean 671ml. At diagnosis 28 patients (47%) (24/55 unilateral; 4/5 bilateral) were hypertensive. Calcium channel blockers were used in first line management for all hypertensive children. Nine children needed a second agent (beta blockers in 7, angiotensin-converting enzyme inhibitors in 2); BP was well controlled prior to surgery. No patient developed hypertensive crisis during nephrectomy. Following nephrectomy, BP normalised in 22/24 patients with unilateral and 2/4 with bilateral tumours. Tumour volume at diagnosis, stage, risk group had no correlation with hypertension. In this study, all 6 relapses among hypertensive patients occurred within 15 months of diagnosis, whilst 6 relapses among non-hypertensive children occurred by 3 years. There was no impact of hypertension on OS (89%). Renal function at last follow-up was normal in both groups.

Conclusions: There was a higher incidence of hypertension in patients with bilateral disease and, following nephrectomy, they were more likely to need medications. It appears that hypertension is associated with an earlier relapse but has no impact on overall survival or renal function. This needs validation in a larger study.

V435 SIOP19-0181 | International Incidence of Childhood Renal Tumours, 2001-2010, A Population-Based Registry Study- On Behalf of IICC-3 Contributors

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Background/Objectives: Renal tumours represent 5% of childhood cancers. Incidence of Wilms tumour (WT), the most common renal tumour in childhood, was shown to vary internationally and with ethnicity. Using the most up-to-date information, extracted from 308 cancer registries contributing to the International Incidence of Childhood Cancer study (IICC-3), we analysed global variations in incidence of renal

tumours in children (age 0-14 years) and adolescents (age 15-19 years).

Design/Methods: Incidence rates were standardised (ASR) to facilitate international comparisons. The cases were classified by the International Classification of Childhood Cancer and the results were presented by 14 geographical regions. Data for the USA were also presented for five racial or ethnic groups. Change in incidence was assessed using the comparable data published in all three IICC volumes.

Results: There were 15,363 cases of renal tumours diagnosed in children aged 0-14 years during 2001-2010 in the contributing registries; 13,876 (90.3%) were WT. ASR of renal tumours were highest in North America and Europe, (9-10/million); they were lowest in most Asian regions (4-5/million). Among the US ethnic groups the highest ASR was seen in Blacks (10.9/million) and the lowest in the Asian and Pacific Islanders (4.2/million). Age-specific incidence of WT peaked at the age of one to three years in all world regions, except in East Asia where the peak was in infancy. The age-specific incidence of renal carcinoma increased with age to 1.3/million at 17 years. In children, between the 1970s and 2000s the incidence of renal carcinomas doubled from 0.1 to 0.2/million (incidence rate ratio (IRR) 2.0 [1.5-2.6]), while the incidence for WT (including other non-epithelial renal tumours in IICC-3) slightly increased from 6.9 to 7.4/million (IRR 1.1 [1.1-1.2]).

Conclusions: The observed international variations are consistent with the mostly genetic origin of WT. The increasing rates of renal carcinomas merit further studies.

V436 SIOP19-1032 | Clinical Outcomes of Children with Wilms Tumour Treated in a Tertiary Care Hospital in Nigeria

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Background/Objectives: Background/Objectives: Survival from Wilms tumour (WT) in sub-Saharan Africa remains dismal as a result of difficulties for patients in accessing health services. The purpose of this study was to analyse the clinical outcome of children with Wilms tumour managed in our centre over a decade.

Design/Methods: Design/Methods: This study is a retrospective review of patients treated at our paediatric surgical oncologic unit between January 2008 and September 2018 by the International Society of Paediatric Oncology (SIOP) protocol.

Results: Eighteen children were treated for Wilms' tumour with this protocol and 72% were girls. The median age at

presentation was 33 months. The majority 15 (83.3%) presented with an abdominal mass. The tumour stage distribution was 7/18 stage II (38.9%), 6/18 stage III (33%), 3/18 stage IV (16.6%) and 2/18 unknown (11%). Most tumours (88.8%, 16/18) showed a response to chemotherapy but 11% (2/18) showed no remarkable responses. Nephrectomy was done for 17/18 (94.4%) of the patient and 1/18 (5.6%) had only incisional biopsy due to unresectable tumour. Postoperative chemotherapy was given according to the SIOP protocol. There was one peri-operative death in a 20month old child with hepatic vein involvement and neuropathy reaction to vincristine. All others made a good postoperative recovery. Three patients did not complete postoperative chemotherapy, two patients had relapsed of disease within 6-9months. During the study period, seven patients (38.9%) died (5cancer-specific, 1 cytotoxicity, and 1 unknown), four (22.2%) patients were lost to follow-up and seven (38.9%) are free of disease with a median follow-up period of 18months. Overall two-year survival is estimated at 50%.

Conclusions: Conclusions: Outcomes for children with Wilms tumour in sub-Sahara Africa are compromised by abandonment of postoperative chemotherapy and lost to follow up. Sharing similar local challenges in the region may helps to identify and implement feasible, sustainable and successful strategies in improving outcomes.

V437 SIOP19-0433 | Characterization of the Immune/Inflammatory Microenvironment of Wilms Tumor in Children

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Background/Objectives: Wilms tumor (WT), composed of three histological subsets (blastemal, stroma, epithelium), is a good model for studying intratumoral heterogeneity. WT microenvironment is known to be infiltrated by innate and adaptive immune cells, but only few studies have addressed the impact of tissue heterogeneity on immune infiltrate. Here we performed a comprehensive analysis of the inflammatory/immune microenvironment of WT, in each histological component separately.

Design/Methods: Fifty-six FFPE samples representing all the subsets, from 31 patients with WT treated in SIOP2001 protocol in our comprehensive cancer center, were retrospectively collected. Manual microdissection of selected areas for each histological subset was performed. We analyzed the

expression of 2,560 transcripts involved in tumorigenesis or immune responses, by targeted sequencing (HTG EdgeSeq®, “Oncology Biomarkers” panel). We also performed multi-color immunofluorescence stainings to identify immune cell populations and their activation states *in situ*. Finally, fresh tumors and blood from patients with WT were collected to perform phenotypic and functional analyzes of immune cells by multicolor flow cytometry.

Results: Transcriptomic analyzes identified 149 specifically up- or down-regulated genes in blastema, with strong over-expression of MYCN-activated genes and downregulation of IL6/JAK/STAT and IFN- γ pathways, along with a trend to lower inflammatory and immune response signatures. *In situ* analyzes identified 3 profiles of immune infiltrate, depending on the tumors: i) strong innate and adaptive immune infiltrate in peri-tumoral areas, including tertiary lymphoid structures and PDL1 expression on macrophages, that are evocative of inflamed tumors; ii) moderate and sparse infiltrate mainly dominated by macrophages inside tumoral areas; iii) very low immune infiltrate that is reminiscent of non-inflamed tumors.

Conclusions: We identified great heterogeneity in WT microenvironment. Blastemal areas are associated with an immunosuppressive microenvironment. Further analysis of correlation with clinical data will help to determine which patients with WT could benefit from immunotherapy.

V438 SIOP19-0303 | Genes Controlled by DNA Methylation are Involved with Formation of Metastasis in Wilms Tumor

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Background/Objectives: Wilms tumors (WTs) have a relapse rate of ~25%. In preoperative chemotherapy treated cases, blastemal predominant WT have a higher risk of relapse and capacity of forming distant metastasis. The aim of this study was to identify mechanisms involved with metastasis formation in WT.

Design/Methods: DNA and RNA were extracted from FFPE and hybridized in the *Infinium Illumina 450K Beadchip arrays* and sequenced by RNA-Seq, respectively, for seven paired cases of normal renal cortex (NK), primary tumor (WT) and pulmonary metastasis (MET) samples. Both data were explored regarding their involvement with WT metastasis formation.

Results: A linear Bayesian framework model identified 497 differentially methylated positions (DMPs, adjP<0.001) between groups which discriminated NK and WT but MET samples were divided in two clusters: one subgroup with methylation profile similar to NK, and second subgroup with similar profile to WT, with high variance of DNA methylation. WT presented an hypomethylation pattern compared to NK, and MET had an hypermethylated pattern compared to both groups. Comparing WT and NK, there were 92 hypo- and 207 hypermethylated regions in WT (FDR<0.05, DB>10%), and 1.100 up and 1.469 downregulated genes in WT (FDR<0.001 and lfcThreshold=0.1), with eight reporting hypomethylation/over-expression and 36 showing hypermethylation/down-expression patterns. These include IGF2/H19 cluster, the tumor suppressor genes *BRCA1*, *HNF4A*, *LTF* and *TNFRSF10A*, suggesting that DNA methylation could be a mechanism for loss of function in a subset of tumors where mutations are not found. Whilst all DEG discriminated samples based on the tissue of origin (WT, MT or NK), when we applied hierarchical clusterization based on the expression levels of the 53 DEG that also had a DMR in the promoter region, the two group of metastatic samples formed, similar to the the methylation cluster.

Conclusions: We suggest that DNA methylation might be involved in the control of genes related to metastasis formation

V439 SIOP19-0109 | Immune Expression in Children with Wilms Tumor: A Pilot Study

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Background/Objectives: Due to improvements in multi-modality therapy, survival among children with Wilms tumor (WT) now exceeds 90%. However, up to 15% of children with favorable WT and up to 50% of children with anaplastic WT will experience tumor recurrence or progression. Survival for these children is dramatically reduced; only 50% survive to adulthood. In adult renal tumors, immune manipulation has been effective at improving survival. However, little is known regarding the immune microenvironment of WT.

Design/Methods: Between 2016 and 2017, we performed a pilot study wherein children with WT underwent *ex vivo* wedge biopsy following their nephrectomy. Fresh tumor tissue and serum were then enzymatically digested to analyze the tumor infiltrating immune infiltrate using flow cytometry. Immune analysis was conducted using a panel for tumor infiltrating and effector cells. Immunohistochemistry was also performed for CD4, CD8, and PD-L1 expression.

Results: 5 patients (median 3 years, 60% male) were included; 2 with unilateral WT (resected prior to chemotherapy), 2 with bilateral WT (resected after neoadjuvant chemotherapy), and one patient with Denys-Drash syndrome, ESRD, and distant history of WT in the contralateral kidney. Immune analysis showed that WT were infiltrated by immune cells prior to and following chemotherapy (Figure 1). There were elevated levels of NK cells infiltrating the tumor specimens; these were higher compared to levels of NK cells circulating in the blood. T cells, mostly of CD8 origin, were also a major cell type in tumors. These displayed an activated cell phenotype (Figure 2). Unlike the $\alpha\beta$ TCR T cells found in the blood, 33% of tumor-infiltrating T cells were positive for TCR $\gamma\delta$ receptors.

Conclusions: These pilot data suggest an inflammatory tumor microenvironment is present within WT, implying that they may be susceptible to immunotherapy similar to adult renal tumors and other adult malignancies. Follow-up studies are currently underway.

V440 SIOP19-0826 | Outcomes of Malignant Renal Tumors in Children: A 15 Year Single Center Experience

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Background/Objectives: This study was performed to evaluate the characteristics and outcomes of malignant renal tumors in children.

Design/Methods: From January 2001 to December 2015, medical records of sixty patients younger than 19 years who were treated for malignant renal tumors were reviewed retrospectively at Asan Medical Center.

Results: Among 60 patients, forty-nine (81.7%) was diagnosed with WT, four (6.7%) with malignant rhabdoid tumor of kidney (MRTK), three (5.0%) with renal cell carcinoma (RCC), and two (3.3%) with clear cell sarcoma of the kidney (CCSK). The mean age at diagnosis was 41.8 months. Sixty-five percent of WT were under age of 2 years at diagnosis. All the patients with CCSK and MRTK were diagnosed between 0-2 years of age. Two patients with RCC were older than age of 10 years. Stage at diagnosed was as followed: Stage I, 36.7% (n=22); Stage II, 21.7% (n=13); Stage III, 16.7% (n=10); Stage IV, 20.0% (n=12); and Stage V, 5.0% (n=3). The most frequent symptom was palpable mass in 55.0% (n=33), followed by hematuria in 31.7% (n=19), abdominal

pain in 26.7% (n=16), abdominal distension in 21.7% (n=13) and fever in 10.0% (n=6). All the patients except four patients with RCC received chemotherapy. Preoperative chemotherapy was done in 20.0% (n=12). Immediate nephrectomy was done in 80% (n=48) and postoperative chemotherapy were performed in 78.6% (n=44). The 5-year overall survival (OS) and event-free survival (EFS) of malignant renal tumors were 85.6% and 77.7%. Twenty-three percent (n=14) experienced relapse and the 5-year OS of relapsed patients was 49.1%. Nine patients of the relapsed patients were treated with high-dose chemotherapy and autologous stem cell transplantation, and the 5-year OS was 66.7%.

Conclusions: This study shows that favorable survival outcomes can be obtained through a multimodal, multidisciplinary treatment in malignant renal tumors in children. In addition, relapsed patients could be rescued using high-dose chemotherapy.

V441 SIOP19-0645 | Amplification Of 4P16.3 and 2P24.3 Cytobands Unveils Worse Outcome in Patients with Diffuse Anaplastic Wilms Tumor (DAWT)

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Background/Objectives: DAWT is known to have worse outcome than favorable histology Wilms Tumor (FHWT). There is a need to identify molecular markers that define prognosis and explain clinical behavior of this entity.

Design/Methods: The National Cancer Institute's "Therapeutically Applicable Research to Generate Effective Treatments" (TARGET) repository includes a set of 652 patients with WT; including a discovery cohort (N=133) of patients with DAWT (N=42) and relapsed FHWT (N=91). Files including genetic mutations, segmentation file and RNA-seq expression table were downloaded via cBioPortal.org. GISTIC was used to analyze copy number alterations (CNA).

Results: Cytobands that showed significant gain in DAWTs (q-value<0.05) were 1q21.3, 2p24.3, 4p16.3, and 19q13.12; while those that showed significant loss were 14q24.1 and 17p11.2. The most significant CNA was amplification of 4p16.3 which was identified in 11 patients (26%) and was associated with worse 5-year-survival (12%vs.70%, p<0.0001). The second most significantly altered cytoband was 2p24.3 (N=9,21%), which was also associated with worse outcome (33%vs.67%, p=0.0052). Amplification of 4p16.3 and 2p24.3 were identified in 2% and 10% of FHWTs, respectively; and were not associated with significant change in survival. TP53 mutations were identified in 52% of DAWT. This

alteration was neither associated with any specific CNA nor difference in survival ($p=0.87$). Six tumors had both TP53 mutation and 4p16.3/2p24.3 amplification. In patients with 4p16.3 amplification, 4 genes only showed significant differential gene expression: RADX, RAB3C, TAFA4 and HAUS3. Gene ontology and KEGG searches failed to report a common process or pathway linking these genes. Overexpression of these genes was identified in 14% of FHWTs and was not associated with worse outcome.

Conclusions: Amplification of 4p16.3 and 2p24.3 were reported in one-third of DAWTs and were associated with worse outcome. These alterations are independent from TP53 mutations, which are reported in half of DAWTs and not associated with outcome difference. These interesting findings deserve further exploration.

V442 SIOP19-1383 | Clear Cell Sarcomas of the Kidney in Children: Analysis of French Patients Treated According to SIOP2001 Protocol

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Background/Objectives: Clear Cell Sarcoma of the Kidney (CCSK) is the second most common pediatric renal tumor after Wilms' Tumor (WT) with a prevalence of nearly 5%. Treatment and outcome of all patients included in the SIOP 93 and 2001 studies were reported previously (Furtwangler, EJC 2013). Our study aims to describe treatment and outcomes of French CCSK patients treated according to SIOP 2001 protocol and their pathological characteristics.

Design/Methods: Every French patient diagnosed with a CCSK and treated according to SIOP 2001 clinical trial was included in this study.

Patients and treatment characteristics, discrepancy between local pathological analysis and national review, histological modification after pre-operative chemotherapy, BCOR status and survival data were studied.

Results: Fifty-seven CCSK patients were analyzed, representing a 5% of 1122 renal tumors in this period. Median

follow-up was 80 months. Median age at diagnosis was 21 months (5-132). 63% were male. 49% were left-sided and 51% right-sided. Local stage distribution for stage I, II, III was 12%, 37% and 50% respectively. Twelve percent were metastatic at diagnosis. Pre-operative chemotherapy was administered to 93% patients. All patients underwent total nephrectomy. All patients but 3 received post-operative 4 drugs: doxorubicine/cyclophosphamide or ifosfamide alternating with etoposide/carboplatin and 78% had radiotherapy. Relapse occurred in 25% of patients. 5years OS and EFS were respectively 87% and 74%. Genotype information was available for 17 patients: thirteen had BCOR internal tandem duplication, 3 were not applicable and one had wild type BCOR genotype. Others samples are going on.

Conclusions: This is the first report of a French cohort of children with CCSK. The outcome of these patients is comparable with previously reported results. This series of alterations in BCOR status is noteworthy.

V443 SIOP19-0863 | The Efficacy and Safety of Defibrotide Treatment in Three Cases with Venous Occlusive Disease due to Actinomycin-D

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Background/Objectives: Venous occlusive disease (VOD) is a potentially life-threatening complication of Actinomycin-D, highly mortal so should be remembered in differential dx of the patients receiving chemotherapy w/wo stem cell transplantation. The clinical signs are hepatomegaly, sudden weight gain w/wo ascites and jaundice.

Design/Methods: Three patients: 9-year-old male, 3-year-old male, 1-year-old male) were admitted with the complaint of abdominal mass and nasal congestion with difficulty in breathing. USG and CT of the abdomen identified solid mass in the right kidney of the 2 patients. Right radical nephroureterectomy was performed, histology revealed Wilms tumor and chemotherapy protocol was started. Third patient w diagnosis of rhabdomyosarcoma on MRI, was put on chemotherapy. Common symptoms were abdominal distension and clinical condition of three patients progressively had worsened after Actinomycin-D therapy. The patients gained weight and the abdominal USG confirmed enlargement of liver and spleen with ascites. Doppler USG revealed reverse hepatic and portal venous flows. Blood tests showed severe thrombocytopenia, very high levels of hepatic enzymes and bilirubin. The coagulation parameters were also abnormal. Defibrotide treatment was started with a dose of 40mg/kg/day in 4 divided doses

Results: The clinical situation and laboratory tests of the patients improved rapidly after defibrotide. Hepatic and portal venous flows were also recorded normal one week after defibrotide treatment, which was continued for 14 days in all of the patients. These patients completed the chemotherapy protocol without any problem and we removed Actinomycin-D from the treatment.

Conclusions: It is a difficult condition for both the patient and the physician because of the fact that the VOD causes morbidity and high mortality. Supportive treatment is a standard approach in these patients. The diagnosis of VOD requires high clinical attention. It seems that Defibrotide, an antithrombotic, anti-ischemic, anti-inflammatory, and thrombolytic single-stranded polydeoxyribonucleotide with fibrinolytic properties, is a safe, well tolerated, and efficacious therapy in VOD.

V444 SIOP19-0427 | Biomarker Candidates of Outcome in Children with Stage IV Nephroblastoma in the SIOP 2001 Study

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Background/Objectives: Determine the prevalence of biomarkers in tumour samples of children with metastatic Wilms tumor (MWT) treated according to the SIOP 2001 protocol and identify their prognostic value.

Design/Methods: Patients were treated with 6w preoperative vincristine, dactinomycin and doxorubicin, followed by nephrectomy and risk-adapted chemotherapy ± local/metastatic RT. Multiplex ligation-dependent probe amplification (MLPA) was used on tumour samples from 7 countries to measure copy number gain or loss of chromosome 1q, 1p, 16q and TP53, WT1, WTX, MYCN and FBXW7. Kaplan-Meier analysis was performed for each biomarker with log rank testing.

Results: Samples of 62/645 (10%) patients with MWT were analysed. Local stage distribution in this cohort was 21/24/42% (13% missing) for stage I/II/III, respectively, with 82% intermediate risk (IR) and 18% high risk (HR) histology (9x diffuse anaplasia (DA) and 2x blastemal type). After a median FU of 73 months 63% of the patients were event-free and 74% alive; 5y-EFS of 74 and 9% for IR and HR, resp ($p < 0.001$). Gain of 1q was observed in 35% of samples (33% of IR; 45% of HR) and was associated with a significantly poorer 5-EFS as compared to no gain (43 vs. 72%, $p = 0.02$), but no significant difference in OS (61 vs. 80%, $p = 0.14$). Loss of 1p/16q/both was observed in 8/16/2% without any significant influence on outcome. Loss of TP53 was observed in 9 patients (15%) and associated with a significant worse 5y-EFS (13 vs. 70%, $p < 0.0001$) and OS (13 vs. 83%, $p < 0.0001$). Seven out of nine samples with TP53 loss had DA. No conclusions could be drawn on loss of WT1, WTX or FBXW7 or gain of MYCN.

Conclusions: Patients with MWT and 1q gain and/or TP53 loss are at high risk of treatment failure with the SIOP 2001 therapeutic strategy. Screening of larger cohorts is needed for clinical evaluation.

V445 SIOP19-1310 | Wilms Tumor Spheroids are a Powerful in Vitro Model for High-Risk Blastemal Wilms Tumor

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Background/Objectives: In vitro models represent a critical tool in cancer research to study tumor biology and to evaluate new treatment options. Unfortunately, there are no effective preclinical models available that represent Wilms tumor (WT) – the most common pediatric renal tumor. Especially high-risk blastemal WT is not represented by the few primary cell lines established until now.

Design/Methods: We describe a new 3D approach for in vitro cultivation of blastemal WT cells. Primary cultures were started from viable tumor material and grown in suspension as cell aggregates (spheroids). Spheroid histology was analyzed by immunohistochemistry in comparison to corresponding tumor sections. WT 3D cultures were further characterized by RNAseq and used for genetic manipulation and to establish mouse xenografts.

Results: WT spheroids could be initiated from different primary tumors and propagated long-term as floating 3D cultures. The spheroids retained the histology of the original tumor and expressed marker genes characteristic of early renal development and blastemal WT elements. Beside blastemal cultures, we could generate spheroids representing epithelial and stromal WT. Primary 3D cultures were amenable to genetic manipulation and they formed xenograft tumors in immune compromised mice that again reflect the primary human tumor.

Conclusions: With this new 3D culture method, we were able to establish long-term blastemal spheroid cultures that represent an in vitro model for this high-risk Wilms tumor subtype.

V446 SIOP19-1111 | Results of Pediatric Renal Tumours Treatment According to Siop Strategy in a Specialized Regional Centre

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Background/Objectives: Renal tumours are common in childhood and account for 6% of all. The objectives of the study were to review the clinical presentation and management of children with renal tumor and the the survival outcomes in Western Ukraine region.

Design/Methods: Analysis included retrospective chart review of 51 children with renal tumors treated and observed at our institution from 2006 to 2018. Diagnosis was confirmed by conventional CT, MRI and sonography and histologically. The strategy of treatment recommended by SIOP was performed.

Results: The neoadjuvant chemotherapy was used as a standard in all cases. No upfront surgeries were performed. Biopsy was done in 5 cases with unusual presentation. Large cohort of patients presented with large primary tumor or metastases: 19 cases (37.2%) were diagnosed as stage III, 11 cases (21.6%) as stage IV, 6 patients (11.8%) as stage I and stage II in 10 children (19.6%). 4-6 weeks of vincristin-dactinomycin regimen was used with response observed in 90.2% of patients. Five cases with bilateral renal tumours (stage V) were observed. 46 patients undergone nephrectomy and 5 children had nephron-sparing surgery.

Unfavourable histological type (including clear cell sarcoma and rhabdoid tumour) was revealed in 17.4%. Adjuvant high risk chemotherapy (CP-Doxo-Carbo-Eto) and use of radiotherapy was performed in 43.5% of children. Intermediate risk chemotherapy (Doxo-ActD-Vcr) was used in 35% of children. Vincristin-dactinomycin regimen was used in 11.7% of patients. The 3-year overall survival (OS) and event free

survival (EFS) rates were 87% and 83%, respectively. The 3-year overall survival (OS) in stage 4 patients was 58%. The 3-year overall survival in children with bilateral disease was 100%.

Conclusions: Primary tumour stage was the most significant factor that influenced the survival. The SIOP strategy with neoadjuvant chemotherapy is effective in the developing country with large amount of advanced stage tumours at diagnosis.

Solid Non Brain Tumours - Retinoblastoma

V447 SIOP19-1220 | Outcome of Unilateral Retinoblastoma: A 10-Year Experience at Children Cancer Hospital in Egypt (CCHE)

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Background/Objectives: A majority of children with retinoblastoma (60%) have a disease in one eye only (unilateral disease). This is a retrospective study to evaluate two different treatment modalities in those patients for saving their lives and vision.

Design/Methods: Four hundred and four patients were diagnosed with unilateral intraocular retinoblastoma at Children Cancer Hospital in Egypt (CCHE) through the period of July/2007 until December/2017. Management strategies included primary enucleation versus ocular salvage treatment.

Results: Patients presented with mean age 24.5 months with range (1.2–154.3 months). According to the international retinoblastoma classification, Group D (n=172, 42%) was the most common, followed by group E (n=142, 35%), group C (n=63, 16%), and group B (n=27, 7%). All patients were alive at the end of follow-up time except four died, with 5-year overall survival 98.3% [CI, (96.5-100%)]. Patients presented with advanced disease and poor visual prognosis (n=241, 59.6%) were undergone primary enucleation with 6 cycles adjuvant chemotherapy if high-risk features were present in the enucleated eye; only four patients out of 241 ended-up either with extraocular metastasis (n=3) or death (n=1). While systemic chemotherapy and focal therapy were the primary treatment for those presented with favorable disease status and good visual prognosis (n=163, 40.4%); seventy-seven patients of them ended up with a pre-defined event (enucleation, EBRT,

off protocol chemotherapy or 2ry malignancy). Ocular survival for patients received primary chemotherapy+focal therapy was [50.9% (CI, 43.5–59.6%)] at 3 years and [46.9% (CI, 39.3–56%)] at 5 years. Comparison between upfront enucleation and primary chemotherapy for the occurrence of extraocular metastasis revealed that is no statistical difference between them except in group D. While for the occurrence of death, no statistical difference in all classification groups.

Conclusions: Primary chemotherapy has a good probability for ocular salvage without increasing the risk of metastasis in comparison with upfront enucleation except in group D.

V448 SIOP19-1584 | Clinical Outcomes in Patients with 13Q Deletion Syndrome and Retinoblastoma: A Single-Centre Experience

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Background/Objectives: Patients with 13q deletion syndrome (a rare genetic disease caused by deletion of some or all of the long arm of chromosome 13) are at risk of developing retinoblastoma (RB) and other clinical features. Limited literature exists regarding chemotherapy toxicity, late effects of treatment and long term outcomes.

Design/Methods: We performed a retrospective case-series review of patients with proven 13q deletion syndrome (n = 22) who underwent treatment for RB at a National Retinoblastoma Referral Centre between 1992 - 2017.

Results: Twenty two patients with 13q deletion syndrome were identified over a 25 year period. Median age at diagnosis was 7 months; 50% of patients presented with leukocoria (median duration of symptoms prior to diagnosis was 8 weeks) and the RB was bilateral in 14 (64%) patients. Ten (45.5%) patients underwent systemic chemotherapy; substantial toxicity was observed in this cohort: 5 (50%) had recurrent infection-related admissions; 4 (40%) had repeated episodes of delayed count recovery and 2 (20%) had vincristine toxicity. Chemotherapy was postponed or dose-adjusted in 4 (40%) and stopped prematurely due to toxicity in 2 (20%). Hearing loss occurred in 6 (27%) patients, 3 (50%) of these patients developed hearing loss in the absence of systemic chemotherapy. At follow up 95% were alive, 90% of patients demonstrated poor growth, 89% global developmental impairment and 59% had ongoing medical/ educational needs. Vision was assessed using age-appropriate testing; 14 (70%) patients had average or above average vision at follow up.

Conclusions: Patients with RB and 13q deletion syndrome are at higher than expected risk of chemotherapy-related toxicity. This knowledge will assist clinicians when planning

treatment: newer, local chemotherapy options may be preferable. Correlation between clinical features and genetics may help predict toxicity more precisely and guide management further.

V449 SIOP19-1528 | Investigating the Aqueous Humor in a Next-Generation Sequencing Panel for Pediatric Malignancies

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Background/Objectives: Recent studies demonstrated that the AH (Aqueous humor) of eyes with retinoblastoma is an important source of tumor-derived DNA to perform genetic analysis and has been purposed as a surrogate tumor biopsy for retinoblastoma. Somatic next-generation sequencing (NGS) panels are designed for adult cancers and therefore are not optimized or do not cover the common genetic alterations found in pediatric tumors. This study aimed to investigate *RB1* (RB transcriptional corepressor 1) gene sequencing and to identify recurrent somatic copy number variations (CNVs), using a next-generation sequencing panel for pediatric malignancies.

Design/Methods: This study included three AH and three retinoblastoma tumors from three patients, after primary enucleation. DNA and RNA were isolated from the 100µl of HA and the matched tumors. After cDNA synthesis, the molecular test was performed using combined DNA and cDNA samples in an OncoPrint™ Childhood Cancer Research Assay panel (OCCRA-ThermoFisher Scientific). The library prep, templating, and chip loading were automated in Ion Chef System and the sequencing data analysis using Ion Torrent S5 (ThermoFisher Scientific).

Results: All the AH samples demonstrated measurable concentrations of DNA and RNA. The CNVs and SNVs between AH and matched tumors showed compatible pattern profiles. Test results obtained with AH identified four exonic SNVs (single nucleotide variants) c.160G>T, c.1072C>T, c.1333C>T, c.1735C>T and one indel c1341_1342insA in *RB1*. In two cases were observed CNVs in *ABL2* (ABL proto-oncogene 2, non-receptor tyrosine kinase) gene.

Conclusions: The results confirmed the molecular potential of HA in retinoblastoma. CNVs in *ABL2* gene has been found in primary solid or blood tumors and are associated to drug efficacy and toxicity. The use of OCCRA assay demonstrated been efficient tool to screening of *RB1* gene and in the identification of recurrent CNVs related to important clinical parameters of retinoblastoma.

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V450 SIOP19-0941 | Challenging in Treating Retinoblastoma in a Developing Country

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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. The purpose of this study was to analyze outcome of RB in a Tunisian pediatric oncologic unit.

Design/Methods: A retrospective review of 79 patients with RB enrolled between January 2006 and December 2018 was done. Data regarding age, sex, stage, laterality, treatment course and outcome were collected. For enucleated eyes, post-operative therapy was decided according to histopathologic exam. For non-enucleated eyes, local treatment was decided after multidisciplinary concertation.

Results: The median age was 18.8 months (range 4-72), the male female ratio was 1.63. There was CNS involvement in 4 cases. 22 patients have bilateral RB (27.8%) while 57 have unilateral RB (72.2%). Unilateral enucleation was performed for the majority of children (93.7%) and 5 children were enucleated both eyes. Neoadjuvant chemotherapy was given in 62% of cases. Conservative treatment was performed for 13 children: thermotherapy (11), laser (2) and intravitreal melphalan (2). Adjuvant chemotherapy was given in 81% of cases. Conformal orbital radiotherapy was performed in 11 children. We analyzed DNA from tumor tissue and from peripheral blood to determine the RB1 mutation status in 37 cases. A multi-step mutation scanning protocol identified bi-allelic inactivation of RB1 gene in 30/37 (81%) of tested samples. We identified 50 somatic RB1 alterations and 7 novel mutations. With a median follow up of 29.2 months (range 1-78), the 5-year Overall survival (OS) was 89.9%. The most significant prognostic factors were the presence of metastasis ($p=10^{-2}$) and the pathologic staging of the tumor ($p<10^{-4}$).

Conclusions: Management of RB needs efficient multidisciplinary team and long term collaborative programs to improve survival. This study provides evidence for the efficacy of systemic chemotherapy and conservative treatment for the management of RB.

V451 SIOP19-0289 | Management Of Unilateral Intraocular Retinoblastoma In Subsaharan Africa: Mali Experience

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Background/Objectives: Retinoblastoma (RB) is the most common malignant intraocular tumor in children and the unilateral form represents 70% of cases. Enucleation at early stage of disease may improve the survival rate in developing countries.

Design/Methods: It was a prospective study from 01/11/2011 to 31/12/2015, aimed to evaluate treatment result of intraocular RB, rehabilitation of orbits after enucleation and survival rates (OS and EFS) in all patients. Were included Intraocular unilateral RB without signs of clinical and radiological extraocular extension. At admission all patients received ophthalmological and oncological assessment. The Tumors were classified according to the IIRC classification. Patients were treated according to the guidelines of the French-African pediatric oncology (GFAOP-RB1).

Results: Fifty patients were included. The median age was 30 months. The sex ratio was 0.6. The majority of patients were Malians (84%). The first symptoms were leucocoria (88%) and strabismus (12%). According to the IIRC classification, group E patients represented 64%, group D (28%) and group B (8%). The enucleation rate was 84%. Twelve percent of patients received primary enucleation. Thirty-five patients (70%) received neoadjuvant chemotherapy. We recorded 38% hematological toxicity and 4% toxic death. The remission rate was 78%, with median follow up of 2.3 years.

Conclusions: Intraocular RB remains a diagnostic challenge for the physicians in sub-Saharan Africa. The enucleation decision must not be delayed because the conservative treatment is inaccessible.

V452 SIOP19-0188 | Reasons for Missed Chemotherapy Appointments in Retinoblastoma Patients at a Tertiary Centre in India

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Background/Objectives: Delays in chemotherapy due to missed-appointments lead to sub-optimal outcomes. Poor adherence has many reasons and is the first cry of help to address known/unknown barriers to treatment. This study was

conducted to understand the reasons responsible for missed appointments in patients with Retinoblastoma (RB).

Design/Methods: We prospectively recorded the causes for missed appointments in RB patients from February 2018–September 2018. A delay of more than 24 hours from the pre-scheduled date of chemotherapy was categorised as a “missed-appointment”.

Results: Out of 870 visits for RB-chemotherapy to our oncology day-care, there were 122 (14%) instances of missed appointments. We excluded the delays due to the patient's illness or unsuitable blood tests, or ones because of delays in getting investigation done. There were 40 children (4.6%) who had missed appointments due to other reasons. These 40 patients had an average age of 41 months with 25 males. 8 families lived within 100 km and 18 travelled more than 500 km for treatment. The median length of delay was 11 days. The median income for these families was about INR-7000 (90€)/month with average members being 8/household. Only 9 families had a cemented accommodation at their original place. Most head of families were illiterate. Twenty-seven patients used train as means of transport and 10 the state-bus. Ten families stayed near the hospital premises (on street/lawns etc) for the chemotherapy cycle, others had some form of local accommodation. The reason for delay were lack of finances ($n=11$), illness of other family-members ($n=21$), transport-related ($n=4$) and absence of an adult to accompany ($n=4$). Sixteen patients had a previous history of missed appointments.

Conclusions: Causes for missed appointments for chemotherapy in RB patients were multifactorial and included distance, lack of local accommodation, illiteracy, low family-income and other family commitments. Establishing centres and expertise across the nation, with more support to treatment from the government will help reduce missed appointments.

V453 SIOP19-0765 | Clinico-Epidemiological Profile and Treatment Outcomes in Children with Retinoblastoma: Experience from a Tertiary Care Cancer Centre in North-East India

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Background/Objectives: Retinoblastoma (RB) is the most common primary intraocular malignancy in children. We sought to provide a comprehensive assessment of epidemiological profile and treatment outcomes of children with retinoblastoma.

Design/Methods: In this retrospective study, we analysed 189 children diagnosed with retinoblastoma at our centre between 2004 and 2017. Survival was analysed with the Kaplan-Meier method and log-rank test.

Results: Median age at presentation was 14 months with male: female ratio 1.2:1. Mean duration between onset of symptoms and presentation was 49 days ($SD \pm 79$). Most common presenting symptom was white pupillary reflex in 60% of children. Family history of RB and other cancers were found in 1 (0.5%) and 7 (4%) children respectively. Primary mode of diagnosis and staging was ocular ultrasonography in 87% of patients. CT scan and MR imaging were done in 124 (66%) and 30 (16%) patients respectively. International staging system (ISS) Grade E disease was found in 144 (76%), extra ocular disease in 55 (29%), bilateral disease in 49 (26%) and trilateral disease in 3 (1.5%) of children. Out of 189 children with RB, 33 (18%) refused treatment and 156 children received treatment [24 children (15%) abandoned treatment midway and 132 (85%) completed treatment]. One hundred children (64%) received systemic therapy as neoadjuvant or adjuvant chemotherapy and 20 (13%) received local therapy. Eyeball and vision salvage rate with chemotherapy was 20 (13%) and 9 (6%) respectively. Cryotherapy was the most common modality of local treatment used in 11 (55%) children. Five-year survival for patients who received treatment was 76% (median survival not reached). In the treatment refusal group median survival was 9 months.

Conclusions: In developing countries, RB is mostly detected in advanced stages resulting in poor outcomes. Increased awareness and accessibility to dedicated centers for treating childhood malignancy can lead to early diagnosis, better prognosis and increased vision salvage.

V454 SIOP19-1125 | Base Editing of Retinoblastoma-Relevant Nonsense Mutations in RB1 Gene

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Background/Objectives: Nonsense mutations are the most prevalent variety of germline and somatic mutations in patients with retinoblastoma. This study aimed to investigate the therapeutic potential of genome editing-based technology in the restoration of *RB1* gene transcripts and retinoblastoma

protein in cells containing nonsense mutations in the *RBI* gene seen in patients with retinoblastoma.

Design/Methods: We prepared human skin fibroblast cells with clinically relevant nonsense mutations in the *RBI* gene by genome editing based on activation-induced cytidine deaminases. Treated cells were cultured from single cells and each single cell-derived clone was used for further experiments. Then, the cells were treated with adenine base editors targeting nonsense mutations. The efficacy of genome editing was evaluated by the next-generation sequencing.

Results: We obtained skin fibroblast cells with nonsense mutations in the *RBI* gene. From these cells, adenine base editors effectively corrected the mutations.

Conclusions: We expect that this genome editing-based technology can help to recover *RBI* gene transcripts and retinoblastoma protein in retinal cells containing nonsense mutations. It might be of therapeutic potential in the treatment of patients with retinoblastoma or people at risk due to germline *RBI* mutations.

V455 SIOP19-1354 | Outcome Comparison of 2 Retinoblastoma Treatment Protocols for Developing Countries as per SIOP-PODC Recommendations

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Background/Objectives: The SIOP-PODC group created recommendations for adapted treatment for children with retinoblastoma in low- and middle-income countries.

We aimed to compare outcomes of children treated with 2 SIOP-PODC recommended retinoblastoma treatment protocols respectively in South Africa (SA) and Cameroon.

Design/Methods: All children diagnosed with retinoblastoma between 2012 and 2016, treated in 6 paediatric oncology units (POUs) in South Africa (SA) and 2 POU in Cameroon (CA) were included (n=281). Treatment in SA, an upper middle-income country, included local intraocular

therapy, or chemotherapy (vincristine, etoposide, carboplatin) and/or surgery and/or radiotherapy for more extensive disease. In Cameroon, a low-income country, treatment included local intraocular therapy or combination chemotherapy (vincristine, cyclophosphamide, adriamycin) and/or surgery. Survival data presented is for 12-month follow-up with p-values for Log Rank Mantel-Cox.

Results: The crude 12-month survival in SA was 78.2% (100/127) and 59.2% (45 of 76) in Cameroon (Chi-Square=9.277, p=0.002), which was significantly affected by stage. All stage 0 patients had a 100% survival in SA (16/16) and Cameroon (2/2). SA patients had a better survival for all stages compared to Cameroonian patients except stage IV: Stage I – SA 92.7% (51/55) versus 58.8% (10/17) in Cameroon (Chi-Square=13.391, p=0.000); Stage II – SA 100% (14/14) versus 75% (9/12) in Cameroon (Chi-Square=3.833, p=0.050); Stage III – SA 75% (6/8) versus 40% (2/5) in Cameroon (Chi-Square = 1.649, no survival difference). Stage IV Cameroonian patients had a better 12-month survival of 67% (8/12) compared to SA with 26% (6/23) (Chi-square=4.026, p=0.045).

Conclusions: The relative lack of diagnostic capabilities may have affected accurate staging in Cameroon. Use of SIOP-PODC recommendations for adapted treatment protocols had an acceptable 12-month OS, for the settings, although patients with advanced stage at diagnosis require intensified treatment for better outcomes.

V456 SIOP19-0253 | Prophylactic Intrathecal Topotecan in the Treatment of Advanced Retinoblastoma Preliminary Report

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Background/Objectives: Retinoblastoma is the most common eye cancer of childhood. In developing countries, diagnosis is frequently made in disease's late stages. When there's extraocular involvement (orbital) at diagnosis, intensive chemotherapy and radiotherapy are mandatory. Up to one third of patients have disease progression and die from tumoral activity despite treatment.

Design/Methods: Since June 2016, the National Institute of Pediatrics group has proposed administering intrathecal Topotecan, given the high drug levels achieved in CSF, as measured in vitreous humor, tear fluid and CNS. Rising doses of Topotecan were administered every 21 days for 4 courses. Adverse effects, survival and relapse event if presented, were analyzed.

CSF was obtained to rule out initial disease. Patients with CNS affection, either by microscopy or image were not included in this publication.

Results: Seventeen patients with orbital stage were evaluated. They received Topotecan once every 21 days for a total of 4 doses (0.2, 0.4, 0.6 and 0.8 mg). 13 out of 17 patients presented with irritability and in 11 of 17 patients oxymetry drop during administration. 9/17 referred pain in the cauda equina. Presently, no patient has relapsed disease.

Conclusions: Conclusions: Though intrathecal therapy is not novel as an alternative for the treatment of advanced retinoblastoma, change of drug of election is. Toxicity is fairly tolerable and thus we have switched from international standard treatment. Longer follow-up and more patients are required in order to present definite conclusions.

V457 SIOP19-1426 | Clinical and MRI Features of Trilateral Retinoblastoma

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Background/Objectives: Trilateral retinoblastoma (TRB) is rare in children, referred to the development of a primary intracranial primitive neuroectodermal tumor in a patient with intraocular retinoblastoma. The clinical features, radiographic findings, and treatments were reviewed from our 8 cases and to promote the better understanding of TRB.

Design/Methods: The imaging and clinical findings of eight children diagnosed with TRB from 2012 to 2018 were reviewed.

Results: Of all 8 patients with bilateral retinoblastoma. Five patients were associated intraocular retinoblastoma with concurrent pineal or suprasellar TRB, with the diagnosed age of 11.8 ± 10.1 months (range from 4 to 26 months). Three patients were associated intraocular retinoblastoma with late onset pineal TRB, with the diagnosed age of 38 ± 20.1 months (range from 25 to 62 months), and bilateral intraocular lesion in a stable period after treatment. The features of all intracranial lesions (5 lesions in the pineal region, 1 lesion in the suprasellar area, 2 case accompanied by pineal gland and suprasellar lesions concurrently) showed circumscribed round or oval masses with the average length of 14.5mm, and all the lesions demonstrated intense enhancement in contrast-enhanced T1WI and significant diffusion restricted in DWI with ADC value of $(0.676 \pm 0.108) \times 10^{-3} \text{mm}^2/\text{s}$. One of pineal TRB was accompanied by leptomeningeal and cerebrospinal dissemination. Of all eight patients, three patients have been given up treatment (death in one patient), and the other five patients have a significant tumor volume reduction after treatment, one of which have gotten complete regression with no recurrence for 12 months follow-up.

Conclusions: The TRB were mostly with bilateral retinoblastoma. The pineal or suprasellar TRB can occur simultaneously or later, with lower age in the concurrent TRB. The

intracranial lesion of TRB mostly occurred in the pineal region, a small number in suprasellar area. Early diagnosis and standardized intravenous chemotherapy can improve the survival rate of patients.

V458 SIOP19-0638 | Retinoblastoma in sub-Saharan Africa: Case Studies of the Republic of Côte D'Ivoire and the Democratic Republic of the Congo on Behalf of GFAOP

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Background/Objectives: In most low-income countries, the diagnosis of retinoblastoma is delayed, resulting in a severe prognosis.

The objectives of this study were to describe the access to diagnosis and care of children diagnosed with retinoblastoma and the challenges in two sub-Saharan African countries: The Republic of Côte d'Ivoire and the Democratic Republic of the Congo.

Design/Methods: A descriptive cross-sectional study was conducted. Data were collected from the medical records of patients admitted during the period of January 1, 2013 to December 31, 2014 in 3 GFAOP pediatric oncology units and an ophthalmologic center. Data were entered and analyzed using Epi Info7.1 software and SAS 9.3.

Results: One hundred sixteen cases of retinoblastoma were collected, including 60 boys and 56 girls. The median diagnosis age was 3 years for both countries. Ninety-eight patients (84%) had unilateral retinoblastoma. Most of the patients presented with advanced disease (76% had extraocular retinoblastoma). Median time between initial symptoms and diagnosis was 8.5 months (range, 0.4 to 116.7 months). Median time between diagnosis and treatment initiation was 31 days (range, 0 to 751 days). The median cost for the treatment of the disease was estimated at \$1,954 per patient.

Conclusions: Late diagnosis of retinoblastoma occurs frequently in both African countries. It is associated with delay in initiating treatment, and the cost of the treatment remains unaffordable for most of the families. Support groups for parents and the support of the Franco-African Pediatric Oncology Group remain important in improving early diagnosis and providing treatment in sub-Saharan African countries.

V459 SIOP19-1170 | Knowledge of Retinoblastoma by Healthcare Professionals in sub-Saharan Africa: Survey Performed in Republic of Côte D'Ivoire and the Democratic Republic of Congo

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Background/Objectives: Diagnostic delay leads to advanced forms of retinoblastoma. The aim of this study was to evaluate the knowledge of health professionals on this disease.

Design/Methods: This survey was carried out among health professionals in the Democratic Republic of Congo (cities of Lubumbashi, Bukavu and Kinshasa) and Côte d'Ivoire (Abidjan). Health professionals were divided into 3 categories: 1) Pediatricians and ophthalmologists 2) Others physicians 3) Paramedics. A questionnaire adapted to each category was used. Scores were calculated to assess the knowledge of each professional according to his / her category. Each professional had an overall score and a score per question. It was maximal at 20 for categories 1 and 2, considered as average at 10, it was maximal of 14 for category 3, considered as average at 7. Descriptive statistical analyzes and association measurements were performed.

Results: A total of 637 health professionals were surveyed, including 69 in category 1, 180 in category 2 and 388 in category 3. Sixty-one per cent of health professionals had an overall score greater than or equal to the average for the category 1, 46% for category 2 and 17% for category 3.

One-quarter of health professionals were aware of the most common retinoblastoma revealing symptoms (leucocoria and strabismus) in category 1, 14% in category 2 and 4% in category 3.

Conclusions: Most health professionals surveyed in DRC and Cote d'Ivoire were not aware of the retinoblastoma revealing symptoms. This contributes to the delay in diagnosis and the poor prognosis of this disease in those countries.

V460 SIOP19-1011 | Trilateral Retinoblastoma - Single Centre Experience Over 60 Years

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Background/Objectives: Trilateral retinoblastoma (TRB) (bilateral retinoblastoma with a histologically similar CNS tumour, usually around the pineal gland) was first described in 1980. It is reported that up to 5% of patients with a germline mutation of the RB1 gene are at risk of developing TRB. The aim of this study was to determine the incidence of TRB in patients presenting to one of the two retinoblastoma (RB) centres in the UK and to define the spectrum of clinical behaviour and outcomes.

Design/Methods: We carried out a retrospective review of the medical records of patients with TRB identified from the West Midlands Children's Tumour Registry which holds data on a population-based cohort of children diagnosed with a malignancy between 1957 and 2019 including data for RB from 2002 when BCH was designated a National RB Referral Centre.

Results: 8 patients with TRB were identified over a 62-year period. 267 of the RB cohort were considered genetic (bilateral disease, positive family history or RB1 mutation positive) with 88 diagnosed before 2002 and 179 since 2002. This results in an overall incidence of trilateral retinoblastoma of 3% in patients with a genetic RB predisposition, but an incidence of 5.7% (5/88) and 1.7% (3/179) in the pre and post 2002 cohorts respectively. None of the 5 patients diagnosed before 2002 survived, however all 3 patients diagnosed subsequently are alive and disease-free following treatment with high dose chemotherapy (median follow-up: 33m).

Conclusions: The overall incidence of TRB (3%) in this series is lower than that reported in the literature, particularly since 2002 (1.7%). We propose this may be a result of the increased use of systemic chemotherapy in patients with RB and provides reassuring evidence in support of the nationally

agreed approach which does not recommend routinely screening patients with genetic RB for trilateral disease.

V461 SIOP19-0149 | Autologous Stem Cell Transplantation as Consolidation Therapy in Metastatic Retinoblastoma, Experience at Instituto Nacional de Pediatría, Mexico

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Background/Objectives: Introduction: Advanced retinoblastoma has a poor prognosis in developing countries. The treatment of this entity is complex and requires a multidisciplinary approach, even more if it is metastatic, where survival is close to 0%. With autologous stem cell transplantation (Auto-SCT), 60% of metastatic retinoblastomas were rescued, although the information is limited at patients treated with this modality.

Objectives: Present the experience of metastatic retinoblastoma treatment with Auto-SCT at Instituto Nacional de Pediatría, Mexico. (INP)

Design/Methods: Materials and Methods: Retrospective review of patients under 18 years old with metastatic retinoblastoma treated at the INP with Auto-SCT, from January 2013 to October 2018.

Results: 6 patients met the inclusion criteria with median age of 25.1 months, Five cases with unilateral affection and one with bilateral affection. Four cases at stage IV B and two patients at stage IV A according to the International stratification System for Retinoblastoma,

The overall survival was 66% (four patients still alive) in a period post transplantation for 57.3 months (range 2-81 months). Two patients present relapse, one patient to bone and the other one to Central Nervous System (CNS) at 7 and 5 months post transplantation respectively, both died.

Conclusions: Conclusions: Metastatic retinoblastoma have a poor prognosis, but with Auto-SCT we have achieved 66% survival, statistics similar to international ones.

V462 SIOP19-1245 | Experience of the Application of Selective Intra Arterial and Intravitreal Chemotherapy in One Institute

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Background/Objectives: Retinoblastoma (RB) is a life threatening cancer disease. A breakthrough in the treatment of children with RB is associated with the improvement of conservative treatment that was administered in at least one of the two tumor-affected eyes in most bilateral cases, that was chemotherapy both systemic and local (selective intra-arterial and intravitreal) in most cases combined with laser therapy, cryotherapy, or brachytherapy.

Design/Methods: The results of the treatment of 110 children (129 eyes) in the N.N. Blokhin Oncology Oncology Center, Moscow, Russia with a diagnosis of intraocular RB from 2011 to 2017 are analyzed.

Results: All children/eyes were divided into 2 groups: the 1st group of treated patients included 99 children (116 eyes) who underwent intraarterial chemotherapy (IACT)±intravitreal chemotherapy (IvCT) with insufficient effectiveness of previous treatment with resistant forms of RB (n=32) and according to the multicenter treatment protocol of RB groups C and D (n=84). The 2nd group of primary local chemotherapy IACT±IvCT included 11 patients (13 eyes) with primary diagnosed RB, who underwent local chemotherapy as the first stage of treatment, including IACT±IvCT

Conclusions: In the 1st group, 95 out of 114 eyes were saved. Eye preservation was 94.5% after 1 year, 88.5% after 2 years, 86.5% after 3 years, 82.9% after 4 years and 78.5% from the 4th to the 6th year. The follow-up period was 30.3 ± 16.81 months, the duration of a relapse-free course was 23.74 ± 12.45 months. 1 patient with bilateral RB was eliminated from the study. In the 2nd group, 11 out of 12 eyes were saved; 1 patient dropped out of the study due to the appearance of a second tumor of a different location. Eye preservation was 92.3% at 1 and 2 years. The follow-up period was 13.5±5.3 months, the duration of a relapse-free course was 9.7±5.2 months. The study demonstrated high efficacy of local chemotherapy.

V463 SIOP19-1258 | Retinoblastoma in Botswana

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Background/Objectives: Retinoblastoma (RB) represents 6% of pediatric cancers at Princess Marina Hospital (PMH), the only pediatric cancer center in Botswana. Ophthalmology services are provided at two different government health centers. Some specialized RB services, like local therapies, are only available in South Africa. To improve the diagnosis and

management of RB in Botswana, further understanding of RB presentations and outcomes was necessary.

Design/Methods: A retrospective review was performed on patients enrolled into the Botswana Paediatric Oncology Database (BPOD), evaluating all patients diagnosed with RB from 2007 to 2018. Summary statistics and survival analyses were performed.

Results: Thirty-two patients with RB were identified in program records. Three were excluded due to a pre-2007 diagnosis and one that was never treated at PMH, leaving 28 for final analysis. The median age at diagnosis of the cohort was 2.5 years (InterQuartile Range 1.3, 3.5), 50% were male, 61% (17) were unilateral, and 32% (9) were bilateral (one each tri-lateral and unknown). Leukocoria (63%) was the most common presenting sign. Two-year overall (2-yr OS) survival was 59% (95% Confidence Interval (CI) 37-75%) with all deaths occurring within two years of diagnosis, 80% of which were in the first year of diagnosis. For patients with unilateral RB, 2-yr OS was 52% (95% CI 25-74%) and bilateral RB was 73% (95% CI 28-93%).

Conclusions: RB survival in Botswana is lower than in high income countries. To further understand and address barriers to diagnosis and survival of RB, the Botswana RB Multidisciplinary Team (MDT) was launched in November 2018, including public/private eye centers and pathology, with a monthly tumor board. The Botswana RB MDT aims to improve community awareness of RB as well as early recognition of RB by health care workers, harmonize treatment strategies among the MDT partners, and expand both systemic and local treatment options available in Botswana.

V464 SIOP19-0680 | Raising Awareness of Retinoblastoma: Think Globally, Act Locally

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Background/Objectives: The very first signs of retinoblastoma are leukocoria and strabismus. With early diagnosis and access to treatment, retinoblastoma is the most survivable paediatric cancer. In both developed or developing countries diagnostic delay is common; however in the absence of systemic symptoms, the early signs of retinoblastoma are often ignored or dismissed by caregivers and healthcare providers alike. Raising awareness of leukocoria has been shown to reduce delays in diagnosis and improve survival. This study aimed to report the frequency of retinoblastoma awareness campaigns conducted worldwide from 2008-2017 and identify the barriers to the delivery of sustainable awareness programs.

Design/Methods: In this cross-sectional study, a secure link to complete a survey was emailed to 146 retinoblastoma treatment centres registered on the One Retinoblastoma World Map (<http://map.1rbw.org>) or retinoblastoma-specific philanthropic organisations. Data collected included: participant's country, frequency of campaigns, clinical signs highlighted and whether impact had been measured. Barriers to conducting awareness campaigns were documented.

Results: Thirty surveys, across 6 continents, representing both developed and developing countries were returned. Accounting for inactive emails a 25.4% participation rate was achieved. Twenty (67%) respondents reported 'ever' having conducted an awareness campaign in the last 10 years. The predominant signs promoted included leukocoria alone (8, 47.1%) or strabismus and leukocoria (9, 52%). Four respondents included 'red eye', 'proptosis' or 'buphthalmos' in their campaigns. The general public, caregivers or healthcare professionals were reported as the target audience. The most commonly identified barriers included: lack of funding, social or cultural barriers, difficulty promoting signs for a rare disease and a lack of understanding among health professionals of the need for awareness.

Conclusions: Despite the demonstrated impact of retinoblastoma awareness campaigns on survival, barriers to their implementation are universal to both developed and developing countries. Understanding these barriers provides an opportunity to develop sustainable awareness campaigns to improve outcomes globally.

V465 SIOP19-1195 | A Glint or a Squint Should Make You Think! Improving Parent Knowledge of the Early Signs of Retinoblastoma: A Double-Blind Randomised Controlled Trial

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Background/Objectives: Early diagnosis of retinoblastoma is critical to achieving optimal outcomes, including survival. The earliest signs of retinoblastoma are leukocoria and strabismus. In the absence of systemic symptoms, these signs are often ignored or dismissed by parents. Whilst raising awareness of leukocoria has been shown to improve survival, as a rare disease, implementing sustainable awareness programs is challenging. Motivated by reducing delayed diagnosis of retinoblastoma, this study aimed to evaluate an

evidence-based, theory-informed paediatric eye-health information pamphlet specifically developed to raise parental awareness of leukocoria and strabismus.

Design/Methods: Five-hundred and eighteen women in their 2nd or 3rd trimester of pregnancy attending a large metropolitan antenatal clinic were enrolled to participate in a double-blind randomised controlled trial. Following completion of the baseline survey, participants were randomly allocated to receive either the intervention or control pamphlet. Two-weeks after baseline, an on-line follow-up survey was completed. Primary outcome measures: change in level of concern if leukocoria or strabismus are observed. Secondary outcome measures: change in help-seeking intention if either leukocoria or strabismus are observed.

Results: Using multiple logistic regression analysis, compared to the control group, participants in the intervention group were more likely to be concerned if leukocoria was observed, (OR 1.711, [CI 1.176-2.497] $p=0.005$) and less likely to delay seeking help (OR 0.560, [0.382-0.817] $p=0.003$). In contrast, whilst participants in the intervention group were no more concerned if they observed strabismus than the control group, they were less likely to delay help-seeking (OR 0.318, [0.125-0.806] $p=0.016$) at follow-up.

Conclusions: Aiming to reduce diagnostic delays for retinoblastoma, providing parents with relevant information, messages to motivate and guidance on behaviour skills can improve their knowledge and subsequent help-seeking intention if leukocoria or strabismus are observed. Delivered in the context of common paediatric eye disease, systematic dissemination of useful eye-health information to parents may improve efficacy and sustainability.

V466 SIOP19-1047 | Whole-Body MRI Screening Programme for Detection of Subsequent Neoplasms in Hereditary Retinoblastoma Survivors

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Background/Objectives: An RB1 germline mutation significantly increases lifelong risk of a second malignancy in survivors of retinoblastoma. A screening programme with whole-body MRI (WB-MRI), performed at yearly intervals, is proposed from the age of eight on.

Design/Methods: This was a retrospective cohort study. Data from two years of the WB-MRI retinoblastoma follow-up programme at Motol University Hospital, Prague were reviewed. WB-MRI were carried out on the Philips Achieva 3T TX MR

system (Philips Healthcare, Eindhoven, Netherlands). The entire body was imaged in coronal and axial plain.

Results: Fourteen patients, 12 of whom had a germline mutation, underwent nineteen WB-MRIs between January 2017 and February 2019. The median age at first WB-MRI was 15.8 years (9.9-32). Five WB-MRIs were reported as normal. No new malignancies were identified. The most common findings were signal abnormalities within the bones or bone marrow of the lower limbs (6/18), followed by non-specific lymph node enlargement (4/18) and abnormal signal of breast tissue. Seven focused ultrasounds, 2 focused MRIs and 2 focused plain radiographs were carried out based on the MRI results.

Conclusions: In a cohort of fourteen patients undergoing WB-MRI for follow-up of retinoblastoma with an RB1 germline mutation, no new malignancies were identified over the two year period of the study. WB-MRI did lead to further imaging. The overall incidence of a second malignancy in our patient cohort appears to be small; of 184 patients treated for retinoblastoma at our institution from 1966 to 2017, only 10 presented with a second malignancy at the median age of 24 years (7-43). Though small, this study suggests the need for a large multicentre prospective cohort study to determine the effect of WB-MRI on mortality in this patient group. Cost effectiveness and the degree of overdiagnosis could also be determined.

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V467 SIOP19-1298 | Vascular Endothelial Growth Factor Expression in Enucleation Material of Advanced Intraocular Retinoblastoma Cases

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Background/Objectives: The primary goal of the treatment of retinoblastoma is to save the patient's life and secondarily to salvage the eye and the vision. All solid tumors need a vascular stroma to grow. Vascular Endothelial Growth Factor (V-EGF) is a potent and specific angiogenic growth factor and may contribute to the formation of vascular tumor stroma *invitro* / *invivo*.

Design/Methods: Sixty-two tumor paraffin blocks of the enucleated bulbus oculi material were studied and V-EGF expression was evaluated by immunohistochemical methods, retrospectively.

Results: The majority of enucleated eyes were in group E; percentage of vascular component and V-EGF expression were evaluated by two different pathologists. Of the patients, 54 (87%) were in intraocular stage E, 6 were stage D, and 2 were stage C. Seven patients had anterior camera, 8 choroid, 24 optic nerve involvement. The enucleation materials were classified according to vascular component expression percentages; 0-5% Group 1, 6-10 Group 2, 11-15 Group 3 and >16 Group 4, respectively. We observed varying degrees of vascularization and V-EGF expression in all groups. However, there were no statistical significance due to the small number of patients ($p>0.05$)

Conclusions: In the literature, there are very few prognostic studies coming from developing countries to demonstrate pathological vascularization in bulbus oculi materials. We aim to share our single center experience with clinicians by demonstrating V-EGF expression in enucleation materials belonging to our patients with retinoblastoma, as in developed countries there are no such high enucleation rates. Therefore, targeting V-EGF in patients with advanced intraocular retinoblastoma may be an effective strategy in the prevention of tumor progression, as In advanced intraocular stage retinoblastoma, disseminated tumor cells are exposed to a hypoxic and nutrition poor environment, which stimulates the tumor cells to secrete more angiogenic factors. Therefore it is hypothesized that Anti-VEGF therapy may have an important therapeutic role in those eyes.

Solid Non Brain Tumours - Soft Tissue Sarcomas

V468 SIOP19-1685 | Regional Lymph Node Evaluation is Underutilized in Pediatric Rhabdomyosarcoma

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Background/Objectives: Regional lymph node (LN) assessment is critical for accurate staging and treatment in pediatric soft tissue sarcomas. Preoperative imaging and clinical examination are often insufficient to correctly determine nodal status. Despite recommendations for histologic examination, reporting on compliance with operative LN sampling is limited. The purpose of this work is to examine the performance of operative LN sampling in pediatric rhabdomyosarcoma using a large national database, and to identify factors associated with variations in practice.

Design/Methods: Demographic and disease-specific data from patients under 25 years of age with a diagnosis of rhabdomyosarcoma were extracted from the National Cancer Database registry. Tumors were classified according to his-

tologic subtype and primary location. Status of operative LN sampling was obtained through the same registry.

Results: This study cohort consisted of 2,410 patients who were diagnosed with rhabdomyosarcoma between 2004 and 2015 with a mean age of 9.5 years. Histologic subtype was embryonal in 46.3% of patients, alveolar in 37.3%, and not specified in the others. Median tumor size was 6.2cm. Distribution included 25.8% in the head/neck, 40.5% chest/abdomen/pelvis, 19.2% extremities, 8.6% bladder/prostate, and 5.8% uterus/female genitalia. Overall, regional LN sampling was performed in 21.7% of patients. Patients were most likely to undergo LN sampling if the tumor was alveolar subtype (25.5%, $p>0.01$) or an extremity tumor (35.3%, $p<0.001$). Preoperative clinical LN staging had a sensitivity of 74% when compared with histologic sampling.

Conclusions: Reliance on preoperative imaging and clinical assessment for regional LN assessment in pediatric rhabdomyosarcoma is imprecise and may result in inaccurate staging and subsequent regional therapy. Operative regional LN sampling is recommended in high risk groups such as extremity tumors, however, compliance remains low and may lead to inadequate staging and treatment. Increased adherence to regional disease evaluation guidelines in pediatric rhabdomyosarcoma could better inform treatment choices and improve outcomes.

V469 SIOP19-0840 | An Unresolved Issue in Rhabdomyosarcoma Treatment: The Duration of Chemotherapy

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Background/Objectives: Over the last five decades, a series of cooperative trials have shown a progressively increased chance for cure for patients with non-metastatic RMS, with a current 5-years survival around 80%.

A series of randomized trials have investigated different chemotherapy regimen but the treatment duration has never been taken into account. Insufficient treatment duration may be unable to kill all the tumor cells even if they are potentially sensitive to chemotherapy. Extended treatment could be unnecessary and increase the risk of late sequelae.

Design/Methods: We analyzed the strategies adopted over the years by North America and European Groups to address this question.

Results: The North American investigators adopted a very long chemotherapy duration in their initial trials (104 weeks) but this was reduced over the time arriving to 24-42 weeks in the most recent trials. In Europe the duration of chemotherapy went from 35 to 48 weeks for low risk patients and from 56

to 72 weeks for high risk patients in the early trials. In the modern era, all European Groups adopted 22 weeks for low risk and 27 weeks for high risk patients as the maximum chemotherapy duration. As patients' survival increased progressively, there was no evidence that the duration of intensive chemotherapy was associated with outcome. However, the recent RMS2005 study a survival advantage was evident for children receiving maintenance, i.e. 6 additional months of chemotherapy using low dose cyclophosphamide and vinorelbine.

Conclusions: Comparisons between sequential studies to evaluate the role of treatment duration is confounded by increased chemotherapy intensity and improvement of supportive care, staging, quality surgery and radiotherapy. The differences in treatment duration between North America and Europe and the results of the RMS2005 trial support investigation of the duration of treatment as a randomized question in future trials.

V470 SIOP19-0426 | Soft Tissue Sarcoma in Children, Adolescents and Young Adults: Outcome Analysis According to Conformity to International Initial Care Guidelines

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Background/Objectives: Outcome of adults with soft tissue sarcomas (STS) is known to be better through management in reference centers. Initial care guidelines advise for 5 main criteria: 1-Imaging before biopsy; 2-Tumor biopsy before surgery; 3-Multidisciplinary team discussion (MTD) before biopsy; 4-Biopsy/Surgery in "expert centers"; 5-Somatic molecular biology feasible. The aim was to describe and assess the prognostic impact of initial management of STS in a young population according to the type of referring centers and the number of optimal criteria.

Design/Methods: Monocentric retrospective analysis of the initial management of 127 youths (0-25 years) with localized STS treated from 2006 to 2015.

Results: Median age at diagnosis was 9.6 years (range: 0-25). Primaries involved limbs (50%), head/neck (28%), and chest

wall (13%). First medical contacts were general practitioners (60%), emergency units (25%). Median delay between first signs and MTD was 3 months (range: 0-82). Patients were referred to Institut Curie by expert centers (59%), general hospitals (19%), other surgical centers (10%). Overall, only 39% patients had 5/5: 39%, 3-4: 29%, ≤ 2 : 32%. No imaging was performed before surgery/biopsy for 21% patients, no biopsy before surgery for 35%. Patients referred by "expert centers" had higher compliance to guidelines ($P=0.025$). Upfront surgery was performed in 59/127 patients (29% R0, 54% R1, 17% R2 margins). Immediate re-operation was inversely related to the number of criteria (0% when 5 criteria vs. 14% for 3-4, 46% if ≤ 2 ; $P<0.001$). Five-year overall (OS) and locoregional relapse-free (LRFS) survivals are 88% (95%IC: 83-95%) and 82% (95%IC: 75-89%) and not influenced by the number of criteria ($P=0.322$; $P=0.887$).

Conclusions: Less than half of the youths with STS are initially managed according to international guidelines, highlighting the need for better information about optimal management. These results plead for immediate management in reference centers to reduce initial burden of therapy.

V471 SIOP19-1356 | Desmoid Tumors in Children and Adults: The Value of Combined Multidisciplinary Care

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Background/Objectives: Fibromatosis (Desmoid Tumor) is a locally aggressive tumor that is amenable to multiple options of local and systemic therapeutics. Our aim is to evaluate treatment options and outcomes of patients treated at our center. A combined adult/pediatric multidisciplinary clinic (MDC) evaluates all patients with musculoskeletal tumors who are managed at our center.

Design/Methods: After IRB approval, we reviewed charts patients with fibromatosis who presented between Jan 2007 and Dec 2017. Main Outcome measures were demographic data, disease location, presenting symptoms, tumor size, treatment modalities, recurrence rate and survival.

Results: A total of 51 patients were included (33 females, 65%; 9 pediatrics, 20%). Median age was 29.4 years (range, 4.9-63.7years). Median tumor size was 7.5cm (range, 2.8-23cm). The most frequent tumor location was the upper and lower extremities. Most patients presented after feeling a mass. The treatment modalities were as follow: 24 patients received chemotherapy, 16 patients received radiotherapy and 37 patients underwent surgery. The most commonly used

agent in our patients was hydroxyurea, which was associated with low toxicity. In average, each patient was discussed 6 times in our weekly combined MDC. Outcome was favorable in general. At the time of data collection, 18 patients are alive without disease and 30 patients are alive with stable disease and two patients were lost for follow up. One patient had died from colon cancer. The 5-year-PFS was $62\% \pm 8.6\%$ for the whole group and no treatment modality showed significantly better outcome. Notably, children had similar PFS when compared to adults ($p=0.74$).

Conclusions: A successful model for treating patients with desmoid tumors was established at our center in a combined MDC. This disease requires long-term meticulous follow up with multiple interventions. Pediatric patients with this rare disease may benefit from all available expertise which frequently requires the input of medical oncologists, radiation oncologists, and musculoskeletal surgeons.

V472 SIOP19-0719 | Outcomes of Metastatic Non-Rhabdomyosarcoma Soft Tissue Sarcomas (NRSTS) Treated Within the Bernie Study: A Randomised, Phase II Study Evaluating the Addition of Bevacizumab to Chemotherapy

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Background/Objectives: The presence of metastatic disease at diagnosis is uncommon in pediatric NRSTS, but generally heralds a dismal outcome. Owing to the lack of studies dedicated to metastatic NRSTS, the EpSSG (in cooperation with ITCC and Roche) included these patients in the same study designed for metastatic rhabdomyosarcoma, i.e. the BERNIE study.

Design/Methods: The study was an open-label, multicentre, randomised phase II study for newly-diagnosed patients < 18 years with metastatic soft tissue sarcomas (BO20924/ITCC-006; ClinicalTrials.gov: NCT00643565). Patients were randomised 1:1 to receive or not bevacizumab added to the standard therapy including 9 courses of IVADo-IVA chemotherapy, followed by 12 months of maintenance therapy with vinorelbine and low-dose cyclophosphamide. Primary end-point was event-free survival (EFS); secondary objectives were objective response rate, overall survival, safety, tolerability, and pharmacokinetic profile of bevacizumab.

Results: From July 2008 and October 2013, 154 patients were included in the study: 49 had NRSTS (12 DSRCT, 9 MPNST, 9 undifferentiated sarcoma, 19 others). The pattern of metastases differed in the different histotypes. Safety data and overall efficacy results for the whole series have been already reported (no improvement with bevacizumab in EFS) (Chisholm et al, Eur J Cancer 2017;83:177-184). As for NRSTS, we observed partial remission in 27.7% of cases (4/18 in standard arm, 6/18 in bevacizumab arm). At median follow-up of 27.7 months, 2-yr EFS was 27.3% (95% CI 13.9-42.5) for all NRSTS series: it was 34.9% and 22.9% for the bevacizumab and standard therapy arm, respectively (p -value=0.1919).

Conclusions: This is the first series of pediatric metastatic NRSTS prospectively treated in a randomised phase II trial including a biologic agent. The study did not demonstrate a benefit for the addition of bevacizumab to chemotherapy. This series may be considered as parameter for this disease category, in particular regarding the development of future investigational studies.

V473 SIOP19-0905 | Non-Parameningeal Head and Neck Rhabdomyosarcoma in Children and Young Adults: Results of the EPSSG RMS 2005 Study

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Background/Objectives: We analyzed outcome of young patients with non-metastatic Head/Neck-non-Paraneoplastic rhabdomyosarcoma (HNnPM-RMS) prospectively included in the European paediatric Soft tissue sarcoma Study Group (EpSSG) RMS2005 protocol for treatment of localized RMS.

Design/Methods: Patients were stratified into four different risk groups, low risk (LR), standard risk (SR), high risk (HR) and very high risk (VHR), based on the following risk factors: pathology (embryonal/alveolar), postsurgical stage (IRS group I-III), site, nodal stage, tumour size (± 5 cm) and patient age (± 10 years). Treatment consisted of risk-adapted chemotherapy, surgery and/or radiation therapy.

Results: Between 2005 and 2015, 136 patients with HNnPM-RMS were enrolled in the EpSSG RMS 2005 study (9% of the cohort): LR 2, SR 60, HR 51 and VHR 23. Median age was 6.6 years (1 month - 25 years). Most common tumour sites were cheek/chin (28%) and nasal ala/nasolabial fold (21%). Pathology was 51% embryonal, 43% alveolar, 3% botryoid, 2% spindle cell and 1% not otherwise specified. The majority of tumours (77%) were < 5 cm in size. Lymph node extension was present in 24%. After a median follow-up of 56 months (range 6-134), 31 (23%) patients experienced an event (local relapse 14, regional lymph node relapse 3, metastatic relapse 2, progressive disease 4, combined relapse 5, secondary tumour 2, toxicity 1), 13 of these patients died. Five-year Event Free Survival and Overall Survival were 76% (95% CI: 67.7-83.1) and 89% (95% CI: 81.8-93.9), respectively.

Conclusions: By adapting treatment according to risk group, treatment results for localized HNnPM RMS were acceptable despite high frequency of alveolar histology and initial lymph node extension. The main challenge remains local tumour control. Even more patients can probably be cured on first line treatment by optimizing and standardizing the local therapy.

V474 SIOP19-0321 | Collagen Gel-Embedded Drug Sensitivity Test of Pazopanib in Childhood Sarcoma

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Background/Objectives: Pazopanib is a multitarget tyrosine kinase inhibitor which is approved for soft tissue sarcoma in Japan. No biomarker has been identified to predict the clinical efficacy of Pazopanib. The objective of this study is to establish the system to evaluate tumor cell sensitivity to Pazopanib.

Design/Methods: The surgically removed tumor tissues from 6 patients with sarcoma (rhabdomyosarcoma: 3, Ewing sarcoma: 2, malignant rhabdoid tumor: 1) were tested for Pazopanib-sensitivity using the collagen gel-embedded drug sensitivity test (CE-DST). The single tumor cell suspension was applied to a collagen gel-embedded culture system in a 96 well plate and exposed to Pazopanib at 60 μ M for 4 days. The number of survival cells per well were measured by a CellTiter-Glo assay. The inhibitory ratio (%IR) by Pazopanib in the tested sample was calculated as follows; %IR = $100 \times (1 - \frac{\text{the number of survival cells in the treated well}}{\text{the number of survival cells in the untreated control well}})$.

Results: %IR by Pazopanib in rhabdomyosarcoma samples was $1.1 \pm 2.0\%$, $7.2 \pm 6.1\%$, or $72.6 \pm 1.2\%$, respectively. It was $57.4 \pm 0.9\%$ or $20.6 \pm 5.4\%$ in Ewing sarcoma samples, and $32.2 \pm 10.5\%$ in malignant rhabdoid tumor.

Case Report: A 14-year-old girl patient developed 2nd relapsed alveolar rhabdomyosarcoma in her posterior mediastinum and left thigh. The resected tumors were tested by CE-DST, showing %IR by Pazopanib of 72.6%. After local irradiation, the new metastatic tumor appeared in her left superior mediastinum. The patient then received Pazopanib at 800 mg/day, which induced tumor reduction (partial response) after 4 months of treatment.

Conclusions: The CE-DST could be a useful tool to predict the clinical efficacy of Pazopanib.

V475 SIOP19-1357 | YWHAE-NUTM2B Translocation in Neonatal Soft Tissue Sarcoma: A Highly Aggressive Entity with an Original Presentation

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Background/Objectives: Neonatal soft tissue sarcoma is a rare entity that encompasses a heterogeneous group of poorly classified tumors. YWHAE-NUTM2B translocation had previously been reported in clear cell renal sarcomas but its description in soft tissue sarcomas is recent.

Design/Methods: We reviewed databases from the two French national referent laboratories in molecular analysis of pediatric sarcomas to describe here clinical presentation of cases of round-cell sarcoma with YWHAE-NUTM2B translocation.

Results: Using RNA-seq, we identified two cases of neonatal sarcoma harboring an *YWHAE-NUTM2B* fusion and expression profiles close to the BCOR-rearranged sarcomas. Both infants presented with an isolated tissue mass of the gluteal region at birth, which histology was compatible with an unclassified round-cell sarcoma. The *YWHAE-NUTM2B* fusion was identified 2 months after tumor discovery. In patient 1, the mass grew rapidly and brain metastases appeared at 3.5 months of life, despite initiation of chemotherapy then interrupted in order to perform the surgical resection of the primary tumor. In patient 2, the mass increased progressively until first-line surgery. Pelvic and abdominal metastases were identified immediately after surgery and rapidly spread to cerebral tissue despite adjuvant treatment with VAC (Vincristine-D-Actinomycin-Cyclophosphamide). Amongst several types of chemotherapy regimens used, only ICE courses (Ifosfamide, Carboplatine, and Etoposide) induced significant volume reduction (patient 1). Difficulties in therapeutic management together with the aggressiveness of these tumors lead to the death of both patients before 4 months of life.

Conclusions: This new entity mimics neonatal immature sacro-coccygeal teratoma. By gathering these two similar clinical situations, we underline their original presentation (pelvic primary tumor, aggressive behavior despite early chemotherapy, and early development of brain metastasis) and the difficulty of therapy adjustment. This leads to recommend a systematic search for somatic translocation in all cases of undifferentiated neonatal round-cell tumors

V476 SIOP19-0551 | Clinical and Prognostic Characteristics of 21 Patients with Extrarenal Extracranial Rhabdoid Tumor in Children

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Background/Objectives: To investigate the clinical characteristics, treatment strategies, and prognosis of extrarenal extracranial malignant rhabdoid tumor (EERT) in children.

Design/Methods: A retrospective analysis was performed in 21 patients with EERT from January 2007 to October 2017 in our hospital.

Results: There were 11 males and 10 females in 21 cases of EERT, with a median age of 46 months (range, 0-122 months). The disease is distributed over a wide range of head and neck (4 cases), posterior mediastinum (7 cases), retroperitoneal (3 cases), pelvis (3 cases), soft tissue of extremities (2 cases), ureter (1 case) and liver (1 case). Tumor rupture occurred in 3 cases during the first diagnosis or treatment. Twenty-one cases of tumor tissues were detected by immunohistochemical of INI1, and all cases were negative. According to the

Surveillance, Epidemiology, and End Results (SEER) staging criteria, there were 3 localized cases, 13 regional, and 5 distant metastases; the most common metastatic site was bone (3 cases), and other common metastases included liver and brain. Although comprehensive treatment with surgery, chemotherapy and radiotherapy was performed on EERT patients, the patients of EERT had a poor prognosis. Among the 21 children with EERT, 6 cases survived, 14 cases died of tumor recurrence and progression, and one case died shortly after diagnosis. Seventy-five percent relapsed within 5 months (including 5 months) after diagnosis. The 3-year and 5-year overall survival rates were 37.5% and 25% respectively.

Conclusions: EERT was a rare, highly aggressive malignancy that presented in infants and young children. It could occur in the soft tissues of the whole body. The tumor was prone to rupture. Distant metastasis is common in the lung, brain and liver. The comprehensive treatment model was recommended that includes surgery, chemotherapy, and radiotherapy. However, tumor relapse occurred early and patients with EERT had a poor prognosis.

V477 SIOP19-0335 | Hyperthermic Intrathoracic Chemotherapy (HITHOC) For the Control of Pleural Dissemination in Pediatric Solid Malignancies: A Single Institutional Experience

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Background/Objectives: Pleural dissemination of pediatric solid malignancies is extremely progressed stage of disease, which is usually unmanageable. In adults, cytoreductive surgery (CRS) combined with hyperthermic intrathoracic chemotherapy (HITHOC) has been used in advanced pleural malignancies such as malignant mesothelioma and metastatic pleural effusion of cancer. Hyperthermic intraperitoneal chemotherapy (HIPEC) for abdominal dissemination has been performed in some cases of pediatric solid malignancies. However, little is known about the efficacy and toxicity of HITHOC in children.

Design/Methods: We retrospectively reviewed the medical files of patients under the age of 18 years with pleural disseminated solid malignancies who had been treated in conjunction with HITHOC in our institution. Basically, hyperthermic chemotherapy had been administered with 100 mg/m² of cisplatin at 41°C perfused continuously for 90 minutes after complete CRS. Recently, We have modulated the

thermal exposure according to the “Thermal dose” basis calculated by exposure duration and temperature.

Results: Five pediatric patients aged 5 to 18 had undergone HITHOC. The underlying diseases include two osteosarcoma, one germ cell tumor, one hepatocellular carcinoma and one malignant rhabdoid tumor. All patients had pleural dissemination identified radiologically or histologically. Total six HITHOC were performed, including one patient with osteosarcoma who was sequentially treated in both sides of thoracic cavity for bilateral pleural metastasis. As a result, two of them (germ cell tumor, osteosarcoma) had no evidence of disease for 2 and 15 months after HITHOC. Though other three were relapsed locally and at other sites, one of osteosarcoma patient could obtain long-term disease control of the site where HITHOC perfused adequately. No severe complications associated with HITHOC had occurred in all cases.

Conclusions: HITHOC is a safe and effective treatment to control pleural dissemination of pediatric solid malignancies.

V478 SIOP19-1644 | How Critical is the Pathology Review of Pediatric Sarcoma Referred to a Cancer Center in a Developing Country

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Background/Objectives: with erroneous diagnoses that can affect significantly the plan of care and the ultimate outcome of Most pediatric soft tissue and bone sarcomas are rare. This rarity makes it more likely to label these tumors affected patients

Design/Methods: In our center, all patients referred from other hospitals are required to have their pathology reviewed by a board-certified pathologist. Difficult cases are discussed in the daily pathology meeting and if necessary cases are sent for international consultation. In this retrospective study, we reviewed medical records of all referred children under the age of 18years at time of referral, who were diagnosis with bone or soft tissue sarcoma in other institutions. All patients who were referred from January 2003 till December 2018 were reviewed. Major changes in pathology diagnoses were considered if they potentially affected patients' management or prognosis.

Results: During the study period a total of 665 pediatric patients were diagnosed with sarcoma. Of these 410 patients had their diagnosis done outside, of those 72 (17.2%) patients had pathology changed, diagnosis of these patients were done in public, private or abroad laboratories. The following referral diagnoses and percentages of patients with major

changes were noticed: Ewing Sarcoma (N=107, 22.4%), Osteosarcoma (N=68,13.2%), Rhabdomyosarcoma (N=148, 9.4%) and other soft tissue sarcomas (N=87, 28.7%).

Conclusions: Major discrepancy in pathological diagnosis was noticed in a significant number of referred patients. Central pathology review should be done for all pediatric sarcomas and building local expertise is probably the most important element in establishing pediatric sarcoma care.

V479 SIOP19-0458 | Efficiency of Immunotherapy Based on Autologous Hematopoietic Cells in Pediatric Cancer

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Background/Objectives: Cell immunotherapy through autologous dendritic cells (DC) presents a hopeful strategy for the treatment of various tumors in adults with an objective response of 30%.

Purpose. To assess results of treatment of children with solid tumors using targeting immunotherapy (dendritic cell vaccine).

Design/Methods: Eight patients aged 5–17 years with solid tumor received adjuvant immunotherapy with autologous DC vaccine between 2016 and 2018. The mean age was 10 years, the median age was 9.5 years (4.5 – 15). There were equal numbers of boys and girls. In the main, soft-tissue sarcoma was diagnosed (6 children or 75%), one patient had Wilms tumor and one had glioblastoma (12.5% each). Half of the children were treated with DC vaccine in combination with the third-line chemotherapy regimens, 2 (25%) – with the second-line chemotherapy and 2 (25%) – with the first-line chemotherapy. To assess treatment effectiveness, the paired-comparison method was used. The control group consisted of 8 patients, who received chemotherapy in a maintenance regimen.

Results: The mean number of DC vaccine administrations was 5 (from 1 to 13). An objective clinical response with a maximum duration of 66 weeks was achieved in 5 patients (62.5%), a recurrence was revealed in one case (12.5%) and the progression of disease was detected in 2 cases (25%). Median follow-up in the experimental (DC vaccine) and control groups was 5.7 months and 2 months, respectively, while the overall survival in the group with dendritic cell vaccine was $57.1 \pm 18.7\%$, and in the control group – 0%. The median time to progression in the experimental group was 2.3 months, in the control group - 1 month; progression-free survival was $29.2 \pm 17.3\%$.

Conclusions: DC immunotherapy is feasible and safe, this treatment may generate tumor-antigen-specific immune responses in many patients, and has high potential in combination therapy of malignant tumors in children.

V480 SIOP19-1705 | Clonal Evolution in Metastatic Rhabdomyosarcoma

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Background/Objectives: Outcomes for patients with rhabdomyosarcoma (RMS) who have relapsed or refractory disease remain poor. Multiple large-scale tumor genomic profiling efforts have been undertaken, however little is known about its spatial intratumoral heterogeneity (ITH) and temporal clonal evolutionary processes.

Design/Methods: To address this issue, we performed 80x whole genome sequencing of 23 metastases and 2 pre-treatment samples from two patients with lethal rhabdomyosarcoma. Multiregion and spatially separated metastases were available through our research autopsy donation program. RA 17-1 had fusion-positive alveolar RMS, while RA 17-10 had Li-Fraumeni Syndrome and anaplastic embryonal RMS.

Results: We observed on average 65 and 98 coding single nucleotide variants (SNV) per sample in RA 17-1 and RA 17-10 respectively. RA 17-1 was found to have the canonical PAX03-FOXO1 fusion along with MYC-N amplification, which was truncal to all samples. A somatic TP53 mutation in combination with TP53 loss of heterozygosity was present in all metastases sequenced at autopsy, which was not present in pre-treatment biopsy. In RA 17-10 each sample exhibited numerous copy number alterations and complex structural variants, including LOH of TP53, which was truncal to all samples. RA 17-10 had more structural and copy number variations than RA 17-1. Phylogenies were derived based on SNV's and demonstrated a branched evolutionary pattern for each patient. When comparing related samples mutational signatures, several dynamics were apparent, including the predominance of signatures 3 and 8 in metastatic samples, consistent with the fact that both patients harbored TP53 mutations.

Conclusions: Defining important elements of ITH within metastases remains a goal for genomic study in pediatrics, especially in patients with germline predisposition syndromes. Our findings demonstrate the dynamic nature of genomic instability processes, highlighting the importance of longitudinal sampling at the time of recurrence to define treatment effect and the changing mutational landscape in these tumors.

V481 SIOP19-0691 | Identification of Novel RNA Markers for Detection of Minimal Residual Disease in Patients with Rhabdomyosarcoma

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Background/Objectives: Real-time quantitative PCR (qPCR)-based detection of minimal residual disease (MRD) in patients with rhabdomyosarcoma (RMS) can be used for initial staging and monitoring therapy response in bone marrow (BM) and peripheral blood (PB). The PAX3/7-FOXO1 fusion transcript is specific but applicable in only a subset of patients. MYOD1 and Myogenin have been identified as MRD markers, but their expression varies between tumors. Therefore, we aim to extend this panel with new markers to increase sensitivity.

Design/Methods: Candidate genes were selected by comparing gene expression data of RMS tumors and hematological cells of healthy controls followed by extensive qPCR testing in samples of tumors (n=11), control BM (n=25) and PB (n=25). The additional value of a panel was determined in liquid biopsy samples from 20 Dutch RMS patients at diagnosis (19 BM and 20 PB).

Results: We identified two panels of specific qPCR markers for MRD detection in RMS patients in addition to MyoD1, Myogenin, PAX3/7-FOXO1: one for analysis of BM samples (ZIC1, ACTC1, MEGF10, PDLIM3) and one for analysis of PB samples (ZIC1, ACTC1, MEGF10, PDLIM3, SNAI2, CDH11, TMEM47). These markers all showed high, although heterogeneous, expression in RMS tumors and low expression in control BM or PB samples. A threshold for positivity was set. Using the established panel of 3 markers, 3 PB and 3 BM tested positive. However, using the new panel 5 additional PB and 1 additional BM sample tested positive.

Conclusions: We identified 7 novel RNA markers for MRD detection in rhabdomyosarcoma. In a small cohort, we demonstrated that these new markers have an additional value compared to the established panel of 3 markers. In a follow-up study, we will validate the clinical relevance of this panel in

a cohort of 120 patients with RMS on PB and BM taken at diagnosis and during treatment.

V482 SIOP19-0344 | Immunohistochemical Markers Associated with the Presence of PAX3/7-FOXO1 Translocation in Rhabdomyosarcoma Tumours

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Background/Objectives: The most frequent histological types of rhabdomyosarcoma (RMS) in children are embryonal (ERMS) and alveolar (ARMS) tumours. Majority of ARMS are characterized by the presence of PAX3/7-FOXO1 gene fusion and have worse prognosis than fusion gene-negative ARMS. However, identification of PAX3/7-FOXO1 fusion status is challenging when using formalin-fixed, paraffin-embedded (FFPE) material. Microarray analyses revealed several genes whose expression is associated with PAX3/7-FOXO1 fusion status. Therefore we investigated, if immunohistochemical approach may detect surrogate marker genes as indicators of fusion gene-positive RMS.

Design/Methods: 28 RMS patients were included in the analysis, 11 patients with ARMS and 17 patients with ERMS. Immunohistochemistry was applied on FFPE tissues collected at diagnosis. Protein expression of three marker genes were investigated: *TFAP2B* gene using rabbit anti-*TFAP2β* antibody (Santa Cruz Biotechnology, dilution 1:500), *ALK* gene using anti-*ALK* antibody clone D5F3 #3633 (Cell Signaling, dilution 1:250) and *OLIG2* gene using antibody EP112 (Cell Marque) at concentration 1.92 ml/ml. Fluorescence in situ hybridization (FISH) was performed on FFPE sections with FOXO1/PAX3 and/or FOXO1/PAX7 probes (Dual Color Single Fusion Probe, Zytovision) according to the protocols of the manufacturer of the probes.

Results: Our analysis revealed that all three immunohistochemical markers are associated with the presence of PAX3/7-FOXO1 fusion: *TFAP2b* ($p < 0.0001$), *ALK* ($p = 0.0001$) and *OLIG2* ($p = 0.0007$). Four out of 11 ARMS had negative PAX3/7-FOXO1 status and none of them displayed positive reaction with analysed markers. Two originally diagnosed ERMS showed positive reaction with all three markers and both had PAX3-FOXO1 gene fusion. Positive reaction with *TFAP2b* alone in >50% of tumour cells (9 tumours) always was associated with the presence of PAX3/7-FOXO1 rearrangement.

Conclusions: Presented results indicate that *TFAP2b*, *ALK* and *OLIG2* may serve as potential surrogate markers for PAX3/7-FOXO1 status. This immunohistochemical approach

may be especially useful when FISH analyses shows inconclusive result.

V483 SIOP19-1506 | Bioinformatic Identification of Key Genes That May Predict Overall Survival in Rhabdomyosarcoma

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Background/Objectives: Rhabdomyosarcoma (RMS) is the most common soft sarcoma in children. However, the underlying molecular mechanism regulating the carcinogenesis and the potential prognostic biomarkers of RMS are poorly known. This study integrated two cohorts profile datasets to detect genes involved in tumor cell growth and survival.

Design/Methods: Gene expression profiles of GSE28511 and GSE68015 were downloaded from gene expression omnibus (GEO) database. R software and bioconductor packages were used to compare and identify the differentially expressed genes (DEGs) between RMS tissues and normal controls. The common Differentially expressed genes (DEGs) were then subjected to gene ontology (GO) enrichment analysis, ingenuity pathway analysis (IPA), protein-protein interaction (PPI) network analysis as well as survival analysis. Then, the expression of these hub genes in RMS and survival analysis were validated by GEPIA in The Cancer Genome Atlas (TCGA) databases.

Results: A total of 232 up-regulated and 241 down-regulated DEGs were identified. Thirteen hub genes including *CDK1*, *CDC20*, *CCNB1*, *CCNA2*, *CCNB2*, *MAD2L1*, *AURKB*, *BUB1*, *KIF11*, *UBE2C*, *KIF2C*, *CDCA8* and *BUB1B* were selected using the Molecular Complex Detection (MCODE). In TCGA database, the expression level of *CDK1*, *CDC20*, *CCNB1*, *CCNA2*, *CCNB2*, *MAD2L1*, *AURKB*, *BUB1*, *KIF11*, *UBE2C*, *KIF2C*, *CDCA8*, and *BUB1B* in RMS tissue were significantly higher than the normal tissue, which were validated by GEPIA. RMS patients with higher expression level of *CCNA2*, *AURKB*, *CDK1*, *CCNB2*, *MAD2L1*, and *KIF11* in tumors suffered from poorer overall survival (OS) than those with lower level of *CCNA2*, *AURKB*, *CDK1*, *CCNB2*, *MAD2L1*, and *KIF11* (all $P < 0.05$), which were validated in TCGA databases through GEPIA.

Conclusions: This study has identified a registry of novel genes and pathways that play important roles in regulating the initiation and development of RMS. A set of robust potential molecular biomarkers is identified for prognostic prediction, which will provide useful guidance for therapeutic applications.

V484 SIOP19-0134 | Compared Management and Outcome of Children and Adolescent/Young Adult (AYA) with Sarcoma in Reference Centers: An Analysis of 4151 Patients of the Nationwide Netsarc Database

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Background/Objectives: Clinical characteristics, management and outcome of children (0-17 yo; N=1360) and adolescent-young adults (AYA) patients (18-30yo; N=2791) registered in the nationwide NETSARC database from 2010 to 2017 were computed.

Design/Methods: NETSARC (netsarc.org) is a national network of 26 reference sarcoma centers with specialized multidisciplinary tumor boards (MDTB), funded by the French NCI. Since 2010, presentation to an MDTB and central pathological review are mandatory for all sarcomas. Children and AYA represented 3.8% & 7.8% of the 35,784 patients registered in the netsarc.org database. SPSS23.0 was used for statistics.

Results: In children and AYA, 74 and 91 different histotypes are respectively listed. There were more male (56% vs 49%), bone tumors (56% vs 36%), lower limb primary (38% vs 30%), and less tumor of intermediate malignancy (all $p < 0.001$) in children. When documented, tumors were larger (87 vs. 76mm), higher grade (grade3: 71% vs 45%) and more frequently N+/M+ (20% vs 13%) (all $p < 0.001$). p53 germline pathologic variants were more frequent in children (0.4% vs 0.1%, $p < 0.03$), while NF1 were less frequent (0.5% vs 1.9%, $p = 0.001$). The management of (1) children, (2) AYA managed & operated in NETSARC centers, (3) AYA managed outside NETSARC centers were compared: rates of biopsy first (79%, 83% and 60%), imaging per guidelines (80%, 86%, 70%) were different in these 3 groups ($p < 0.0001$ all); Documented R2 resection rates were 7.5%, 4.2%, 17.1% respectively, with 5%, 6% and 12% reoperations ($p < 0.0001$ all). Five years EFS and OS were significantly lower in group (3) ($p < 0.001$) but

similar between group (1) and (2) ($p = 0.1$). In multivariate analysis, group-3 patients had significantly worse EFS and OS, while age < 18 was not an independent parameter.

Conclusions: In this nationwide series, children and AYA with sarcomas had similar OS and EFS. Management of AYA outside NETSARC reference centers yielded worse OS & EFS in uni and multivariate analyses.

V485 SIOP19-1384 | Early Lymphocyte Recovery and Sarcomas: An Extensively Available and Potentially Useful Biomarker as a Good Prognosis Factor

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Background/Objectives: Several authors suggest that an early lymphocyte recovery (ELR) after the first cycle of chemotherapy (ChT) is a favorable prognostic factor in Ewing sarcoma (ES) and osteosarcoma in children. The aim of our study is to determine the association of absolute lymphocyte and neutrophil count (ALC and ANC) post-ChT with overall survival (OS) in children and adolescents with ES, osteosarcoma, rhabdomyosarcoma and non-rhabdomyosarcoma soft tissue sarcomas (NRSTS).

Design/Methods: Retrospective unicentric and observational study in patients younger than 21 years with ES, osteosarcoma, rhabdomyosarcoma and NRSTS, histologically diagnosed between November 1999 and October 2019. Medical records were reviewed and demographic, clinical, analytical and survival data were collected, including ALC at diagnosis and ANC and ALC on day 14 ± 1 post-ChT. Patients with immune pathology, post-transplant tumors, previous ChT or incomplete records were excluded. All patients were treated according to the current international protocols.

Results: Forty-nine patients were included, with 12.79 years of median age at diagnosis. The diagnoses were: eighteen ES (36.7%), 12 osteosarcomas (24.5%), 12 rhabdomyosarcomas (24.5%) and 7 NRSTS (14.3%). Fifteen (30.6%) were metastatic at diagnosis. The 2-year OS and 5-year OS were 85.7% and 72.8%, respectively, without taking into account those patients who have not completed that follow-up time. In ES group, there is a trend towards statistical significance ($p = 0.051$) with greater survival if ALC pre-ChT was ≥ 1400 . In osteosarcoma group, there are statistically significant differences in survival in favor of patients with ANC-14 ≥ 1500 . In rhabdomyosarcoma, there was a trend towards significance ($p = 0.065$) with greater survival if ALC-14 was ≥ 1000 , as well as in relapse probability if ALC-14 < 800 ($p = 0.053$).

Conclusions: In rhabdomyosarcoma, ELR (ALC ≥ 1000 in day +14 post-ChT) may act as a prognostic and potentially useful factor in the stratification of risk. Larger studies should be implemented for these sarcomas in order to verify these results.

V486 SIOP19-0043 | Infant VGLL2-NCOA2 Transcript Sarcoma Does Not Always Have a Benign Behavior

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Background/Objectives: Congenital/infantile spindle cell “rhabdomyosarcomas” with VGLL2-NCOA2 transcript are a rare situation and nowadays better recognized and clearly different from “classical rhabdomyosarcomas” [Mosquera 2013; Alaggio 2016]. As this tumor is associated with a very favorable outcome, the lack of already known metastatic potential might advocate against the need for systemic chemotherapy if they can be adequately excised.

Design/Methods: We present an original case of patient, born with a VGLL2-NCOA2 transcript tumor, who died after delayed malignant transformation.

Results: This boy was born in 2012 after a spontaneous twin pregnancy. Antenatally, US then MRI discovered an isolated right shoulder mass. Delivery was unremarkable at terms. Biopsy at day3 of life showed a spindle cell proliferation without any atypia, nor mitotic activity. At this time, multiplex PCR did not reveal any sarcoma transcript presence (SYT-SSX, ETV6-NTRK3, EWS-FLI-1, PAX-FKHR, EWS-WT1) and suggested diagnosis was “fibromatosis”. Due to the severe shoulder limitation, a medical therapy with intravenous methotrexate-vinblastine was started against this unresectable lesion. Hematologic tolerance was poor, and therapy was stopped after 3 months after a minor local response (-25%). Residual mass progressively spontaneously reduced during subsequent years. At 3 year of age, a homolateral supraclavicular nodal mass occurred concomitant to the increase of the residual shoulder mass. New biopsies showed a high grade malignant proliferative sarcoma aspect, with a dramatic change in the pathologic aspect. In 2015, new somatic molecular somatic characterization found a VGLL2-NCOA2 fusion transcript, retrospectively present at birth in the initial “benign” lesion. Patient died from bone and pulmonary metastasis despite multiples aggressive chemotherapy regimens 20 months after malignant transformation.

Conclusions: Even if all cases of sarcoma with VGLL2-NCOA2 transcript published in literature to date do favorably with a quite conservative strategy, we present a unique, biologically well documented, unfavorable case. This case adds to the general knowledge of infantile sarcoma with VGLL2-NCOA2.

V487 SIOP19-0259 | First Experience of LOXO-292 in the Management of Pediatric Patients with RET-Altered Cancers

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Background/Objectives: Genomic alterations of *RET* kinase, including chromosomal fusions and activating point mutations, have been identified as oncogenic drivers in pediatric and adult cancers. Multikinase inhibitors have modest activity against *RET*-altered cancers and are associated with significant toxicity. LOXO-292 is a potent, ATP-competitive, small molecule *RET* inhibitor with high selectivity for *RET*, preclinical activity in the brain and excellent pharmacokinetic properties. In an ongoing phase 1/2 study of adult and adolescent patients with advanced *RET*-altered cancers, LOXO-292 demonstrated marked antitumor activity and was well tolerated

Design/Methods: Pediatric patients with *RET*-altered cancers who were unable to access LOXO-292 through the phase 1/2 clinical trial were enrolled using FDA-allowed, IRB-approved single patient protocols. Patients received LOXO-292 (capsule/liquid formulation) orally, continuously, at a starting dose of 90 mg/m²BID. Response was assessed locally by investigators.

Results: As of March 31, 2019, 5 patients (4 female, 1 male) aged 13 months–8 years were enrolled from the Republic of Korea (papillary thyroid cancer, n=1), France (medullary thyroid cancer, n=1) and the USA (infantile myofibroma/hemangiopericytoma, n=1; congenital mesoblastic nephroma/infantile fibrosarcoma, n=1; lipofibromatosis, n=1). All tumors harbored *RET* gene fusions (5' partners: *CCDC6*, *MYH10*, *SPECCIL*, and *NCOA4*, respectively) or activating *RET* mutations (C918), detected by next-generation sequencing. Previous therapies included surgery/iodine 131 (n=1); vandetanib (n=2); surgery/chemotherapy (n=1); 1 patient was treatment-naïve. Duration of treatment ranged from 3–179 days and all patients

remain on treatment. There were no dose modifications or discontinuations due to adverse events. There were no treatment-related adverse events $\geq$ grade 3. Four patients who were evaluable for response had partial responses (all ongoing, 2 confirmed, 2 unconfirmed pending confirmation).

Conclusions: These preliminary data from a real-world setting suggest that LOXO-292 is effective and safe in pediatric patients whose tumors harbor *RET* gene fusions.

V488 SIOP19-0802 | Extra Skeletal Ewing's Sarcoma. Treatment and Prognosis at the National Institute of Pediatrics in Mexico

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Background/Objectives: Introduction: Ewing's sarcoma is the second most common bone tumor in childhood, the annual incidence is 2.9: 100,000. The time between the onset of symptoms and the diagnosis is between 2 and 9 months. The bones are the most frequent site of presentation, however it can present as an extra skeletal tumor, which corresponds to 5 to 15% of cases.

Objective: To evaluate the frequency of presentation of extra skeletal Ewing's sarcoma, as well as the treatment and survival at the National Institute of Pediatrics.

Design/Methods: Methods: A cohort study was conducted in patients with Ewing Sarcoma from January 2007 to July 2018, at the National Institute of Pediatrics in Mexico.

Results: In the study period, 50 patients with Ewing's Sarcoma were included, of which 11 (22%) were of extra skeletal presentation. Of these, the most frequent presentation sites were: muscle 63.3% (thigh 36.3%, parasternal 18.2%, and subscapular 9.1%), visceral 27.3% (kidney 18.2%, pancreas 9.1%) and others 9.1%. 7 (63.3%) patients presented metastasis at diagnosis. All were treated with chemotherapy with the national protocol corresponding to 9 courses of vincristine, doxorubicin, and cyclophosphamide, alternated with ifosfamide and etoposide, and radiotherapy. 50% of patients with metastasis at diagnosis received consolidation treatment with autologous bone marrow transplant. 2 patients had progression of the disease, received second line of treatment with irinotecan, temozolamide and bevacizumab, without response, both patients died of progressive disease. Overall survival was 81.8%, compared to patients with bone Ewing's sarcoma who had a total survival of 69% ($p = 0.05$).

Conclusions: Conclusions: The extra skeletal Ewing's sarcoma is uncommon in the pediatric population, with adequate treatment with chemotherapy, radiotherapy and consolidation with autologous transplantation, the possibility of survival

is high compared to those patients with bone presentation. Patients with progression of the disease have an unfavorable prognosis.

V489 SIOP19-0903 | Dramatic Response to Imatinib in Generalized Type of Infantile Myofibromatosis

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Background/Objectives: Generalized Infantile myofibromatosis (G-IM) is exceptional, develops during infancy and is characterized by numerous tumors in skin, subcutaneous tissues, muscles, bones and, viscera. In life-threatening situation, low-dosage chemotherapy is used with nevertheless slow efficiency. Mutations in the coding sequence of *PDGFR- β* were identified in most sporadic multicentric forms of the disease.

Design/Methods: We present a biologically well documented original case of an infant with life-threatening G-IM who presented a dramatic response to imatinib-mesylate, a tyrosine kinase inhibitor (TKI) against *PDGFR*.

Results: A foetal multicentric G-IM was evoked at 36 weeks of gestation on ultrasound. MRI performed immediately after birth showed disseminated lesions in skin diffuse multiple skin, subcutaneous tissue, skeletal muscle, bone and pulmonary lesions. Diagnosis was confirmed by the histological analysis of a skin lesion. Immunohistochemistry was negative for *PDGFR*. The new-born developed severe exudative enteropathy at day 15 of life and worsened with signs of respiratory distress due to multiple bilateral lung lesions. He required intensive care unit transfer, and despite intravenous steroid and vinblastine-methotrexate started at day 22, needed an artificial ventilation. Due to severe respiratory insufficiency with refractory hypoxemia and hypoxic bradycardia, a compassionate oral imatinib treatment (20 mg/d) was added at day 31. The respiratory status dramatically improved in 48h allowing tube removal 9 days after initiation of imatinib. Patient was discharged 20 days later. Chemotherapy was continued for 6 months, and imatinib for 9 months with regular dosages with an excellent tolerance. Complete remis-

sion was reached after six months and is maintained 2 years later. Somatic genetic analyses retrospectively confirmed a PDGFR- β gene mutation (Asn666Lys).

Conclusions: Despite the rarity of this disease, this original experience of the efficacy of imatinib gives a new efficient option in the armamentarium of systemic therapy in life-threatening situations for generalized infantile myofibromatosis.

V490 SIOP19-0502 | Pediatric Prostate/Bladder Rhabdomyosarcoma: Single Center Experience in Russia

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Background/Objectives: Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma in childhood and 15% to 20% arise from the genitourinary tract. The aim of the study was to analyze the results of therapy of prostate/bladder RMS (PB-RMS) in children treated in federal center in Russian Federation.

Design/Methods: All prospectively registered patients with PB-RMS treated during the period 02.2012 - 02.2018 were included. Diagnosis was confirmed by histology. All patients were examined and stratified according to the GPOH Cooperative Weichteilsarkom Study (CWS) Group guidance 2009.

Results: Eleven patients with a median age at diagnosis of 23.7 months (range 0.33–49.6) have been included. Male to female ratio was 2.6:1. Tumor was detected prenatally in 1/11 (9%). Histopathologic types of RMS included embryonal (n=9;82%), alveolar (n=1;9%), spindle cell (n=1; 9%). In 8/11 (72%) patient tumor size was more than 5 cm. The median tumor volume was 120.5 ml (range 9–3120 ml). In 2/11 (18%) patients tumor invaded prostate. 2/11 (18%) had IRS group II, while 7/11 (63%) - group III, 2/11 (18%) - group IV. All patients received chemotherapy. Initial surgery included biopsy in 6/11 (55%), surgery – 5/11 (45%) (R1- 2, R2- 3 patients). Local control was provided to all patients: only radiotherapy in 2/11 (18%), only surgery in 2/11 (18%), distant radiotherapy and surgery in 6/11 (55%), brachytherapy and surgery in 1/11 (9%). Second-look surgery was performed in 4/11 (36%) (cystectomy -2, bladder resection -2). Median follow-up time was 40.2 months (range 7.8-72.5). 1/11 (9%) event was observed (local relapse). 10 patients

were alive, 1 died. 3-year overall and event-free survival was 88.9%±10.4%.

Conclusions: The prognosis of patients with PB-RMS receiving program therapy was favorable. Mutilating surgery was avoided in 82% of cases, but at the cost of widespread use of radiation therapy.

V491 SIOP19-0089 | Endothelial Cell Malignancies in Infants, Children and Adolescents: Treatment Results of Three Cooperative Weichteilsarkom Studiengruppe (CWS) Trials and One Registry

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Background/Objectives: Objective. To analyze clinical course, treatment and outcome in patients with endothelial cell malignancies treated within the CWS-91, -96, -2002P trials and the registry SoTiSaR (1991-2017).

Background. Endothelial cell malignancies are extremely rare in childhood. New identification of genetic abnormalities (WTR1:CAMTA1 translocation) help to recognize potential therapeutic targets. Little is known about treatment and outcome of these patients.

Design/Methods: Methods. Patients had angiosarcoma (AS) (n=12), epithelioid hemangioendothelioma (HE) (n=16) and kaposiform HE (HEkap) (n=13). Therapy consisted of chemotherapy (CHT) (n=24/41), interferon or new agent therapy (n=6), resection (n=21/41) and radiotherapy (n=9/41).

Results: Median age was 5.39 years [range: 0.8–17.34], 32 patients had localized disease (LD), 9 patients had metastatic disease (MD) (AS n=3, HE n=6). Objective response (OR) to CHT was 6/12 (50%), stable disease in 5/12 (42%), OR to new

agent therapy 1/4 (25%). Two patients (HEkap) had watch and wait strategy resulting in stable disease. Complete resection was possible in 10 patients with LD, complete remission was achieved in 25/41 (61%) patients. Relapse occurred after a median time of 1.03 years (range 0.13-1.99) in 4 patients. The 5-year EFS and OS for patients with AS was 64% ($\pm$ 29 CI 95%) and 80% ($\pm$ 25, CI 95%), with HE 62% ($\pm$ 24, CI 95%) and 78% ($\pm$ 23, CI 95%), and with HEkap 33% ($\pm$ 34, CI 95%) and 92% ($\pm$ 15, CI 95%), respectively. The only significant prognostic factor was metastatic disease for poor OS.

Conclusions: Endothelial cell malignancies in childhood have a fair outcome with multimodal treatment. New treatment options are needed for metastatic disease.

V492 SIOP19-1325 | Liquid Biopsy in Soft Tissue Sarcoma (STS) - Project of the CWS (Cooperative Weichteilsarkom Studiengruppe)

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Background/Objectives: The principal possibility for application of cell free (cf) DNA/RNA as tumor specific and non invasive liquid biopsy biomarker in patients with STS is investigated in a CWS accompanying biological project and provides first results.

Design/Methods: Twenty four patients with alveolar Rhabdomyosarcoma (ARMS) and tumors positive for PAX3-FOXO1 fusion, all entered in the CWS SoTiSaR registry, were included in our preliminary analysis. Six patients had initially localized tumors (IRS I n=1, IRS III n=5), 18 patients were initially metastasized (IRS IV). From initial blood samples plasma fractions were collected, cryoconserved and used for isolation of cf exosomal RNA. By RT-PCR analysis we searched for PAX3-FOXO1 fusion transcripts.

Results: PAX3-FOXO1 fusion transcripts were not found in plasma from patients with primary localized disease. Half of IRS IV patients were positive for PAX3-FOXO1 fusion transcripts in plasma (n=9). Seven of these patients had bone marrow (bm) involvement.

Conclusions: Detection of PAX3-FOXO1 fusion transcripts by RT-PCR in blood plasma originating cf exosomal RNA from patients with ARMS is possible. There is a good correlation between tumor dissemination and positivity of blood plasma. PAX-FOXO1 fusion transcripts represent promising biomarkers for non invasive liquid biopsy procedures in ARMS. Further optimization, validation and the application of liquid biopsy to other cfRNA/cfDNA markers in diagnostics and monitoring of Soft Tissue Sarcoma is ongoing.

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V493 SIOP19-0532 | Clinical Characteristics and Treatment Outcome of Synovial Sarcoma in Children- A Single Centre Experience from South India

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Background/Objectives: Soft tissue sarcoma (STS) comprises 7% of all malignancies in children. Synovial sarcoma (SS) accounts for 7-8% of STS in children. There is scarcity of data regarding outcome in resource limited countries.

Design/Methods: Children, $\leq$ 14 years of age, diagnosed as SS from January 2007 to December 2017, were included for retrospective analysis. 3 year event free survival (EFS) and overall survival (OS) were noted and outcomes were correlated with stage, and post surgery margin status.

Results: Fifty nine children were diagnosed as non-rhabdomyosarcoma soft tissue sarcoma, of which 15 (25%) had SS. Mean age at the time of presentation was 122 months (Range 54 - 168). Stage I, II, III and IV disease were seen in 0 (0%), 9 (60%), 5 (33%) and 1 (7%) children, respectively. Four (27%), 4 (27%), 6 (40%), and 1 (6%) children had group I, II, III and IV disease, respectively. One child was lost to follow up. All 14 children, who received treatment, underwent surgery. Eleven (78%) children received chemotherapy and 8 (57%) received radiation. Four (28%) children had relapse and 1 (7%) had progressive disease, out of which 3 children died. At a median follow up of 50 months (Range 18-125) 3 year EFS and OS were 76.2% and 85.1%, respectively. 3 year EFS for stage II, III and IV disease was 72.9%, 40%, and 100%, respectively (P=0.674). 3 year OS for stage II, III and IV disease was 87%, 80%, and 100%, respectively (P=0.247). 3 year EFS of children with post surgery margin positive and negative status was 55.6% and 72.9%, respectively. (P=0.717).

Conclusions: 3 year EFS and OS of children with SS in India are comparable to western countries. Advanced stage, and post surgery residual disease did not affect outcome in children with SS.

V494 SIOP19-1228 | Pattern of Relapse in Localized Limbs Rhabdomyosarcomas According to Loco-Regional Therapies: The French SFCE Contribution

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Background/Objectives: Radiotherapy is the treatment of choice of involved lymph node area in localized limbs rhabdomyosarcomas (L-RMS) without considering intermediary relays. We analyzed the correlation between the pattern of relapse of non-metastatic L-RMS and initial therapies delivered.

Design/Methods: Patients with localized L-RMS±positive regional lymph nodes at diagnosis treated in France from 2005 to 2013 in RMS-05 protocol were selected. All patients received chemotherapy according to risk factors. Local treatment included surgery and radiotherapy to primary site ±involved lymph nodes area. Initial extent of the disease was determined using clinical, imaging, and surgical methods.

Results: We identified 47 patients, median age 4.7years (range: 1 month-18 years). Initial tumor assessment comprised MRI in 41 patients and PET in 26 patients. Among 2 patients with clinical enlarge nodes and 23 with abnormal imaging, only 15 patients (32%) were confirmed to have lymph node involvement after histologic confirmation, only present in inguinal or axillar area. Non guided surgical biopsy detected 12/15 nodal involvement and sentinel node biopsy reveals 2 tumor spreads. Primary surgery was performed in 43 patients (10 immediate and 37 delayed surgery, including 2 both) and 35 received radiotherapy (on primary 19 cases; with regional nodal area 15 cases; only nodes 1 case). After a median follow-up of 69 months (range, 6-129), 13 relapses occurred: 7 local (3 in previous irradiated fields), 3 nodal (2 in irradiated fields), 3 metastatic, and 1 combined (nodal previously irradiated and metastatic). Five-year Event Free Survival is 63.9%, IC95%[51.2%-79.9%], and Overall Survival 73.5%, IC95%[60.4%-89.4%].

Conclusions: Limbs RMS failures are mainly local (54%). Isolated nodal failures are rare (6%) with systematic irradiation of initial involved area. This study pleads against systematic expand of regional nodal irradiation fields to non-involved area in L-RMS. To propose an optimal tumor assessment, systematic nodal biopsy could be more systematically advised in this poor primary location.

V495 SIOP19-0580 | ADMG-MYOGP-E1-5/3F, MYOG Promoter-Controlled Oncolytic Adenovirus, Kills Rhabdomyosarcoma Cells Selectively In Vivo

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Background/Objectives: The specific cytogenetic abnormality of about 80% of patients with alveolar Rhabdomyosarcoma (ARMS) is *PAX3-FOXO1* fusion-gene, and the prognosis of *PAX3-FOXO1*⁺ ARMS is much worse than that of the others. Novel therapeutics for the treatment of *PAX3-FOXO1*⁺ ARMS are desperately needed.

Myogenic regulatory factors, MYOD1 and myogenin (MYOG), play important roles for the process of skeletal muscle differentiation. Interestingly, when the MEF2 binding site in MYOG promoter (MYOGp) was mutated (mMEF2), MYOD transactivation was abolished, but the *PAX3-FOXO1* transactivation was not affected. This means MYOGp-controlled OAd with mMEF2 can be activated in only *PAX3-FOXO1*⁺ RMS cells.

Design/Methods: To analyze the antitumor effect in an *in vivo* model, 2×10^6 of Rh30 cells were inoculated subcutaneously into the nude mice, and 3×10^{10} vp of the selected or control viruses were intratumorally injected. The tumor diameter was measured twice a week. In a separate experiment under the same conditions, the mice were killed at day 5 and 10. The DNA of the tumor specimens was purified from frozen tumor tissue, and the adenoviral DNA copy number was quantified by qPCR. Additionally, the expression of adenoviral hexon protein in the tumor was analyzed by immunostaining.

Results: The administration of AdMG-MYOGp-5/3F with or without mMEF2 exhibited significant antitumor effect *in vivo*. The virus copy number in tumors treated with both MYOGp-controlled OAds showed the similar degree as AdMG-5/3F. The staining of virus hexon in the tumor specimens at days 5 and 10 after injection showed the vast majority of cells in the Rh30 tumors treated with MYOGp-controlled OAds expressed high levels of hexon protein.

Conclusions: Our findings indicated the applicability of MYOGp for the design of oncolytic adenovirus for RMS. With mutation in MEF2 binding site, MYOGp-controlled OAd might be more useful to enhance its specificity and safety.

V496 SIOP19-1008 | Efficacy of Second Line Therapy in Young Patients After Relapsed or Refractory Orbital Rhabdomyosarcoma

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Background/Objectives: Localized orbital rhabdomyosarcoma (o-RMS) has an overall favorable prognosis with more than 90% of survival. Little is known about the best strategy in case of recurrent/refractory (R/R) situation. Aim is to examine the characteristics of patients with R/R-oRMS focusing on local therapy.

Design/Methods: Monocentric retrospective analysis of all consecutive young patients (<30 years) with R/R-oRMS treated from 1989 to 2018 in Institut Curie.

Results: Twenty-two patients out of 133 patients with oRMS (17%) presented R/R disease. Alveolar RMS concerned 5 patients (23%) with 3 parameningeal extension (14%). During first-line, 16 patients (72%) had orbital radiotherapy and none had surgery. All patients received chemotherapy as first and second line. Median age at R/R was 8.4 years (ranges: 4.2- 28.1) after a delay of 19.4 months from diagnosis (ranges: 3.3-33.4). Tumor events was refractory disease (3 cases), local relapse (17 cases), metastatic relapse (2 cases), and no cervical relapse. Second line local treatment comprised orbital radiotherapy (16 cases, including brachytherapy 1case), surgery (exenteration 6 cases, with R0 margins in all cases; wide eyelid resection 1 case with R0margins) and metastasis removal (2 cases). After a median follow-up of 89 months (ranges: 10-231), 3 patients died of disease, 19 were in complete remission (CR) without treatment (CR218patients, CR31 patient). Three year-event-free survival (EFS) and overall survival (OS) after tumor event are respectively 83.3% (74.5%- 92.1%) and 86.3% (81.5%-96.3%).

Conclusions: R/R-oRMS is a rare situation. Second line therapy is efficient but at the price of mutilating surgery up to 37% of survivors that can be lifesaving. Second line local therapy should therefore include orbital radiotherapy (in the absence of previous irradiation) or complete R0 surgery aimed to be complete, even at the cost of an exenteration (if relapse occurred after irradiation).

Survivorship

V497 SIOP19-1394 | Clusters of Health Behaviors and Their Determinants Among Adult Survivors of Childhood Cancer

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Background/Objectives: Health behaviors are generally studied separately, despite the existing evidence suggesting that health risk behaviors were not independent. To our knowledge, there are few studies have examined the clustering of healthy risk behaviors among childhood cancer survivors.

Design/Methods: The present study focused on the 3149 patients treated in France for solid cancers in childhood who sent back the questionnaire. Latent class analysis was used to identify health behavior patterns using data regarding physical activity, unhealthy eating behaviors (current body mass index), smoking, cannabis use, and alcohol consumption. Multinomial logistic regression analysis was used to examine the associations between these latent health behavior patterns and demographic, social, health, and treatment-related risk factors.

Results: Three health behavior patterns emerged: 'Low-risk' (n = 1099, 34.90%), included the participants who exhibited the lowest probabilities for all risk behaviors; 'Insufficiently active' (n = 1459, 46.33%), and 'High-risk' (n = 591, 18.77%) for survivors who exhibited the highest probabilities for smoking (≤10 cigarettes per day, 11 to 20 cigarettes per day, or ≥ 21 cigarettes per day), cannabis use, and alcohol consumption (≥ 3 drinks per week). The multinomial logistic regression analysis revealed that males survivors, with beyond high school, age at first cancer from 12 years, and treated by radiation therapy alone or no radiotherapy and nor chemotherapy were significantly more likely to be in the high-risk group than the low-risk group.

Conclusions: As childhood cancer survivors remain a vulnerable population, to characterize survivor groups according to their health risk behaviors and to identify its potential predictors are important to motivate behavioral change. Ours findings are important for clinicians supervising this population's health care for targeted health interventions on modifiable behaviors for the high-risk group in particular.

V498 SIOP19-1648 | Risk of Developing Leukemia After Chemotherapy and Radiotherapy for Childhood Cancer: An International Pooled Analysis

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Background/Objectives: Previous studies of childhood cancer survivors have demonstrated increased risk for therapy-related leukemias. However, studies had limited numbers of subjects, limiting understanding of risks associated with specific treatments.

Design/Methods: We initiated collaborative analyses of studies with detailed treatment data to more thoroughly investigate the respective roles of radiotherapy and chemotherapy in the occurrence of therapy-related leukemia after childhood cancer, pooling 147 therapy-related leukemia cases and 522 individually-matched controls (childhood cancer survivors with no secondary leukemia) from France, Great Britain, and an American-led consortium. Radiation dose to the active bone marrow and cumulative doses of chemotherapy were calculated based on data abstracted from medical records; pooled multivariable odds ratios (OR) were calculated using conditional logistic regression.

Results: For the combined data, the unadjusted OR associated was significantly elevated for both chemotherapy (OR = 6.2, 95% CI: 2.9–13.3) and radiotherapy (OR = 1.6, 95% CI: 1.0–2.4). However, when chemotherapy and radiotherapy were included simultaneously in a multivariable analysis, the OR for chemotherapy remained similar (OR = 6.1, 95% CI: 2.8–13.2), but the radiotherapy-related risk estimate was slightly attenuated (OR = 1.5, 95% CI: 0.98–2.3). In the multivariable model including radiation dose to the active bone marrow and cumulative exposure to topoisomerase II inhibitors (anthracyclines and epipodophyllotoxins), alkylating agents, platinum compounds, and vinca-alkaloids, only topoisomerase II inhibitors were independently associated with an increased therapy-related leukemia risk (OR = 4.1, 95% CI: 2.2–7.7) and the risk increased with increasing cumulative dose of topoisomerase II inhibitors (P-trend = 0.0002). Risk was even higher (OR = 14.5, 95%CI: 5.2–40.3) when patients received both topoisomerase II inhibitors and alkylating agents, compared to childhood cancer survivors who did not receive chemotherapy.

Conclusions: These results are particularly important given increases in topoisomerase II inhibitors use in current treatment approaches and have implications for the follow-up of childhood cancer survivors for therapy-related leukemia.

V499 SIOP19-1582 | Lipid Factors Associated to Metabolic Syndrome in Childhood Cancer Survivors

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Background/Objectives: Survivors of childhood cancer appear to have an increased risk for metabolic syndrome (MetS), type 2 diabetes and cardiovascular disease. The diagnostic criteria of MetS include abdominal obesity, high triglyceride (TG $\geq$ 150mg/dl), low high-density lipoprotein cholesterol (HDL-C $<$ 40mg/dl), high blood pressure and high fasting glucose (GLU $\geq$ 100 mg/dl). There are studies showing that individuals with MetS have higher uric acid (UA) levels. The purpose of this study was to investigate the frequency of associated to MetS factors in childhood cancer survivors.

Design/Methods: Children and adolescents with hematologic malignancies, at least six months after chemotherapy completion underwent clinical evaluation, liver ultrasonography, fasting blood lipid profile, GLU and UA assessment. Body mass index (BMI) was also calculated.

Results: A total of 30 patients, 18 with acute leukemia (mean age $\pm$ SD; 12.7 $\pm$ 3.8 years) and 12 with lymphoma (14.5 $\pm$ 3.3 years) participated in the study. Patients had already completed treatment 21.6 $\pm$ 13.6 months (leukemia group) and 19.3 $\pm$ 11.5 months (lymphoma group). Among patients with leukemia, 23.5% had normal weight and 76.5% were overweight/obese, whereas among patients with lymphoma, 58.3% had normal weight and 41.7% were overweight/obese. GLU concentration in leukemia group was 82,72 $\pm$ 9,3 mg/dl and lipids' concentrations were HDL 57,5 $\pm$ 13 mg/dl, TG 76,9 $\pm$ 30,5 mg/dl, UA 4,8 $\pm$ 1.7 mg/dl, while in lymphoma group we found: GLU 81,17 $\pm$ 7,37 mg/dl, HDL 63,3 $\pm$ 14,7 mg/dl, TG 67,1 $\pm$ 26 mg/dl and UA 4,5 $\pm$ 1,5 mg/dl. Fatty liver infiltration had 33,3% and 16,7%, among patients with leukemia and lymphoma, respectively.

Conclusions: Although in this cohort GLU, TG and HDL-C were not diagnostic for MetS, childhood cancer survivors should have thorough long-term metabolic evaluation in order to detect, manage or prevent cardiovascular disease.

V500 SIOP19-1467 | Feasibility of Ready Steady Go and Worry Memory Thermometer as a Patient Experience Tool in the Transition Pathway in a Tertiary Long Term Follow-Up Service

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Background/Objectives: Over two-thirds of childhood cancer survivors develop late effects related to their treatment. Key challenges are engaging the cancer survivor in education and empowering their self-care through a sustainable transition pathway. In our tertiary paediatric/Teenage and Young Adolescent (TYA) oncology long-term follow-up (LTFU) service we initiated a transition programme. “Ready Steady Go (RSG)” and a psychological screening tool, “Worry and Memory Thermometer (WMT)” to deliver a pathway that encompassed education and self-management in an integrated transition process. We describe this process and patient experience.

Design/Methods: We established a patient pathway including, age appropriate consultations. Treatment summaries and care plans were utilised to support holistic multidisciplinary team decisions. On attending clinic, survivors completed the RSG to identify existing knowledge and skills, and any gaps to be addressed in the clinic. We calculated attendance, discharges, usage of RSG and WMT, and clinic outcomes. Patient experience was collected by verbal feedback following the consultation.

Results: In a 24 month period 178 patients attended 59 clinics, 43 did not attend. RSG was completed by 89 patients aged 12 and over. 20 patients were discharged to primary care, 158 continued hospital follow up. Patients were also transitioned to young adult LTFU or BMT LTFU clinics with support. Issues of self-esteem and coping with life were identified needing clinical psychology referral. Patient experience with RSG was reported as “good to be given the opportunity”, “empowering”, “not daunting”.

Conclusions: RSG and WMT are feasible in a busy LTFU clinic with the appropriate nursing support. These tools enabled delivery of a needs-led service that can equip and empower young cancer survivors, and identified patients who benefited from referral to clinical psychology. The patient/carer experience was positive. Further developments are planned including shared electronic health records to improve the efficiency and engagement in this transition.

V501 SIOP19-0059 | The Evaluation of Late Effects During 16-Year Follow-Up of Pediatric Hodgkin Lymphoma Survivors: The Ankara University Faculty of Medicine Pediatric Oncology Department Experience

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Background/Objectives: Hodgkin lymphoma (HL) is a curable malignancy. However, survivors experience pulmonary, cardiovascular, endocrine sequelae and secondary malignancies. The purpose of this study was to compare health status of HL survivors (HLS) and apparently healthy population (their siblings) matched by age, gender.

Design/Methods: A total of 51 patients who completed their HL treatment between 2003 and 2019 were included in the study. The data related to heart, kidney disease, thyroid dysfunction, smoking, alcohol consumption, marital and parenting status, education, the use of health care services of the HLS were compared with their own siblings (n= 56). Information was obtained retrospectively from the patient charts and by contacting the families by phone. Kaplan-Meier life analysis, Chi-square and independent sample t-test were used as statistical methods.

Results: The age and gender ratios were similar in the HLSs and the control group. The rates of kidney (p = 0.033), heart disease (p = 0.016), thyroid dysfunction (p = 0.002), health care service admissions (p < 0.001), physical function limitations (p < 0.001) and pulmonary disease (p = 0.02) were significantly higher in the survivors than in the siblings. The rates of being married (p = 0.004), parenting (p = 0.007), being educated (p = 0.003), smoking (p = 0.022) were significantly higher in the control group than in the HLSs. The alcohol use and psychiatric treatment were similar in both groups. Secondary malignancy was not detected in HLS group. Thyroid dysfunction was higher in the neck radiotherapy (RT) group (p < 0.01). We couldn't show association between thorax radiotherapy and cardiotoxicity probably due to only involved field RT.

Conclusions: Heart, kidney disease, physical and thyroid dysfunction were significantly higher in survivors with HL than their siblings during the 16 years of follow-up. The social status (marriage, parenting, education) of the patients was also found to be markedly affected negatively. Thyroid dysfunction was strongly associated with neck radiotherapy.

V502 SIOP19-0314 | Report of Cancer Therapy-Related Late Sequelae Among Long-Term Osteosarcoma Survivors Treated Between 1997-2015 at Instituto Nacional de Pediatría, Mexico City, Mexico

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Background/Objectives: Osteosarcoma is the most common primary malignant tumor of bone in children and adolescents. Nowadays, with combined systemic chemotherapy and local surgical control the 5-year disease-free survival rate is 60-70% in localized disease. Survival of patients with limited and resectable metastases can reach up to 50%. Due to the increasing number of osteosarcoma survivors, adequate knowledge of therapy-related long-term complications for their timely approach and prevention is necessary.

Design/Methods: Retrospective and clinical study of late sequelae among patients with osteosarcoma treated at Instituto Nacional de Pediatría between 1997-2015.

Results: 101 patients with osteosarcoma were included. At diagnosis a similar gender incidence and a mean age of 11.44 years (2-17 years old range) were observed, most frequent involvement sites were long bones of lower extremities (80%), with the osteoblastic type predominating (60%); most common symptoms were pain (76%), volume increase (58%), functional limitation (31%), and pathological fracture (9%); 63% presented with metastases (97% pulmonary). Ninety five percent of patients received a chemotherapy scheme based on doxorubicin, cisplatin, methotrexate, cyclophosphamide or ifosfamide, and etoposide, 32% underwent an amputation surgery, 27% had a disarticulation, and 24% a limb-sparing surgery; 57.4% presented some type of toxicity (acute and/or chronic) and 83% of these cases presented one or more late sequelae. In the long-term follow-up, most frequently observed late effects were ototoxicity (19%), nephrotoxicity (17%), cardiotoxicity (8%) and neurotoxicity (6%); 19% presented some type of psychological disorder, depression associated with anxiety was the most frequent. One case of second malignant neoplasia was documented (acute lymphoblastic leukemia) 84 months after treatment. Fifty five percent of the patients remain under surveillance without tumor activity at 119 months follow-up.

Conclusions: We observed a high number of therapy-related long-term sequelae among patients with osteosarcoma, implementation of protocols to prevent and decrease them are necessary.

V503 SIOP19-0316 | Cancer Therapy-Related Late Effects Among Long-Term Wilms Tumor Survivors in a 20-Year Period at Instituto Nacional de Pediatría, Mexico City, Mexico

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Background/Objectives: Therapy with surgery, chemotherapy and radiation therapy (RT) cures more than 90% of chil-

dren with Wilms tumor (WT), however, despite adequate rationalization of these treatments, risk of presenting therapy-related short- and long-term sequelae remains latent and intensifies over time and may not become apparent until years later as the child matures. Our results provided a notion of therapy-related late effects in our patients with WT and a guide for their approach and prevention.

Design/Methods: Retrospective and clinical study of late effects among WT survivors treated at Instituto Nacional de Pediatría between 1990-2010.

Results: Forty eight patients were included, 26 girls (54%) and 22 boys (46%). At diagnosis, median age was 32.4 months (6-96 months range), 2 had associated genetic syndromes (AGS), Denys-Drash and Beckwith-Wiedemann syndromes, there were 4 (8.3%) stage-I, 3 (6.2%) stage-II, 20 (41.6%) stage-III, 14 (29%) stage-IV (pulmonary metastases) and 7 (14.5%) stage-V. Three (6.2%) had diffuse anaplasia. All patients received a clinical-trials-NWTSG-based treatment. Median follow-up time was 10-year (5-20-year range). EFS and OS rates over 10-year for unilateral and bilateral WT were 83.3% and 88.9%, and 60% and 85.7%, respectively. Chronic conditions development cumulative incidence among long-term WT survivors was 18.4%. There were 2% doxorubicin-induced late cardiotoxicity (> 250mg/m2 cumulative dose, RR 0.16), 4.1% no-related AGS end-stage renal disease, and 8.3% RT-related musculoskeletal disorders (RR 0.7). There was not RT-induced lung damage or second malignancies. Twenty-year mortality rate was 16.1%.

Conclusions: Long-term WT survivors at our institution have a morbidity and mortality risk and survival rates similar to survivors population of other countries. Due increased number of worldwide WT survivors, a lifelong surveillance systematic plan for these patients is necessary in all hospitals treating childhood cancer, focused on prevention, early diagnosis and treatment of their chronic comorbid health conditions.

V504 SIOP19-0465 | Incidence and 5 Years Survival Rates of Childhood Cancer Diagnosed Less Than 1 Year Old in Ireland 2007-2017

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Background/Objectives: According to the National Cancer Registry of Ireland, an average of 137 cancers were diagnosed per year in children under the age of 15 between 1994 and 2014. The 5-year overall survival rate for this entire cohort was 81%. It is well documented that survival rates in paediatric oncology vary depending on specific cancer diagnosis, age of the patient at diagnosis and disease stage. We describe the incidence of cancer in very young children and the

influence of age on outcome in children diagnosed with cancer in Ireland under the age of 1 between 2007-2017.

Design/Methods: Data were extracted from the database of the National Children's Cancer Service (NCCS) based at Our Lady's Children's Hospital, Dublin. The data presented refer to the International Classification of Childhood Cancer (ICCC) version 3 with the inclusion of Langerhans Cell Histiocytosis (LCH).

Results: 185 patients were diagnosed with paediatric cancer under the age of 1 at the time of their initial diagnosis. 159 (85.5%) patients were diagnosed with solid tumours or LCH. 86 (46.5%) were male. The average age at diagnosis was 5.24 (range 0-12) months. Nineteen (10.3%) patients were diagnosed following an abnormal antenatal scan. The most common cancers diagnosed were neuroblastoma (22.7%), central nervous system (CNS) tumours (19.5%) and leukaemia (13.5%). 158 (85.5%) patients received treatment. 124 (78.4%) and 20 (12.7%) patients received chemotherapy and radiotherapy as part of their treatment respectively. The mean age for radiotherapy was 1.35 years (range 0.17-4). The cumulative overall survival rate at 5 years is 80%. CNS tumours have the worst prognosis followed by leukaemias.

Conclusions: Incidence rates of specific paediatric cancer types vary according to the age at diagnosis. There is no difference in survival rates between children diagnosed with cancer under 1 year of age and older children. Outcomes at the NCCS compare favourably with international standards.

V505 SIOP19-0169 | Vascular Malformations and Endocrinopathies After Radiotherapy in Patients with Cancer

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Background/Objectives: Review all paediatric oncology patients that were treated with radiotherapy (RT) in our Hospital and summarize the relevant manifestations of radiation-induced CVD and endocrinopathies.

Design/Methods: This was a descriptive retrospective study performed at Hospital Universitario Central de Asturias, in Oviedo (Spain) from January 1, 2007, to December 31, 2017. Inclusion criteria were patients ≤ 18 years of age presenting any type of tumours and having received radiotherapy as a part of their treatment. For the purpose of this review, the following data were collected: age at the time of radiotherapy, sex, diagnosis and site of malignancy, total radiation dosage and vascular /endocrinopathy alterations observed.

Results: Between 2007 and 2017, a total of 145 new solid tumours and Hodgkin Lymphomas cases were diagnosed in our Hospital (excluded leukemias and non Hodgkin Lymphomas). Radiotherapy was performed in 37 cases (17

females and 20 males). The average age of this therapy was 9,7 years $\pm$ 5 years. There were eighteen cases of cerebral tumours. Three of them, presented any vascular malformation during their follow up. First one (PNET) telangiectasias plus cavernomas observed 23 months after radiotherapy. Second one (pinealoblastoma) presented an aneurysm that was operated (20 months after radiotherapy). Third one (medulloblastoma) presented telangiectasias 39 months after radiotherapy. All of them had also, at least, one endocrinology alteration.

Conclusions: The number of childhood cancer survivors entering adulthood is increasing. This means that previously unknown complications / sequels are increasingly frequent in this group of patients. A strict follow-up is strongly necessary in order to treat and prevent some complications. Although endocrinological complications are well known, others, like vascular complications, are still a little known group of radiotherapy sequels. They can carry lots of morbidity, including death. It is important to have them in mind in order to find them early and treat if it would be necessary.

V506 SIOP19-1013 | Risk and Predictors of Adverse Long-Term Mental Health Outcomes Among Survivors of Adolescent and Young Adult (AYA) Cancer: A Population-Based Impact Cohort Study

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Background/Objectives: The long-term risk of adverse mental health outcomes among survivors of AYA cancer is not well characterized. We used population-based clinical and health administrative databases to determine this risk and identify associated predictors.

Design/Methods: 5-year survivors were identified using IMPACT, a population-based database of all Ontario, Canada AYA, diagnosed with one of six common cancer types at 15-21 years of age between 1992-2011. We compared several outcomes between survivors and sex, age, and area-matched controls by linking to provincial health services data: rate of outpatient visits for a psychiatric indication (general practitioner, psychiatrist) and time to a severe psychiatric event (emergency room visit, hospitalization, suicide). Demographic-, disease-, and treatment-related predictors of outcomes were assessed in survivors. The association between cancer treatment setting (adult vs. pediatric centre) and long-term mental health outcomes was also examined.

Results: We identified 1,700 survivors and 8,042 controls (median 19 years of age; IQR 18-20). Compared to controls, survivors experienced elevated rates of outpatient psychiatry-related visits [adjusted rate ratio (RR) 1.37; 95% confidence interval (95CI) 1.13-1.67; $p=0.002$] and increased risk of severe psychiatric events (adjusted hazard ratio 1.24; 95CI 1.06-1.45, $p=0.006$). In multivariable analysis, higher outpatient rates were associated with demographics (female sex, rural residence) and treatment modalities (cranial radiation, high-dose methotrexate). In adjusted analysis, survivors initially treated in adult settings had twice the visit rate of those treated in pediatric settings (RR 2.04; 95CI 1.32-3.13; $p=0.001$). Increased risk of severe events was associated with rural residence and previous mental healthcare use.

Conclusions: Survivors of AYA cancer are at higher risk of adverse mental health outcomes, including severe events, compared to controls. Highest risk survivors can be identified using demographic, disease, and treatment characteristics. Survivors treated in adult settings are at dramatically elevated risk compared to those treated in pediatric settings and may benefit from increased psychosocial support.

V507 SIOP19-1445 | Providing A Life Line for Young Adult Survivors Through A Unique Wellness Intervention

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Background/Objectives: Background: Adult survivors (LTS) of childhood cancer frequently have difficulty adjusting to life. The Periwinkle Foundation (TPF), which provides programming for our pediatric cancer patients, recognized this challenge and recently developed a LTS program to provide a strong support network through positive peer interactions. LTS (>age 18) are invited to participate in monthly socials, weekend retreats and volunteer opportunities.

Design/Methods: 46 LTS ages 19-43 (median 27 years) participated in the program in 2018. Survivor diagnoses included brain tumors (16); leukemia (14); lymphoma (4); neuroblastoma (3); Ewings/Wilm's (2 each); miscellaneous (5). Of these, 13 have significant physical/neurologic sequela. LTS activities included attending sporting/arts events, educational/career counseling sessions and volunteer activities. Data on program participation was collected and LTS were surveyed to determine the impact of this program on their psychological wellness.

Results: LTS participants had 366 combined years of survivorship; 420 LTS program encounters; and 1237 volunteer hours with TPF. In a survey, LTS rated the importance of the program to them from 1 (not important) to 5 (incredibly

important). Results including the percent of LTS selecting a specific response follow: 1) building self-confidence (5-78%; 4-22%); 2) improving sense of well-being (5-90%; 4-10%); 3) helping adjustment to cancer history (5-90%; 4-10%); 4) help dealing with ongoing late effects (5-100%); 5) help establishing/maintaining relationships with others: (5-90%; 4-10%). Comments from LTS included: "Periwinkle makes me feel hopeful, this is my safe haven"; "This group helps me come to terms with my long-term effects"; "My mental wellness is the most important part of LTS care"; "This program is my family – these are my siblings".

Conclusions: Establishing a social network of LTS in a non-medical environment provides critically important peer support which enhances the survivors' psychological wellness. Social programming directed at older LTS is a key intervention positively impacting survivor mental health.

V508 SIOP19-1148 | Cost-Effectiveness of Screening Guidelines to Prevent Heart Failure in Childhood Cancer Survivors: A Report from the Childhood Cancer Survivor Study (CCSS)

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Background/Objectives: Childhood cancer survivors treated with anthracyclines or chest radiation therapy (RT) are at risk for left ventricular dysfunction (LVD) and subsequent heart failure (HF). The International Guideline Harmonization Group (IGHG) recommends risk-based screening echocardiograms for LVD, but evidence supporting its frequency and cost-effectiveness is limited.

Design/Methods: Using data from the CCSS, we developed a microsimulation model of the clinical course of LVD and HF to estimate long-term health and economic outcomes associated with screening for IGHG-defined risk groups (low [anthracycline 1-99 mg/m² and/or RT <15 Gy], moderate [100 to <250 mg/m² or 15 to <35 Gy], high [≥ 250 mg/m² or ≥ 35 Gy or (≥ 100 mg/m² and ≥ 15 Gy)]). We compared 1-, 2-, and 5-year interval-based screening to no screening. Screening performance and pharmacological treatment effectiveness were based on published studies. Costs and quality of life weights were based on US averages and published

studies. Outcomes included lifetime HF risk, quality-adjusted life years (QALYs), lifetime costs, and incremental cost-effectiveness ratios (ICERs). Strategies with ICERs <\$100,000/QALY gained were considered cost-effective.

Results: Among the IGHG risk groups, the lifetime HF risk in the absence of screening was 37% (high), 25% (moderate) and 17% (low). Screening every 2 years was cost-effective for the high-risk group (ICER \$77,900/QALY) and every 5 years for the moderate-risk group (ICER \$98,700/QALY). In contrast, routine screening was not cost-effective for the low risk group (ICER >\$100,000/QALY), representing ~40% of those for whom screening is currently recommended. These findings were consistent across a wide screening and treatment efficacy ranges.

Conclusions: Our findings can inform screening guidelines and suggest that elimination of LVD/HF surveillance for low-risk survivors warrants consideration.

V509 SIOP19-1117 | Development of a School Support Website for Children and Adolescents with Cancer (for Educational Day Series: Gaps and Models of Care for Schooling After Cancer)

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Background/Objectives: Identifying ways to best support Australian students with cancer remain engaged in schooling is needed to ensure ongoing academic achievement and psychosocial health for these students. Therefore we aimed to develop a website for students with cancer (Ready Steady School) that provides tailored school support to students, parents and teachers.

Design/Methods: We conducted a systematic review of existing school re-entry programs and semi-structured telephone interviews with parents of students with cancer, teachers, school-hospital liaison staff and healthcare professionals to understand preferences for school support programs. Using the review and interview data we developed the Ready Steady School website and conducted an Expert Panel Review of the website.

Results: Our review identified the following common features of school support programs (n=15): planned education and psychosocial support; teacher and peer education; school-hospital liaison personnel to facilitate communication between the school, family and hospital. Similarly, interview participants (n=20) indicated dedicated school liaison person-

nel and provision of tailored information for peers and teachers improved communication. Formalised education planning and psychosocial support were important. Web-based support was preferred. Based on these results, we developed the Ready Steady School website for students with cancer, parents and educators, across primary (7-12 years) and secondary school (13-20 years). The website is personalised by users completing screening questions and an education needs assessment. Expert panel review (n=13) indicated that overall, website feedback was positive, with 93% of the content meeting its aims and 100% of reviewers endorsing agree or strongly agree for readability for all users. Appropriateness was high, 100% of reviewers reported agreeing or strongly agreeing with information, resources and strategies provided.

Conclusions: Development of online resources for students with cancer has the potential to facilitate communication between students, families, healthcare professionals and teachers. Provision of tailored education strategies and information can help minimise the disruption to education that cancer causes.

V510 SIOP19-1676 | Fear of Cancer Recurrence: The Impact of Late Effects of Treatment on Fear of Cancer Recurrence

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Background/Objectives: Fear of cancer recurrence (FoCR) is a significant concern in adult cancer survivors – predicting anxiety, depression, and increased healthcare usage. Yet, little is known about FoCR in survivors of pediatric cancer. Survivors of pediatric cancer undergo a variety of toxic therapies and are at risk of experiencing relapse and late effects resulting from their treatment. Up to 80% of survivors experience late effect that can severely impact their physical and psychosocial health. Thus, we aimed to investigate study investigates the effect of late effects on FoCR.

Design/Methods: Survivors completed a health assessment as part of their regular long-term survivor clinic appointment including a yes/no question: "Are you concerned about the following health issues: Fear of cancer coming back?" and were screened for late effects according to the Common Terminology Criteria for Adverse Effects (CTECA v5) guidelines. Predictors of FoCR, such as clinical demographics and late effects, were explored through odds ratios.

Results: Participants (N= 218, male= 123 [56%]), ranged from 4-21 years of age (M= 13.50 SD= 4.25) at their most recent follow-up appointment. Overall, 41% (n = 90) of

survivors reported FoCR at least once across all clinic visits. Twenty three percent ($n = 50$) reported FoCR at more than one clinic visit. Factors related to FoCR include: experiencing 2 or more late effects ($OR = 3.60$, 95% $CI = 1.37-9.45$), experiencing late effects grade 3 or higher ($OR = 3.10$, 95% $CI = 1.24-7.71$) and reporting 2 or more current health problems ($OR = 4.78$, 95% $CI = 2.09-10.93$). Health problems found to be related to FoCR include disturbed sleep ($OR = 4.13$, 95% $CI = 1.44-11.83$), and depressive symptomatology ($OR = 4.35$, 95% $CI = 1.64-11.54$).

Conclusions: FoCR is a concern in pediatric cancer survivors and effects quality of life and healthcare usage. Careful screening of patients at risk of developing FoCR is warranted.

V511 SIOP19-0448 | New Insights in Cisplatin and Radiation-Induced Ototoxicity: A French Childhood Cancer Survivors Study (FCCSS)

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Background/Objectives: Platinum chemotherapy and cranial radiotherapy (RT) are risk factors of ototoxicity. Effects of RT dose at inner ear and of other chemotherapy agents were investigated.

Design/Methods: Of 7670 5-year French CCS treated for solid cancer in 1942-2000 before 20years of age, 5243 with ototoxicity data were included. Severe ototoxicity, defined as the need of hearing aids or Brock grade 3-4 hearing loss, was identified from self-administrated questionnaires, clinical visits and cohort linkage with the French Hospital Database and health insurance information system (SNIIRAM). The mean RT dose at inner ear was estimated using home-made software. Multivariable Cox models adjusted for gender, age at diagnosis, time period and social deprivation index was used to identify risk factors.

Results: After a mean follow-up=30 years, 199 severe ototoxicity cases were identified. Cumulative incidences (CumInc) at 30 and 50years of age were 2.8% (95% $CI=2.4-3.3$) and 5.5% (4.6-6.5). Mean RT dose at inner ear (Hazard Ratio $HR=1.6$ (95% $CI=1.0-2.5$), 4.5 (2.7-7.2), 5.7 (3.0-10.8) and 14.0 (9.2-21.2) for 0-<5, 5-<30, 30-<40 and ≥ 40 Gy), cisplatin ($HR=2.8$, 95% $CI=1.9-4.0$), mel-

phalan ($HR=3.3$, 95% $CI=1.9-5.7$) and busulfan exposure ($HR=2.6$, 95% $CI=1.6-4.4$) were significantly associated with severe ototoxicity. Concerning melphalan, almost all cases were identified in patients with neuroblastoma (NBL) who also received cisplatin 200mg/m²/cycle (26/92 NBL, 30y-CumInc=36.4% vs. 3/107 non-NBL, 30y-CumInc=1.6%). Concerning busulfan, all cases were identified in NBL ($n=16/63$, all treated with melphalan-cisplatin) and brain tumors ($n=13/28$, all treated with RT at inner ear ≥ 5 Gy). The 30y-CumInc in patients with RT at inner ear ≥ 5 Gy was 39.8% (22.5-60.0) with busulfan vs. 7.4% (95% $CI=5.7-9.6$) without.

Conclusions: RT at inner ear has significant deleterious impact on audition, with cumulative incidence still worsening >30years after RT, and with likely potentiation by busulfan. The deleterious effect of melphalan could be explained by an interaction with cisplatin, or by the high cisplatin dose by cycle used in NBL.

V512 SIOP19-0736 | Suitability of Who Criteria for Quality Assessment in Teenage Boys Undergoing Sperm Banking for Fertility Preservation Prior to Potentially Gonadotoxic Treatment

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Background/Objectives: Semen quality as classified by 2010 WHO criteria is validated against data from males aged 17 and older. A validated reference range does not exist in younger males.

Design/Methods: We present a series of 62 ≤ 17 year old males who stored sperm prior to gonadotoxic treatment between 2008 and 2017. Data were collected retrospectively and analysed by age, ethnicity and indication for banking using STATA 14 statistics software.

Results: Mean age at storage was 16.0years (SEM 0.2, range 13-17). 4.8% of males were aged 13, 5.8% were 14, 4.4% were 15, 15.6% were 16, 22.6% were 17. White British was the largest ethnic group (66.1%), South East Asian accounted for 3.6%. The indication for storage was cancer in 91.9%. (Sarcoma (31.0%), Lymphoma (27.6%), Testicular (17.2%), Leukaemia (13.8%), CNS (5.2%) and Renal, Thyroid and Unknown Primary (1.7%)). Applying the 2010 WHO criteria,

20.5% of samples at storage met the normal parameters. Analysis according to age revealed that; 0% of samples from 13 and 14 olds reached normal threshold. 20.0%, 17.6% and 33.3% did so in 15, 16 and 17 year olds respectively. The likelihood of meeting WHO criteria increased with each increasing year of age, OR 2.3 (95% C.I. 1.0-5.3). Ethnicity, diagnosis, and previous orchidectomy had no significant impact.

Conclusions: Despite limitations, we confirm sperm storage is possible in males younger than 18 years old, and in this population, age at storage conveys the greatest bearing on whether the sample meets the WHO parameters. Pre- and post-treatment analysis is complex for this age group, for whom the 2010 WHO criteria is not validated. Given the time lag between pre- and post-treatment semen analysis the impact of treatment may be underestimated if patients were classified as storing an abnormal sample when in fact their semen parameters were normal for their age group.

V513 SIOP19-0732 | Risks of Azoospermia in Teenagers Following Chemotherapy: A Comparison of Pre- and Post-Treatment Semen Analysis

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Background/Objectives: Infertility is a recognised late effect of treatment with cytotoxic drugs. Little is known about the true extent of the risk.

Design/Methods: 43 males aged ≤ 18 years stored sperm at our unit between 2008 and 2017 prior to potentially gonadotoxic treatment and subsequently provided follow-up semen analysis (89 cases in total provided pre-treatment samples). Data on cancer diagnosis, chemotherapy exposure and sperm quality at initial storage, and at follow-up was collected for those with follow-up samples available. Validated parameters for semen quality in males < 17 years old is not available, consequently we report azoospermia as the single outcome. To avoid overestimating subtle changes, azoospermia was defined as a sample with < 100 sperm/ejaculate.

Results: Mean age at storage was 16.4 ± 0.2 years (Range 13-18) and follow-up 19.9 ± 0.4 years (Range 14-25). Mean time to follow-up sample was 3.5 ± 0.34 years (Range 1-8). The commonest indication for storage was cancer (88.0%), primar-

ily lymphoma (31.5%). 81.4% of the 43 received chemotherapy. 4.7% of all initial samples and 30.3% at follow-up contained < 100 sperm/ejaculate ($p=0.0034$, RR 1.36 95% C.I. 1.11-1.62). Of those receiving chemotherapy: 5.7% initial samples contained < 100 sperm, versus 45.8% at follow-up ($p=0.0118$, RR 1.38 95% C.I. 1.08-1.75). Of those receiving an alkylating agent: 4.2% initial samples contained < 100 sperm/ejaculate, versus 32.0% at follow-up ($p=0.0232$, RR 1.41 95% C.I. 1.07 -1.87). Of those receiving platinum-based chemotherapy: 0% initial samples had < 100 sperm/ejaculate, versus 14.3% at follow-up ($p=1.00$, RR 1.17 95% C.I. 0.86-1.58).

Conclusions: Elevated risk of azoospermia post chemotherapy is confirmed, the highest risk being receipt of alkylating agents. Reassuringly, 70% were able to produce some sperm 4 years after treatment and consequently may be suitable for assisted reproductive support if natural conception is not feasible. Prediction of the precise response to treatment in an individual remains difficult and will require very large studies to formally evaluate.

V514 SIOP19-1633 | Passport for Care: Integrating User-Specified Content to Engage Survivors and Promote Survivor Education on Risk for Late Effects

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Background/Objectives: The Passport for Care Survivor Website (PFCSW) launched in 2015 as an ancillary website to the PFC Clinician Website, a patient-centered decision support tool currently used in 8 countries worldwide that provides clinicians, survivors, and their families with a personalized cancer treatment summary, Survivorship Care Plan, and recommendations for follow-up screening based on the Children's Oncology Group Long-Term Follow-Up Guidelines. The PFCSW was developed to provide survivor families with direct access to these recommendations. With the objective of expanding PFCSW functionality, we employed a user-centered strategy to identify content priorities for ongoing SW adaptation.

Design/Methods: Key stakeholders including survivors and survivor caregivers were consented to participate in interviews centered around PFCSW content preferences under an IRB-approved research protocol. Responses were condensed into key themes and prioritized for adaptation together with the website development team.

Results: An analysis of responses (55% survivors, 45% caregivers) who participated in semi-structured interviews

revealed that most participants viewed the PFCSW as having the potential to significantly facilitate the transition from active treatment to survivorship. Respondents expressed interest in maintaining PFCSW simplicity and ease of use, while identifying specific targets for adaptation that were grouped into the following themes: a) networking and social support, b) informational resources, c) peer mentorship, d) testimonials. The PFCSW was then adapted to include content that is reflective of these priorities, and deployed in April 2019.

Conclusions: Web-based platforms can be an effective means for delivering educational materials to survivors regarding the risks for late effects after cancer treatment, but should address user-specified priorities in order to maximize website utility. Here, we employed a user-centered strategy to identify key themes for content adaptation that are responsive to survivor needs, and introduced a simplified outcomes search tool that generates surveillance recommendations from user-entered exposures.

V515 SIOP19-0254 | Incidence and Predictors of Significant Hearing Loss Requiring Hearing Assistive Devices Among Childhood Cancer Survivors: A Population-Based Study

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Background/Objectives: Though hearing loss is a significant late effect among childhood cancer survivors, recent guidelines note insufficient evidence to quantify natural history or risk associated with specific exposures. We examined the long-term incidence and predictors of hearing loss requiring hearing amplification devices (HAD) using population-based healthcare data.

Design/Methods: In Ontario, Canada, HAD costs are subsidized by the provincial Assistive Devices Program (ADP). Ontario children age <18 years at cancer diagnosis between 1987-2016 were identified using a pediatric cancer registry and linked to ADP claims. The cumulative incidence of HAD use was compared between cases and matched controls. Patient, disease, and treatment predictors of HAD were examined.

Results: We identified 11,842 cases and 59,210 matched controls. Cases were at higher risk of HAD [hazard ratio (HR) 12.8, 95% confidence interval (95CI) 9.8-16.7; $p < 0.001$]. The cumulative incidence of HAD among survivors was 2.1% (95CI 1.7-2.5%) at 20 years and 6.4% (95CI 2.8-12.1%)

at 30 years. 30-year incidence was highest in survivors of neuroblastoma (10.7%, 95CI 3.8-21.7%) and hepatoblastoma (16.2%, 95CI 8.6-26.0%). Predictors of HAD in multivariable analyses included age 0-4 years at diagnosis (vs. 5-9 years, HR 2.2, 95CI 1.4-3.3; $p < 0.001$). Relative to no cisplatin exposure, patients receiving 1-200mg/m² were not at greater risk, unlike those receiving higher cumulative doses (201-399mg/m² HR 3.1, 95CI 1.8-5.5; $p < 0.001$; ≥ 400 mg HR 4.7, 95CI 3.0-7.4; $p < 0.001$). Relative to no radiation, those receiving ≤ 32 Gy were at no higher risk, unlike while those receiving > 32 Gy (HR 2.4, 95CI 1.6-3.7; $p < 0.001$). Carboplatin exposure was not associated with HAD.

Conclusions: Childhood cancer survivors are at elevated risk of requiring HAD which continues to rise between 20 and 30 years from diagnosis. Thresholds of cisplatin and radiation exposure exist above which risk substantially increases. Prolonged monitoring and trials of otoprotective agents are warranted in high-risk populations.

V516 SIOP19-0032 | Long-Term Health Status of High-Risk Neuroblastoma Survivors Treated with High-Dose Chemotherapy and Hematopoietic Stem Cell Transplantation

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Background/Objectives: Current treatment strategies including high-dose chemotherapy with stem cell transplantation rescue (HDC-SCT) have improved 5-year event-free survival for patients with high-risk neuroblastoma (HRNB), but with an increased risk of late treatment-related toxicities.

Design/Methods: Between 1980 and 2012, 439 children were treated for HRNB with HDC-SCT in Gustave Roussy (GR), among which 145 were alive and disease-free at 5-year post-SCT. Long-term health data have been collected for those 145 patients, prospectively within the long-term follow-up clinic in GR or retrospectively from pediatric consultations.

Results: With a median follow-up post-SCT of 15 years (range 5-34), we observed 6 late relapses, 11 second cancers (including 3 papillary thyroid carcinomas; median delay = 20 years post-SCT [18-22]) and 9 deaths. Event-free and overall survival at 20-year post-SCT were 82% (95%CI = 70-90) and 89% (95%CI = 78-95), respectively. A second health event was observed in 135 patients (median = 3/patient), including 103 patients with at least 1 severe event (median = 1/patient).

Cumulative incidence at 15-year post-SCT of second cancers is 4%, cardiac diseases 8%, thyroid 11%, renal 7%, hepatic focal nodular hyperplasia 14%, dental mal-development 70%, and severe hearing loss 20%. Height-for-age z-score was ≤ -2 for 30 patients (21%) and ≤ -3 for 12 patients (8%). After busulfan-melphalan conditioning regimen, 40/43 females and 33/35 males had a gonadal insufficiency.

Conclusions: Long-term consequences of HRNB treatment including HDC are frequent and disabling, mainly due to hearing loss and gonadal insufficiency.

V517 SIOP19-0280 | Psychometric Properties of the Chinese Version of the Pittsburgh Sleep Quality Index in Hong Kong Chinese Childhood Cancer Survivors

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Background/Objectives: Sleep disturbance is a prevalent symptom reported by children after they complete the treatment for cancer. Nonetheless, no validated instrument is currently available for assessing this symptom, especially in the Hong Kong Chinese Context. To address the literature gap, this study translated the Pittsburgh Sleep Quality Index (PSQI) from English into Chinese, and examined its psychometric properties among Hong Kong Chinese childhood cancer survivors. This study also examined the factorial structure of the Chinese version of the PSQI using confirmatory factor analysis.

Design/Methods: A cross-sectional study was conducted. A total of 200 Hong Kong Chinese childhood cancer survivors who had medical follow-ups in the outpatients were invited for this study. We assessed the translated PSQI for internal consistency, content validity, construct validity and 2-week test-retest reliability.

Results: The content validity index was 0.90. The test-retest reliability at 2 weeks was 0.82. The internal consistency was 0.87. There was a positive correlation between levels of sleep disturbance and depressive symptoms, and a negative correlation between levels of sleep disturbance and quality of life. The mean level of sleep disturbance of the survivors was statistically significantly lower than that of those receiving cancer treatment, but statistically significantly higher than that of their healthy counterparts. Confirmatory factor analysis indicated a 3-factor structure underlying the Chinese version of the PSQI.

Conclusions: This study confirmed that the Chinese version of the PSQI was a reliable and valid instrument in assessing sleep disturbance among Hong Kong Chinese children surviving cancer. This validated instrument can be further applied to

document and monitor the severity of sleep disturbance in this group of population.

V518 SIOP19-1299 | Childhood Cancer Survival in Abidjan, Kampala and Harare in 2017: A Population-Based Cancer Registry Study

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Background/Objectives: Childhood cancers in Africa, are often under-diagnosed; with few studies that document the survival experience of African children with cancers at a population-level. As part of the project to expand childhood cancer registration in sub-Saharan Africa, a one-year pilot study within the framework of the My Child Matters Programme was carried out in 2017/2018.

Design/Methods: This pilot study had two components, the follow-up of the more common cancers of childhood and to calculate survival. Three cancer registries for which follow-up for a minimum of 3 years was feasible were chosen (Abidjan, Cote d'Ivoire (cases from 2014-2016); Harare, Zimbabwe (cases from 2005-2014) and Kampala, Uganda (cases from 2010-2014)). All three registries had been recording contact details of the parents/next of kin of registered childhood cancer cases, to facilitate follow up after discharge from the hospital. We included children with acute lymphoid leukemia, Hodgkin lymphoma, NHL, Burkitt lymphoma, retinoblastoma, Wilms tumour, osteosarcoma, rhabdomyosarcoma and Kaposi Sarcoma.

Results: There were 667 patients with childhood cancers included; 179 from Abidjan, 217 from Harare and 271 from Kampala. Of the 667 patients, 48.9% were female and 51.1% were male. 538 cases (80.7%) were included for survival analyses. Loss to follow up was greatest in the first year, estimated at 26.1% in Abidjan, 19.1% in Harare and 17.2% in Kampala. For all cases combined the overall observed survival at 5-years was 32.9% in Abidjan, 28.2% in Harare and 41.0% in Kampala. However, survival experience varied by the cancer type and by registry. Patients with Wilms tumour had the best survival experience in Abidjan and Harare, while this was poorest in Kampala, while for patients with Burkitt lymphoma, patients in Kampala had the most favourable survival outcomes.

Conclusions: Continuous efforts will have to be made to maintain registration and improve the care and follow-up of children with cancers in Africa.

V519 SIOP19-1466 | Body Composition by Dexascan and Determinants of Adiposity in Survivors of Childhood Acute Lymphoblastic Leukemia (ALL): A Single Institutional Study from India

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Background/Objectives: High adiposity is an emerging long-term complication of childhood cancer survivors. Its importance stems from its association with cardio-metabolic complications like hypertension, diabetes and stroke. Hence, this study was undertaken to evaluate adiposity and its risk factors in survivors of childhood ALL.

Design/Methods: The cases included 65 survivors of ALL treated with BFM-95 protocol and off-therapy for at least 5 years, while the control group constituted 50 age and sex-matched healthy siblings. Physical examination, anthropometry and DEXAscan was performed for all and lipid profile for the cases alone. Body mass index (BMI), body fat (BF) percentage, trunk fat (TF) percentage, lean body mass (LBM) and trunk lean mass (TLM) were calculated. Overweight ($\geq 85^{\text{th}}$ centile) and obesity ($\geq 95^{\text{th}}$ centile) were defined by McCarthy's body fat reference data and compared with BMI cut-offs from Centre for Disease Control. Univariate analysis was done to explore the association of demographic, disease and treatment-related factors with high adiposity.

Results: Median age of patients at diagnosis and follow-up were 6 years (1.3-19.5) and 15 years (7.7-27.5) respectively, 80% were male. Median duration from diagnosis was 7 years (5-18). Median BF% and TF% [35 (16.6-51.2), 32.4 (16.1-48.1)] were higher in cases compared to controls [31 (16.1-46.3), 27.5 (14.4-45.4)] ($p=0.001$, 1.00). While median LBM and TLM were lower in the cases (sarcopenia) ($p=0.03$, 0.03). Higher prevalence of adiposity (overweight and obesity) was detected amongst survivors (34/65, 50/65, 77%) as compared to controls (24/50, 48%; overweight) using BF% ($p=0.001$). BMI underestimated the incidence of adiposity in cases (44/65, 67%) and controls (6/50, 12%), although the pattern was similar ($p=0.001$). On univariate analysis, age ≤ 10 years old at follow-up was the only factor associated with high adiposity ($p=0.05$).

Conclusions: High prevalence of adiposity in young survivors of ALL especially from a developing country is a matter of concern demanding monitoring and aggressive intervention for lifestyle modification.

V520 SIOP19-0290 | Incidence of Anthracycline-Induced Cardiotoxicity in Long Term Survivors of Pediatric Cancer: A Population Based Study

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Background/Objectives: Population-based data on the long term incidence of anthracycline induced cardiotoxicity (AIC) in children is scant. This study was designed to determine the incidence of AIC in long term survivors of pediatric cancer.

Design/Methods: Following ethics approval, a retrospective population-based study was conducted using the following data sources (i) patient charts (ii) oncology database at the IWK health centre. All children with cancer treated with anthracycline in the long-term follow up clinic (up to 18 years of age or 5 years after the end of therapy) at the IWK health centre were included. Cardiotoxicity was defined as deviations in echocardiogram (ECHO) parameters including ejection fraction (EF); shortening fraction (FS) and symptomatic cardiotoxicity. Regression analysis and correlation were used to determine the relationship of cardiac changes to hematopoietic stem cell transplant (HSCT), chest radiation, ≤ 5 years at diagnosis, and cumulative dose of anthracycline.

Results: Of the 175 (95 males) patients, only 8 were reported to have AIC. Only 1 patient required intervention for cardiotoxicity. Mean age at diagnosis was 65.9 months. Follow-up time ranged from 7-24 years and the elapsed time from treatment to an event ranged from 1-24 years. Of the 8 patients, 6 received a cumulative anthracycline dose > 300 mg/m², 5 were ≤ 5 years at diagnosis, 1 had chest radiation, 2 had HSCT, 1 had LV wall thinning, 2 had cardiomyopathy and 6 had decreased EF and FS. Only a cumulative dose of ≥ 250 mg/m² ($p<0.001$) had a significant relationship with cardiac changes.

Conclusions: The current study shows that AIC has a low incidence (5%) while cardiotoxicity warranting intervention is rare (0.5%). A cumulative dose ≥ 250 mg/m² had a significant relationship with cardiac changes. Future studies may consider AIC incidence and risk factors with a larger population.

V521 SIOP19-0811 | Use of Electronic Patient Data Warehouse for Calculating the Risk Category of Late-Effects in Childhood Cancer Survivors

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Background/Objectives: There are currently over 4600 adult childhood cancer survivors in Finland. Despite high survival rates, it is known that only one third of the survivors stay as healthy as their age-mates. Some of the late-effects may occur decades later. One of the growing challenges is to provide appropriate care for childhood and adolescent cancer survivors after transitioning to the adult health care. Missing systematic follow-up plan (Survivorship Passport) may lead to excessive use of healthcare services and delays in interventions.

International guidelines for determining the risk for late-effects were adapted to serve as a nation-wide guideline for health care authorities in Finland. Turku University Hospital got a task to develop an automatized system for calculating the risk based on electronic patient records saved in Hospital Data Lake.

Design/Methods: We created an electronic algorithm that uses exposure-based health screening guidelines published by the Children's Oncology Group. The three risk-categories are based on the type of cancer, details of treatment modalities, and cumulative doses of certain chemotherapies. The results gathered by the algorithm (patients treated 1.1.2004-31.12.2017) were compared with those calculated manually by an experienced clinician.

Results: A significant concordance between manual and algorithm based risk classification was found in this retrospective analysis. A total of 355 patients received a classification through the algorithm and 325 of those fully matched with manual categorization producing a Cohen coefficient of 0.91 (95% CI 0.88-0.95).

Conclusions: The process of creating an electronic algorithm for late-effect risk categorization showed that already by the tools/definitions in a developmental phase, it was possible to get a more than 90% accurate result when compared with the one set by an experienced clinician. With the most recent innovations of registering structured data in to the Hospital Data Warehouse, we assume that the accuracy of the algorithm has still improved.

V522 SIOP19-1216 | Occupational and Financial Changes Following Cancer Therapy in Young Adults with Cancer in Germany

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Background/Objectives: Cancer survivors have a significantly increased risk for unemployment, early retirement and moreover, significant health expenditures. For young adult cancer patients (AYA), who are at the beginning stages of

work and vocational development and who often have lower earnings, this strain might be especially relevant. Not much is known about changes in the professional and financial situation of AYA after cancer therapy.

Design/Methods: Young patients (aged 18-39 years at time of diagnosis) with all malignant cancer sites within the last 4 years were assessed in Germany. At two time points we measured the employment status, the strength of occupational and financial changes (FLZ-M subscales work/profession and income/financial security) as well as perceived financial burden (EORTC QLQ-C30 subscale financial difficulties through illness).

Results: N=514 AYA (mean age at diagnosis 29.6 years; SD=6.1) completed the survey at both time points. At t1 N=248 (48.2%) of patients noted high changes regarding their occupational situation and N=195 (37.9%) concerning their financial situation since cancer diagnosis. N=216 (42.1%) of patients described financial burden at t1- those declined significantly to t2 (N=157; 30.5%) (T=5.428; p<0.0001). At t2 n=362 (70.4%) of the 514 patients were (again) employed and n=63 (12.3%) were students or on vocational training. N=102 (20%) reported at t2, that they felt under pressure to take up work after cancer. This was mainly for financial reasons.

Conclusions: Cancer diagnosis in AYA age entails major professional and financial changes. Even though a large number of AYA patients are back to work up to two years after cancer therapy, approximately 40% of AYA patients in Germany experienced financial burden on a high level. Health policy should focus more on the issue. Further, more investigation on direct and indirect costs AYA patients and their supporting families have is needed in order to support AYA cancer patients.

V523 SIOP19-0334 | A Swedish Nationwide Population-based Register Study of Children Treated for a Brain Tumor and Their Grades from Year 9 in Practical and Aesthetic Subjects

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Background/Objectives: Children treated for a brain tumor are at high risk of experiencing neurocognitive, physical and psychosocial late effects which can all negatively affect school performance. Previous studies concerning school grades from year 9 have mainly focused on theoretical subjects, such as native and foreign language as well as mathematics. This has revealed that children treated for a brain tumor are at risk of lower school grades compared to controls. Grades in differ-

ent practical and aesthetic subjects have been investigated to a very limited extent although the syllabuses for these school subjects train skills that are important to strengthen social, physical, aesthetic, and practical skills, of children. Those subjects may also possibly positively affect some of the late effects as well as the psychological burden of the diagnosis and treatment.

Design/Methods: We identified 475 children with available grades from year nine, born between 1988 and 1996, and diagnosed with a brain tumor before their 15th birthday. We used chi-square tests to compare their grades with the grades from 2,197 matched controls in the subjects 'Home and consumer studies', 'Physical education and health', 'Art', 'Crafts' and 'Music'.

Results: The preliminary results show that children treated for a brain tumor received a lower grade or failed in one or more subject to a significantly higher extent than controls in all the assessed subjects except in 'Art'. Females were more affected than males in most subjects compared to their controls, although they still had the highest grade to a greater extent than males in all subjects except in 'Physical education and health'.

Conclusions: As many children treated for a brain tumor seem to be at risk of lower grades or failing in the practical and aesthetic subjects, individualized support should be provided due to the benefits of these school subjects.

V524 SIOP19-0345 | Late Effects of Childhood Cancer on Cognition

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Background/Objectives: With 80% of children surviving into adulthood after childhood cancer, there is a growing population of adults living with the long-term sequelae of cancer and its treatment. Cognitive difficulties are reported; this study aims to explore this problem.

Design/Methods: This retrospective study gathered data from 216 patients in a single-centre tertiary late-effects clinic. Cancer diagnoses were: Brain Tumour n=32, Haematological (including bone marrow transplant) n=118, other Solid Tumour n=66. Each patient completed a mood questionnaire and Cognitive Failures Questionnaire (CFQ). For those attending clinic with a relative/carer, this person (the informant) completed the Everyday Cognition questionnaire (ECog).

Results: The mean patient age was 25 years old (range 17 – 48 years); mean diagnosis age 9 years (1 month – 17 years), mean interval was 16 years from diagnosis (3 years – 44

years). Based on ECog scores, 28 patients experience persistent cognitive impairment. 7 of these were patients with brain tumours. Self-reported scores correlate poorly with informant scores. There was no correlation between mood and cognition in this group. 3/216 patients were referred to a formal memory loss clinic.

Conclusions: This new information confirms this young patient group experience symptoms of cognitive impairment which is not related to low mood. They may benefit from formal neuropsychological testing to objectively ascertain the nature and severity of their complaints. This would allow provision of services during and after treatment, which may improve daily functioning and health-related quality of life.

V525 SIOP19-0412 | Psychological Distress in Parents of Long-Term Childhood Cancer Survivors

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Background/Objectives: Even long after the experience of a life-threatening disease of a child, parents might suffer from psychological distress. We 1) compared distress in parents of childhood cancer survivors (CCS) with the Swiss general population, and 2) described characteristics of CCS parents with significant psychological distress.

Design/Methods: Swiss parents of CCS aged <16 years at cancer diagnosis and >20 years at study, and a representative sample of the Swiss general population (N=1238; 58.2% female) completed a questionnaire. To measure psychological distress, we used the Brief Symptom Inventory (BSI; scales: *Somatisation*, *Obsessive-compulsive tendencies*, *Interpersonal sensitivity*, *Depression*, *Anxiety*, *Hostility*, *Phobic anxiety*, *Paranoid ideation*, *Psychoticism*, and a *Global Severity Index* (GSI)). Raw scores were T-standardized. Participants were considered cases with significant psychological distress if they reached T≥63 on two scales, or T≥63 on GSI.

Results: In total, 778 CCS parents completed at least one scale of the BSI (women n=458, 58.9%; mean age 62.2 years, SD=6.9; mean time since diagnosis 23.8 years, SD=6.7). Parents reported significantly lower distress than the Swiss general population on all scales (all p<0.05) apart from *Somatization*. Fewer CCS parents (n=97; 13.1%) were considered cases with significant psychological distress compared to the general population (18.1%; p<0.001). Multivariable logistic regression analysis showed that CCS parents with a migration background (OR=2.03, 95%CI:1.12-3.68) and those from the Italian-speaking part of Switzerland (OR=3.59, 95%CI:1.44-

8.94) were more likely to experience significant distress. None of the clinical characteristics of the CCS were associated with parents' psychological distress.

Conclusions: Their child's survival of a life-threatening disease might have strengthened overall psychological well-being of parents. Parents with migration background should be paid special attention to help them cope with psychological distress.

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V526 SIOP19-0772 | Motivation and Challenges of Making Career Choices During the Growth Process After Treatment Completion in Child Cancer Survivors

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Background/Objectives: Background/ Objectives:

COG recommends preventive support for late psychosocial complications during the growth process after the completion of treatment in child cancer survivors. In Japan, importance has been increasingly placed on psychosocial support through interdisciplinary hospital-community care.

Design/Methods: The purpose of this study was to identify motivation and challenges faced when making career choices during the growth process after the completion of treatment in child cancer survivors receiving in-hospital education and to explore an ideal method for long-term psychosocial follow-up. Fourteen subjects aged 18 to 26 years were enrolled, and one-hour semi-structured interviews and qualitative descriptive analysis were conducted.

Results: With respect to the motivation for making career choices, six categories were extracted: "Want to help patients from my experience with child cancer or relationships with people," "Interested in medical and welfare work," "Want to be a teacher from experience in taking in-hospital classes," "Chose work that connected an area of my interest to child cancer experience," "Interchanging with peers helped me decide my career," and "Chose work based on advice from parents, medical practitioners, or teachers." For challenges faced in making career choices, two categories were extracted: "Difficulties experienced due to side effects, reduced physical strength, and delays in learning" and "Difficulty in proceeding to higher education or finding work due to experience of illness."

Conclusions: Hospitalization experience, their relationship with care staff and teachers, and interaction with friends helped motivate participants to make career choices. Hindering factors included late stage complications, reduced physical strength, delayed learning, and social factors. These findings suggest the need for care staff and teachers to work together to provide career choice support for these patients from the start, as well as during, and after treatment.

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V527 SIOP19-0553 | Prevalence and Predictors of Overweight and Obesity Among Survivors of Childhood Acute Lymphoblastic Leukemia: A Single Center Experience from South India

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Background/Objectives: Survivors of Childhood Acute Lymphoblastic leukemia (ALL) are at increased risk of obesity and related diseases like hypertension, insulin resistance, and diabetes. This study was conducted to find out the prevalence of overweight and obesity in the survivors of childhood ALL and to assess the risk factors for overweight and obesity.

Design/Methods: This is an observational study conducted at tertiary Cancer Centre among survivors of childhood ALL who were ≤ 14 years of age at diagnosis and had completed therapy at least 2 years earlier. Obesity was studied by determining the body mass index (BMI). Survivors were classified as underweight, normal weight, overweight, or obese on the basis of their BMI at the current follow-up visit

Results: One hundred and seventy five survivors of childhood ALL survivors were enrolled in this study with a median follow-up of 47 months (25-136 months). The median age at the time of diagnosis and enrollment was 4.5 years (1-14) and 12 years (6.6-25) respectively. The median BMI z-score at diagnosis and at follow up was -1.03 and 0.00 respectively. Prevalence of overweight and obesity was 24% (BMI z score according to WHO standards) in survivors. A meta-analysis on childhood obesity in India (N=92,862; age 2-18 years) described overweight and obesity in 16% individuals. BMI z-score at diagnosis was associated with overweight/obesity among survivors at follow-up (OR=1.605; 95% CI= 1.17-2.18, p value=0.003).

Conclusions: The prevalence of overweight and obesity in survivors of ALL is greater than the general population. BMI

z-score at diagnosis is one of the most important predictors for overweight and obesity.

V530 SIOP19-0671 | The Pain of Survival: An Examination of the Prevalence, Patterns, and Predictors of Pain in Long-Term Survivors of Childhood Cancer

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Background/Objectives: Over 30,000 long-term survivors of childhood cancer (LTSCCs) reside in Canada and survival rates are growing. Approximately two thirds of LTSCCs will experience late- and long-term effects from their original disease and treatments, including pain. To date, the experience of pain has not been well characterized in this population. Thus, the aim of the current study is to examine the prevalence, patterns, and predictors of pain in LTSCCs.

Design/Methods: Survivors of childhood cancer (n=318, 50.6% male; current mean age=17.70[4.11-40.33] years; 10.27[2.51-33.51] years off therapy) completed a health assessment as part of their regular long-term survivor appointment. Latent class analysis (LCA) was used to identify patterns of pain across multiple clinic appointments. Logistic regression analyses examined demographic, clinical, and psychosocial variables associated with patterns of pain.

Results: Fifty-two percent of survivors reported pain during at least one clinic visit. Headaches were most frequently reported (30.0%) and survivors of pediatric Wilms' (63.6%) and Ewings' sarcoma (60%) reported the highest rates of pain. LCA revealed two clinically relevant profiles labelled "low pain" (75.1%) and "persistent pain" (24.9%). Biopsychosocial factors related to persistent pain included female sex (OR=1.78, 95% CI, 1.01-3.13), longer time off treatment (OR=1.08, 95% CI, 1.03-1.14), depressive symptomatology (OR=3.42, 95% CI, 1.08-10.91), and drinking to intoxication (OR=3.00, 95% CI, 1.05-8.54).

Conclusions: Findings from the current study support the notion that persistent pain is a prevalent concern in LTSCCs. Pain management is undoubtedly an essential component in supporting the health and well-being of children diagnosed with cancer. As longer time off treatment was associated with persistent pain, screening for pain and pain management strategies should continue well beyond treatment completion. Future research should aim to disentangle pain as a multidimensional construct to better understand what contributes to poorer pain-related outcomes and inform pain management interventions from diagnosis and throughout survivorship.

V531 SIOP19-1413 | Ten-Year Childhood Cancer Survival - France, 2000-2015, Influence of Local Socioeconomic Disparities

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Background/Objectives: This study aimed to describe the evolution of nationwide survival 5 years and 10 years after a diagnosis of childhood cancer in France and the influence of deprivation on survival.

Design/Methods: We included all the 28,073 primary cases of cancer aged less than 15 years old registered by the French National Registry of Childhood Cancers between 2000 and 2015. For each case, geolocation of residence at time of diagnosis allowed to affect residential address to an IRIS (the smallest census unit available) and so to assign two deprivation scores (European index EDI and French deprivation index Fdep), based on the 2007 population census data. Vital status was determined at censoring date October 31, 2018. Survival at 5 and 10 years was described by diagnostic group using Kaplan-Meier method. Adjusted differences in survival by age at diagnosis, gender, period of diagnosis and deprivation were assessed with Cox models.

Results: The overall survival for all cancers was 82.8% [82.4-83.3] at 5 years and 80.8% [80.3-81.3] at 10 years. Altogether, the 10-year conditional survival after having survived 5 years was 97.5% [97.3-97.7]. Five-year survival has increased from 80.2% [79.2-81.1] in 2000-2003 to 84.2% [83.3-85.1] in 2012-2015 (p<0.0001). The overall survival varied by diagnostic groups and subgroups but did not differ significantly according to gender or age. Overall there was no heterogeneity of survival over urban status and deprivation index categories, except for neuroblastomas, for which survival seemed lower in most deprived Fdep quintile.

Conclusions: Our findings provide additional justifications to the right to be forgotten, in view of the long-term evolution of survival after a childhood cancer. This study also suggests that there are no substantial socioeconomic and territorial disparities in childhood cancer overall survival in France.

V532 SIOP19-0001 | Multimorbidity Over Time Among Children, Adolescents and Young Adult Cancer Survivors in British Columbia (BC), Canada

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Background: Little is known about the extent of multimorbidity among young cancer survivors over time periods post therapy. This data would aid in service planning. We describe the risk of multiple late morbidities and different types of morbidity (Aggregated Diagnosis Groups (ADGs)) for young cancer survivors, and whether the survivors are at an increased risk of multiple late morbidities compared to the general population.

Methods: The survivor group consisted of patients diagnosed with cancer aged 0 to 24 years from 1970 to 2005, resident in BC at diagnosis, survived five or more years from diagnosis, and were alive from January 1, 1991. They were linked to the provincial health insurance plan for health care usage from January 1, 1991 to Dec 31, 2010, or death, or loss to follow-up. A population comparison group consisted of five randomly-chosen British Columbia residents from the universal health insurance Client Registry for each survivor, individually matched by gender, birth year and followed for the same period as the matched survivor.

Results: Survivors diagnosed as children (aged 0 to 14 years ($n=1892$)), adolescents (aged 15-19 years ($n=1,074$)), and young adults (aged 20-24 years ($n=1,596$)) were analysed separately at 5-year intervals from 5 years post-diagnosis. By 30 years post-diagnosis, 7.7%, 6.4%, and 7.8% survivors had died from each age at diagnosis group, compared to 0.7%, 0.9%, and 1.3% of comparators. Approximately 0.9%, 2.9%, and 2.8% of survivors respectively experienced no recorded morbidity (0 ADGs), compared to 7.1%, 6.6%, and 6.0% of comparators. An estimated 46.7%, 50.3%, 48.7% of survivors in each group experienced 7 or more different types of morbidity (as classified by ADGs) since diagnosis, compared to 21.3%, 28.4%, and 30.6% of the general population group.

Conclusions: Primary care physicians need to be aware of ongoing excess risks of mortality and multimorbidity among these survivors.

V533 SIOP19-1673 | Examining the Impact of Late Effects on Depressive Symptoms in Survivors of Childhood Cancer

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Background/Objectives: With the survival rate of childhood cancer approaching 80%, many individuals are living with the physical and psychosocial of late effects of cancer treatment. However, our understanding of psychosocial late effects remains limited. What is known is that some survivors of childhood cancer increasingly experience depressive

symptoms into adulthood. As such, this study investigates the impact of late effects on depressive symptoms.

Design/Methods: Survivors attending a local survivorship clinic complete a comprehensive questionnaire detailing ongoing health concerns and behaviors at each appointment. Depressive symptoms are assessed through five yes-no items based on the Diagnostic and Statistical Manual-V criteria. Additionally, late effects of treatment were recorded by clinical staff using the Common Terminology Criteria for Adverse Events (CTCAE) v5.0. The total number of late effects were calculated and grade severity (i.e., Grade 1 or 2 = mild/moderate and Grade 3 or 4 = severe/life threatening) was assigned to each survivor. Linear regression was conducted to determine the impact of late effects on depressive symptoms.

Results: The most recent questionnaires filled out by 314 survivors were analyzed (53.8% males; mean=19.80 years of age [$SD = 6.72$], mean time since diagnosis = 13.03 years [$SD = 5.42$]). Severity of late effects, sex, age and time since diagnosis were not significant predictors of depressive symptoms. However, the number of late effects ($F(4, 305) = 3.88, p = 0.004$; $t(305) = 3.25, p = 0.001$) was a significant predictor of depressive symptoms.

Conclusions: Number of late effects is a significant predictor of depressive symptoms in childhood cancer survivors. Survivors experiencing multiple late effects should be carefully monitored by healthcare providers to ensure adequate support. Further research could help guide future interventions to support survivors who may be at risk for developing clinical depression.

V534 SIOP19-1449 | Adult Survivors of Childhood CNS Tumours: Late Effects and the Impact of Recall Assessment

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Background/Objectives: Adult childhood cancer survivors (ACCS) treated for CNS (brain and spinal) tumors are at significant risk of late effects (LEs) or long-term health problems occurring over 5 years after treatment.

To assess the burden of LEs in ACCS treated for CNS tumors and determine if previously unrecognized LEs are detected by recall assessment in ACCS "lost to follow up" (not seen at a cancer center for 5 years or more).

Design/Methods: We identified all CNS ACCS treated with radiation therapy (RT) at age 18 years or less in BC, between 1969 to 2002 and lost to follow-up. 201 patients were identified, 110 patients were recalled for assessment. In total 27 patients have attended. Data collected included demographics, original therapy details, LEs detected prior to and at recall;

evidence of previous screening as per COG guideline recommendations.

Results: Of the 27 patients, the median age was 40 years, seen an average 30 years since therapy. 22% had experienced at least one CVA (Cerebrovascular accident), 44% had ongoing headaches, 30% had seizures (50% on anti-epileptics). 66% had hearing loss (73% bilateral), 66% patients had visual problems, 22% patients required ophthalmology referral. 16 patients (60%) had a psychiatric diagnosis and 2 patients required psychiatric referral. 6 patients had primary hypothyroidism, 6 had panhypopituitarism, 16 patients (60%) required referral to endocrinology (only 2 were already followed). Prior to clinic 5 patients had a thyroid US, 9 patients had meningioma screening, 4 patients had lipid profile testing. Clinic assessment diagnosed 11 of 12 patients with thyroid nodules, 3 of 6 patients with meningioma, 4 of 8 hypertensive patients and 9 of 12 patients with hypercholesterolemia.

Conclusions: ACCS lost to follow up and previously treated for CNS malignancies have significant LEs and were not receiving adequate follow-up and screening. A recall program detects a significant number of previously unrecognised LEs.

V535 SIOP19-0761 | Echocardiographic Long-Term Follow-up in Adult Survivors of Pediatric Cancer Treated with Dexrazoxane-Anthracyclines Association

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Background/Objectives: Co-administration of Dexrazoxane has been shown to reduce short and mid-term anthracyclines cardiotoxicity in children. The usefulness of dexrazoxane in preventing late (>10 years) anthracycline cardiotoxicity is under investigation, yet. Aim of this study was to assess cardiac function in long-term (>10 years) survivors of childhood tumors treated with dexrazoxane/anthracycline association.

Design/Methods: Adult survivors previously treated with co-administration of anthracyclines/dexrazoxane for childhood renal tumors or sarcoma from 1992 to 2008 at Pediatric Oncology Unit of "Sapienza" University were eligible. Healthy non-athletic subjects comparable for age, sex and body surface area were enrolled as control group. Echocardiographic measurements included 3D left ventricular (LV) ejection fraction (LVEF) and LV and right ventricular (RV) global longitudinal strain (GLS).

Results: Twenty dexrazoxane-treated survivors (9M/11F), median age at diagnosis 5 years (range 1-17) and at study enrollment 26 years (range 18-35) were evaluated at median

follow-up of 21.5 years (range 10-26). The median cumulative doses of doxorubicin and epirubicin were 210 mg/m² and 300 mg/m², respectively. No evidence of cardiac toxicity, as defined by current guidelines, was reported in all survivors. No significant differences in standard and deformation imaging parameters were observed between survivors and controls (3D LVEF 58 ± 3% vs 60 ± 5% p=NS; LV GLS -21 ± 1% vs -21 ± 2% p= NS; RV GLS -23 ± 2% vs -23 ± 5% p= NS). Moreover, considering survivors who received a cumulative dose of anthracyclines above the median (>210 mg/m² for doxorubicin and >300 mg/m² for epirubicin) no significant differences were found with the group that received a lower dose. No second tumor was registered in dexrazoxane-treated survivors.

Conclusions: 2D and 3D Echocardiography assessment and 2D Strain analysis did not show subclinical myocardial dysfunction in adult survivors who received dexrazoxane-anthracyclines in childhood.

V536 SIOP19-1569 | High Hospitalization Rates for Symptoms Without an Underlying Diagnosis in 5,650 Long-Term Childhood Cancer Survivors: A Dcog-Later Linkage Study

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Background/Objectives: Insight in hospitalizations in long-term childhood cancer survivors (CCS) is useful to understand the impact of long-term morbidity. We aimed to investigate hospitalization rates and underlying types of diagnoses in a Dutch nationwide CCS cohort compared to matched controls, and to investigate the determinants.

Design/Methods: We linked 5,650 five-year CCS from the DCOG-LATER cohort and 109,605 age- and sex-matched controls to the Dutch Hospital Discharge register, which

contained detailed information on day- and inpatient hospitalizations from 1995-2016. Relative hospitalization rates (RHRs) were calculated using a Poisson regression model. Adjusting for multiple hospitalizations per person via generalized estimated equations, using a Poisson model, we investigated determinants for hospitalizations for all types of underlying diagnoses among CCS.

Results: CCS were twice as likely to be hospitalized than reference persons (RHR 2.0, 95% confidence interval (CI) 1.9-2.2). Although CCS had more hospitalizations for 17 types of underlying diagnoses, they were especially more likely to be hospitalized for endocrine conditions, (RHR: 6.0, 95% CI 4.6-7.7), subsequent neoplasms (RHR: 5.6, 95% CI 4.6-6.7) and symptoms without underlying diagnoses (RHR: 5.2, 95% CI 4.6-5.8) For those types of conditions, female sex and radiotherapy were determinants.

Conclusions: This study provides new insights the high risk of hospitalizations for many types of underlying diagnoses in CCS and treatment related determinants. CCS are especially at high risk for hospitalizations for endocrine conditions, subsequent neoplasms and symptoms without an underlying diagnosis. This new knowledge is important for survivorship care and to identify possible preventable hospitalizations among CCS.

V537 SIOP19-1587 | Primary Health Care Use for Childhood Cancer Survivors - A DCOG-LATER Linkage Study

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Background/Objectives: Childhood cancer survivors are at risk of developing long-term morbidity, which is very likely to be presented to a primary care physician. Therefore, insight in primary care use in survivors is needed. We aimed to

investigate the volume of primary care use among long-term childhood cancer survivors, underlying health problems and determinants.

Design/Methods: Data from a Dutch nationwide cohort of five-year survivors was linked to the Nivel Primary Care database, which contains detailed data on primary care use from a representative sample of 10% of all Dutch primary care physicians. For every survivor included in the study, two matched controls were selected. Primary outcome was the number of contacts with the primary care physician per year of follow-up, secondary outcome was the reason for contact. We used negative binomial regression to compare the number of contacts between survivors and the reference population, and to identify determinants for having more contacts among survivors.

Results: A total of 602 survivors and 1,204 controls were included. Survivors were 1.3 times more likely to contact their primary care physician than controls (95% confidence interval (CI) 1.2-1.5), up to 1.5 times at an attained age over 40 years (95% CI 1.2-1.8). Compared to the reference population, survivors were 4.9 times more likely to seek contact for new types of malignancies, 3.1 times for hematological conditions and 2.8 times for endocrine conditions. Female sex, higher attained age and treatment with radiotherapy were determinants for having more contacts among survivors.

Conclusions: Childhood cancer survivors have a high health care use in the primary care practice as compared to matched controls. Especially females, those who are older and those treated with radiotherapy are at risk. Our results emphasize importance of disseminating the current knowledge on long-term morbidity in childhood cancer survivors among primary care physicians.

V538 SIOP19-0363 | Necessary Management in the Long-Term Follow-Up System for Supporting Childhood Cancer Survivors of the Adolescent and Young Adult Generation in Japan

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Background/Objectives: Long-term follow-up (LTFU) for childhood cancer survivors (CCSs) is critically important for the early detection and treatment of late-stage complications, however, many CCSs who have reached their adolescent and young adult (AYA) phases discontinue medical visits. LTFU in medical institutions faces difficulties with researching CCSs and supporting them adequately. The purpose of this

study was developed to clarify necessary management in the LTFU system for supporting CCSs in AYA generation.

Design/Methods: We conducted a survey (questionnaire and/or interview) of 117 CCSs aged ≥ 18 years old in collaboration with the Patient Associations, Japan.

Results: The follow-up rate for 20- and 40-year-old CCSs was 87.2% and 46.5%, respectively. Discontinuation of medical visits was due to physicians' perspectives (34.9%) and CCSs' own decision based on "no physical problems, keeping busy, financial difficulty" (65.1%). Multivariate analysis demonstrated that lacking the understanding of LTFU levels, and marriage was an independent factor of dropout ($P = 0.0290$ and $P = 0.0470$, respectively). Among all CCSs, 58.4% required multiple medical consultations per year, and 72.3% had to visit more than two medical departments. Notably, 49.4% of CCSs requested convenience for LTFU such as consultations on weekends or in their residential neighborhood clinics. Late-stage complication was the most common problem in CCSs (43.8%), followed by anxiety about future health (30.1%), difficulty in medical visits (28.8%), and anxiety at a specific life stage (28.8%). Moreover, CCSs needed supportive care for medical expenses (26.8%), followed by rehabilitation in society (25.6%), societal support (23.2%), medical support such as provision of a treatment summary (22.0%), and an explanation of late-stage complications (22.2%).

Conclusions: It is necessary that both physicians and CCSs understand the need for LTFU to detect late-stage complications. Moreover, improving the convenience of medical visits and support, such as for medical costs, is imperative.

V539 SIOP19-0368 | Perceived Life Satisfaction, Psychological Symptomatology, Cognitive Problems and Coping Strategies in AYA Cancer Survivors and Controls

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Background/Objectives: This study compared life satisfaction, psychological symptomatology, cognitive problems and coping strategies adoption of adolescent and young adult (AYA) cancer survivors with those of a control group of peers with no history of serious illness. The links between socio-demographic and medical factors and AYA cancer survivor outcomes were investigated.

Design/Methods: The participants included AYA cancer survivors ($n = 205$) recruited during follow-up visits, and AYA peers ($n = 205$) recruited from the secondary schools, youth groups and universities, matched for gender and age. All of

the participants filled in self-report questionnaires regarding life perceptions, psychological symptoms, cognitive problems and adopted coping strategies. In addition, medical and socio-demographic information were collected.

Results: There were statistically significant differences adopting chi-square or paired-samples t-tests between survivors and controls in terms of education level, cognitive reported problems, past life perception and coping strategies adoption, while no significant difference was found for psychological symptomatology. Cancer survivors attended school for fewer years, had a worse perception of their past life, lower reported cognitive problems and more positive coping strategies than controls. The results showed no clear gender or age differences along the examined variables; only females reported more mood problems than males. Hematopoietic stem cell transplantation (HSCT) experience ($\beta = -0.29$; $p = 0.01$) and worse past life perception ($\beta = -0.18$; $p = 0.02$) were recognized as predictors of higher psychological symptoms in survivors ($R^2 = 0.25$, $F = 3.46$; $p = 0.001$).

Conclusions: Adolescent and young adult cancer survivors reported an equal frequency of psychological symptoms, more positive coping strategies, lower cognitive problems and lower past life perception than controls. The AYA cancer survivors more at risk for psychological symptomatology were those underwent HSCT and those who declared a worse past life perception. Future studies should aim to investigate better post-traumatic growth using qualitative narratives.

V540 SIOP19-1001 | Frailty and its Determinants in Long-Term Dutch Adult Survivors of Childhood Acute Myeloid Leukemia, Wilms Tumor and Neuroblastoma

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Background/Objectives: Several simultaneous impairments in physical ability may be an indication of frail health in adult survivors of childhood cancer. The primary aim of our study was to assess the occurrence of frailty in a selected Dutch cohort of adult survivors of childhood cancer and compare this to healthy controls. The secondary aim was to explore determinants of frailty.

Design/Methods: In this cross-sectional study, we used data of 71 very long-term survivors (median age 28.8 years (IQR: 18.8-62.8 years)) of acute myeloid leukemia (AML)($n=17$), neuroblastoma (NBL)($n=26$) and Wilms tumor (WT)($n=28$),

and 75 age and sex-matched healthy controls (median age 26.9 years (IQR: 17.9-61.7 years)). Prefrailty and frailty were respectively defined as having 2 and ≥ 3 of the following five indicators: low body weight (body mass index $<20\text{kg/m}^2$), muscle weakness (lowest 20% of hand grip strength and/or jump peak power), slow walking speed (lowest 20% of the six-minute walk test), physical inactivity (beneath Dutch exercise standard) and self-rated physical limitations in activities of daily living. Potential determinants included sociodemographic, cancer and treatment related characteristics and lifestyle.

Results: Thirty-two percent of the survivors and 16% of the controls were classified as frail ($p=0.03$); prefrailty occurred in 37% of the survivors and 24% of the controls ($p=0.15$). The occurrence of frailty was highest in survivors of AML (82%) compared to NBL (65.4%) or WT (64.3%). Being a survivor of childhood cancer and being overweight/obese ($\text{BMI}>25$) increased the odds of frail health, respectively, OR: 3.2 (95% CI: 1.6-6.5), OR: 2.6 (95% CI: 1.2-5.5). Five survivors underwent myeloablative autologous stem cell transplantation (ASCT), all five were either prefrail or frail.

Conclusions: In conclusion, survivors of childhood AML, NBL and WT carry a relatively high risk of frailty. AML survivors, particularly those who underwent ASCT, and people with overweight and obesity appeared to have the highest risk of frailty.

V541 SIOP19-0535 | Childhood Cancer Survivors Treated Before The Age of One Year: Long-Term Outcomes

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Background/Objectives: Age at diagnosis <5 years is associated with more frequent and severe late effects of childhood cancer therapy. But little is known concerning long-term follow-up (LTFU) of infants. The aim of this study was to describe the long-term outcomes of childhood cancer survivors (CCS) aged <1 year at diagnosis.

Design/Methods: Five-year CCS from the FCCSS (*French Childhood Cancer Survivor Study*) treated at Gustave Roussy (GR) before 1 year of age from 1946 to 2000 for solid cancer were included. Epidemiological data concerning mortality, second malignant neoplasms (SMN) and cardiac diseases were obtained by mortality registry, self-administrated questionnaires, clinical visits and cohort linkage with the health insurance information system (SNIIRAM). Other late effects

were identified in adult patients who had LTFU visits at GR between 01/2012 and 12/2017.

Results: 796 patients were included (sex ratio M/F=1.24; 50% neuroblastoma and 17% Wilms tumor; 353 diagnosed before 1980, 256 in 1980-1989 and 187 in 1990-2000; 70% received chemotherapy and 38% radiation therapy RT). With a median follow-up of 31 years (range=6-53), the overall mortality rate was 11%. Main deaths causes were primary tumor (22%) and SMN (34%). The 35-year-cumulative incidences of SMN and cardiac diseases were 5%. Forty-four SMN were registered including 17 sarcomas, 13 carcinomas and 3 hematologic malignancies. Thirty-seven patients suffered from cardiac diseases, including 20 cardiac failures and 7 valvular disorders. A LTFU visit was performed in 112 patients at a median age of 35 years and identified ≥ 1 late effects in 97% of the patients: thyroid disorders (47%), endocrine (42%), musculoskeletal (49%, mainly due to laminectomy or thoracic/abdominal RT), renal (21%, 64% of patients with Wilms tumor), neurocognitive (29%) and sensory (22%). More than 25% reported psychological or psychiatric trouble.

Conclusions: Patients treated before the age of 1 year are at very high risk of late effects and need specific and multidisciplinary very long-term follow-up.

V542 SIOP19-1146 | Patterns and Predictors of Perceived Health Among Long-Term Survivors of Childhood Cancer

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Background/Objectives: Survivors of childhood cancer are at increased risk of experiencing treatment related late effects. Perceived health can serve as an indicator of overall health. This study aims to understand how the perceived health of survivors: a) varies overtime; b) compares to the perceived health of the general Canadian population and; c) varies with respect to clinical variables (e.g., diagnosis), health problems (e.g., headaches) and lifestyle factors (e.g., physical activity).

Design/Methods: A total of 233 survivors (124 males; mean age at diagnosis=6.76 years; mean time off treatment=10.29 years) were included in the analyses. Survivors completed annual health assessments as part of their long-term survivor clinic appointments, including a question on perceived health answered on a 5-point Likert scale, where 1 is excellent and 5 is poor. Linear regression was used to calculate change in perceived health across 2014, 2015 and 2016 clinic appointments. Linear regression was used to assess factors

associated with patterns of perceived health. Perceived health of survivors was compared to the general Canadian population using data from the 2014 Canadian Community Health Survey.

Results: Most survivors (73%) reported excellent or very good health. The majority of survivors' perceived health remained stable across clinic appointments. The mean perceived health of survivors (2.14 ± 0.87) was not statistically different from the general Canadian population (2.17 ± 0.87). Time off treatment ($B=0.027$; CI 95%, 0.008 to 0.046; $p=0.006$), pain ($B=0.321$; CI 95%, 0.193 to 0.449; $p<0.0005$), depression ($B=0.092$; CI 95%, 0.006 to 0.179; $p=0.036$), and physical activity ($B=-0.334$; CI 95%, -0.629 to -0.039; $p=0.026$) were significant predictors of survivors' perceived health.

Conclusions: The majority of survivors reported excellent or very good health. Factors shown to influence survivor perceived health, including pain, depression and physical activity, may inform targeted interventions. Insight into how survivors develop their conception of health may be warranted.

V543 SIOP19-1624 | High Prevalence of Adenomatous Polyps in Patients Treated with Abdominal Irradiation in Childhood - Slovenian Experience

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Background/Objectives: Patients treated with abdominal irradiation for childhood cancer especially when in combination with alkylating agents are at high risk of second colon cancer. The Children's Oncology Group recommends screening with colonoscopy 10 years after abdominal irradiation in patients after the age of 35 years, but reports about findings in such screening programs are scarce. In 2015, we started with screening colonoscopy in long-term survivors of childhood cancer in our follow-up clinic at the Institute of Oncology in Ljubljana.

Design/Methods: Between 1968 and 1995, 202 pts 0-16 years of age were treated for Hodgkin disease (117), Wilms tumour (76) or dysgerminoma (9) in Slovenia. In January 2015, 146 patients were alive. Second colon cancer was cause of death in one of 56 pts who had died. In December 2018, 120 pts were 35 years of age or more. Fifty-five of them received abdominal irradiation with 10 to 46 (med 30) Gy at the age of 3 months to 16 (median 10) years and were referred to screening colonoscopy. Twenty-four pts undergone colonoscopy until December 2018 at the age of 35 to 57 (median 49) years. Fourteen of them received chemotherapy with alkylating agents as well.

Results: In 15 pts (62%), tubular adenomas were found and removed (in one with partial colectomy). In 3 pts, hyperplastic polyps were found and another 2 pts had inflammatory changes of mucosa. In only 4 of the 24 patients, colonoscopy did not reveal any abnormalities. They got abdominal irradiation with 24 to 36 Gy and 3 pts received alkylating agents as well.

Conclusions: Screening colonoscopy serves as a very efficient tool for prevention and early detection of second colon cancer in patients after abdominal irradiation in childhood. We suggest it in patients who received abdominal irradiation with the dose below 30 Gy as well.

V544 SIOP19-1566 | Components of Metabolic Syndrome in Children and Adolescents Who Have Completed Leukemia Therapy

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Background/Objectives: During treatment of children and adolescents with leukemia, the misbalance of carbohydrates and minerals metabolism may occur leading to clinical manifestations of the components of metabolic syndrome. The purpose of the work was to study the frequency and manifestation degree of different clinical features associated with metabolic syndrome in a cohort of patients from the Clinical Rehabilitation Research Center "Russkoye Pole".

Design/Methods: The group of 100 leukemia survivors in 2017-2018 years was formed with an exhaustive clinical examination, including toxicity analysis on the chemotherapy, family history, physical and psychological status. In total, more than 50 characteristics were determined in all patients, including biochemical parameters, like insulin level, HOMA index, lipid profile and so on, as well as BMI, bioimpedance, exercise tolerance, sphygmometry, psychological testing. The statistical analysis was done using Statistica 8.0 software package (StatSoft Inc., USA).

Results: The reduced level of high-density lipoproteins was observed in 67% of patients; an increased BMI in 42% of patients, which corresponded to the disproportion of fat and muscle tissue. The insulin resistance determined as HOMA index higher than 3.2 was registered in 21% of patients and arterial hypertension in 16% of patients. There are tendencies, that obesity, insulin resistance and arterial hypertension had an adverse effect on the physical and psychological status. Genetic testing revealed statistically significant association of polymorphisms rs11091046 in the AGTR2 gene and rs4833095 in the TLR1 gene with insulin resistance developed after chemotherapy.

Conclusions: Thus, the algorithm described allows identifying the combination of three potential components of metabolic syndrome in 32% of leukemia survivors. The data obtained may contribute to development of individualized rehabilitation program for the prevention and treatment of metabolic syndrome in patients receiving antitumor therapy in childhood.

Treatment and Care - Immunotherapy

V545 SIOP19-0849 | Fever Management in High-Risk Neuroblastoma During Immunotherapy

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Background/Objectives: Clinical guidelines for fever management with immunotherapy are not well established. Although fever is a known secondary effect due to this therapy, patients also have risk factors for infection such as disease, immunosuppression, intravascular catheter and long-term hospitalization. The aim of this study is to assess the causes of fever and their management during immunotherapy in patients with High-Risk Neuroblastoma (HR-NB).

Design/Methods: Descriptive retrospective review of medical records of patients with HR-NB treated with immunotherapy (anti-GD2 +/- IL-2) as first line treatment according to HRNBL1/SIOPEN protocol, between January-2013 and December-2018.

Results: Eleven patients received immunotherapy, 7 girls and 4 boys with a median age at diagnosis of 2 years (range 8 months-10 years). As protocol randomization, 64% were treated with anti-GD2 and 36% with anti-GD2 and IL-2. Before and during each cycle, all of patients received prophylactic antipyretic. Ten out of eleven patients presented fever during hospitalization. In 55 administered cycles, 35 fever episodes (64%) were recorded: 48% of cycles with anti-GD2 (17/35) and 90% with anti-GD and IL-2 (18/20). None of the patients presented severe neutropenia. Empiric antibiotherapy was started in 66% of patients with fever. The infectious cause was identified in 40% (14/35) of episodes of fever such as bacteraemia, urinary infection or viroses. The most frequently isolated germs were gram positive bacteria (50%) in catheter-related bloodstream infections. None of the episodes were severe and the discharge only was delayed in two patients.

Conclusions: Despite the prophylactic measures, fever due to immunotherapy appeared in 3 out of 5 patients, most of them with anti-GD2 and IL-2. Infectious aetiology was observed in less than a half of cases, therefore not always might be indicated to start an empirical antibiotherapy. However, more studies are needed in order to develop recommendations for fever management in these patients.

V546 SIOP19-1509 | Adapter Chimeric Antigen Receptor (ADCAR)-Engineered NK-92 Cells Targeting Neuroblastoma

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Background/Objectives: Treatment of high-risk neuroblastoma still remains a major challenge in pediatric oncology despite intensive multimodal therapies. To enhance the therapeutic utility of NK cells for adoptive immunotherapy, we have recently developed a universal adapter CAR (AdCAR) system based on the unique properties of a novel single chain variable fragment (scFv) recognizing a "neo"-epitope comprising the endogenous vitamin biotin in the context of a specific linker, referred to as linker-label epitope (LLE) conjugated to an adapter molecule (AM) e.g. a monoclonal antibody.

Design/Methods: NK-92 cells were obtained from ATCC and transduced with a second generation AdCAR construct containing CD28 co-stimulatory plus CD3- ζ signaling domains. Using single cell sorting, AdCAR NK-92 clones with the highest CAR expression were selected and tested in combination with LLE-tagged therapeutic antibodies targeting a variety of antigens expressed on different neuroblastoma cell lines. Calcein AM-based cytotoxicity assays, real-time impedance measurements and flow cytometry analysis were used to evaluate the specificity and activity of AdCAR NK-92 cells *in vitro*.

Results: AdCAR NK-92 in contrast to parental NK-92 cells induced specific and potent neuroblastoma cell lysis in an antibody and antigen dose-dependent manner. The selective cytotoxicity of AdCAR NK-92 cells stringently relied on the presence of LLE-conjugated antibodies, verifying the specificity and flexibility of the AdCAR system.

Conclusions: The AdCAR NK-92 cell line, whose effector function can be tightly regulated and redirected against one or multiple antigens, allows tunable and flexible antigen targeting, thus counteracting tumor immune escape mechanisms. Moreover, AdCAR NK-92 cells can be manufactured as an "off-the-shelf on demand" standardized product improv-

ing the practicality of CAR NK cell therapy combined with the possibility of tailoring a LLE-AM platform for patient-individualized neuroblastoma treatment.

V547 SIOP19-0970 | Regulation of the Functions of Expanded Natural Killer (NK) Cells by N-820, an IL-15 Superagonist with 4 Single-Chain Anti-CD20 Antibody Domains Against Burkitt Lymphoma (BL)

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Background/Objectives: Children with relapsed/refractory BL have a poor prognosis (Cairo et al BJH, 2018). NK cells play a major role in the rejection of tumors. However, NK therapy is limited by small numbers of active NK cells, lack of tumor targeting specificity, and multiple mechanisms of tumor escape from NK immunosurveillance (Chu/Cairo et al BJH, 2019). Our group has successfully expanded functional and active NK cells (exPBNK) with irradiated feeder cells (Chu/Cairo, et al, *Can Imm Res* 2015). N-820 was generated by fusing N-803 (ALT-803, IL-15 superagonist) to four single-chains of the tumor-targeting monoclonal antibody, rituximab (Liu/Wong, et al, *JBC*, 2016).

To investigate N-820 mediated-crosstalk between BL and exPBNK cells and the anti-tumor effects of N-820 combined with exPBNK against rituximab-sensitive and -resistant BL.

Design/Methods: NK cells were expanded with irradiated K562-mbIL21-41BBL. N-803 and N-820 were generously provided by Altor Bioscience. Rituximab-sensitive Raji and -resistant Raji-2R and Raji-4RH were used as targets. The levels of mRNA and proteins of cytokines, chemokines and growth factors were monitored by real-time PCR and ELISAs, respectively. *In-vitro* cytotoxicity was performed and BL xenografted NSG mice were generated as we described (Chu/Cairo, et al, *Oncoimmunology* 2017).

Results: N-820 significantly enhanced exPBNK cells cytotoxicity against Raji, Raji-2R and Raji-4RH compared to controls ($p < 0.001$). N-820 significantly enhanced IFN- γ , granzyme B, and GM-CSF release from exPBNK against Raji-2R and Raji-4RH compared to controls ($p < 0.001$). We also found that N-820 significantly reduced CCL22 release from Raji-2R compared to controls ($p < 0.05$). In NSG mice bearing BL tumor, we found that N-820 added to exPBNK significantly reduced tumor burden ($p < 0.05$) and increased BL xenografted NSG mice survival ($p < 0.05$) compared to control groups.

Conclusions: N-820 significantly enhanced exPBNK cytotoxicity, IFN- γ , granzyme B, GM-CSF release from exPBNK, inhibited CCL22 release from BL and increased anti-tumor activity against BL xenografted NSG mice.

V548 SIOP19-1671 | Analysis of Ex Vivo Expanded and Activated Clinical Grade Human NK Cells After Cryopreservation

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Background/Objectives: Natural killer cells can display potent anti-tumor activity. However, one factor limiting their clinical use is the difficulty generating large numbers of cells to allow for multiple sequential infusions into patients. Consequently, several methods have been developed to expand and activate NK cells in vitro. Infusion of fresh NK cells is generally preferred to the administration of cryopreserved cells because of concern that cryopreservation diminishes NK cell activity. However, little data is available to compare freshly expanded/activated NK cells to those that have been cryopreserved.

Design/Methods: We performed 5 qualification runs incubating NK cells in a WAVE bioreactor with IL-2 and a feeder cell line (K562-CD137L-mbIL15) under GMP conditions. The resulting fresh and cryopreserved NK cell products were characterized and compared.

Results: Following an 11-day incubation period, NK cells expanded 28 – 194 fold (median 56 fold) with a purity of 72 – 93% (median 86%). Purity increased to 80 – 99% (median 99%) after CD3 depletion using the CliniMACS® cell processing system. Analysis of cryopreserved NK cell products demonstrated excellent recovery and viability of CD56+ cells. Both fresh and cryopreserved NK cell products showed increases in Granzyme B and NKG2D, but not in PD-1. Both NK cell products exhibited enhanced killing capacity compared to pre-expanded PBMC. Freshly expanded/activated NK cells generated high levels of IFN γ , which was abrogated by JAK1/JAK2 inhibition with ruxolitinib. In contrast, cryopreserved NK cells showed lower production of IFN γ compared to pre-expanded PBMCs, and IFN γ levels were unaffected by JAK1/JAK2 inhibition.

Conclusions: NK cells that have been expanded and activated using IL-2 and the K562-CD137L-mbIL15 feeder cell line show significantly enhanced functional capacity, even after cryopreservation. The use of sequential NK cell infusions, (along with an anti-GD2 immunocytokine) is currently being

tested in a clinical trial for children with relapsed neuroblastoma (NCT03209869).

V549 SIOP19-0231 | Development of Piggybac Transposon Mediated CAR-T Cells Targeting EPHB4 for Pediatric Solid Tumors

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Background/Objectives: Chimeric antigen receptor T cell (CAR-T) therapy has recently produced spectacular success in the treatment of hematologic malignancies. However, comparable responses in targeting solid malignancies have not been achieved. CAR-T cells engineered by non-viral gene transfer, including *piggyBac* transposon (PB)-based gene transfer by electroporation, can be produced at an extremely low cost as compared to virally engineered CAR-T cells. Here, we developed novel chimeric antigen receptor T cells using *piggyBac* (PB) transposon-based gene transfer for the clinical application of these cells in the treatment of pediatric solid tumors.

Design/Methods: Using rhabdomyosarcoma (RMS) as a model, we generated PB-based CAR-T cells specific to EPHB4 molecules which is strongly expressed and associated with the malignant phenotype of RMS, by using the optimized electroporation and culture protocol we developed. The phenotypes and the expression of exhaustion markers on CAR-T cells were assessed using flow cytometry. To evaluate the cytotoxic activity, the CAR-T cells were co-cultured with tumor cells at different effector:target ratios, and the number of live tumor cells were analyzed by real time cell analyzer or flow cytometry. For in vivo experiment, the EPHB4-CAR-T cells were injected via tail vein of RMS xenograft-bearing mice.

Results: We successfully generated EPHB4-CAR-T cells with 40-70% of CAR positivity. Notably, EPHB4-CAR-T cells exhibited naïve/memory stem cell phenotype, indicating their proliferative potential in response to antigen stimulation. EPHB4-CAR-T cells demonstrated sustained killing activity against tumor cells, even in multiple tumor re-challenges in vitro. Moreover, EPHB4-CAR-T cells debulked EPHB4-positive tumors in vivo.

Conclusions: PB-based EPHB4-CAR-T cell therapy is promising for the treatment of RMS. A non-clinical study of PB-based CAR-T cell therapy targeting pediatric soft tissue sarcoma is underway, precluding future clinical trials in Japan.

Treatment and Care - New Drugs - Experimental Therapeutics

V550 SIOP19-0900 | Phase I Study of Fluvastatin-Celecoxib Combination in Children with Relapsing/Refractory Optico-Chiasmatic Low-Grade Glioma or High Grade Glioma (FLUVABREX): First Results

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Background/Objectives: Preclinical data support the anti-cancer activity of celecoxib and fluvastatin in high grade (HGG) and optico-chiasmatic low grade gliomas (LGG). Therefore, a Phase I study was designed to evaluate this combination in children with refractory/relapsed HGG and LGG. The aims of the study were to assess the safety, pharmacokinetics (PK), maximum tolerated dose, Recommended Dose for Phase II study (RDP2), in children with recurrent/refractory LGG or HGG.

Design/Methods: This is a multicenter national phase I trial, including patients aged 6 to 21 year old. Fluvastatin starting dose was 2 mg/kg/day, 14/28 days, with fixed dose of celecoxib (200 mg to 800 mg /day according to weight). Four dose levels of fluvastatin (2, 4, 6, 8 mg/kg/day) were evaluated. A Continual Reassessment Method was used for fluvastatin dose escalation. Dose-limiting toxicities (DLT) were determined on the 1st cycle of treatment using the NCI-CTC v4.0 scale. PK samples were obtained for fluvastatin and celecoxib at D1 & D14 of cycle 1 and pre-dose of cycle 2.

Results: Twenty patients were enrolled with a median age of 12 years (range, 5.9-19 years). They previously received a median of 3 (range 1-7) lines of treatment. Ten patients were treated for LGG and 10 for HGG, receiving a median of 3 cycles of fluvastatin-celecoxib (1-18). Patients with LGG received a median of 5 cycles (1-18). Among the 17 patients evaluable for DLT, 2 DLTs were reported: 1 grade 3

maculo-papular rash (4 mg/kg), and 1 grade 4 increase of CPK (6 mg/kg). The RP2D of fluvastatin is 6 mg/kg/day. No additional grade 3 related adverse event was reported.

Conclusions: In children with refractory/relapsed glioma, the RDP2 of fluvastatin associated with celecoxib is 6 mg/kg/day. This combination is well tolerated encouraging a phase 2 study.

V551 SIOP19-0942 | Securing Access to Innovative Anticancer Therapies for Children, Adolescents and Young Adults Outside Clinical Trials: The SACHA Study of the French Society of Pediatric Oncology

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Background/Objectives: Access to innovative anticancer therapies for children, adolescents and young adults within clinical trials in France is steadily increasing in the last years. Thanks to the French precision medicine MAPPY-ACTS (NCT02613962), more than 400 molecular profiles of pediatric/adolescent patients with recurrent/refractory malignancies at relapse/progression have been performed in France since 2016 and more than 100 patients have been included in the proof-of concept AcSé-ESMART trial (NCT02813135). However, clinical trials portfolio is still insufficient and access to new treatment outside their marketing authorization is still needed. In order to secure the access to these innovative therapies outside the frame of clinical trials, the French Society of Pediatric Oncology (SFCE) has developed the SACHA (Secured Access to innovative medicines for Children with cAncer) study in collaboration with the 7 inter-regional-multidisciplinary tumor boards (RCCPI) of the French National Cancer Institute (INCa).

Design/Methods: French observational study consisting on prospective collection of toxicity and efficacy data of off-label administration of anticancer therapies with marketing authorization > 01/01/2007, to patients ≤ 25 years-old with pediatric tumors outside the frame of clinical trials. Data will be collected by the validated pharmacovigilance tool VIGINOM. Study duration will be 3 years with 450 expected patients.

Results: Expected results; to analyze current landscape of innovative anticancer therapies administered to children, ado-

lescents and young adults in France outside their marketing authorization. This analysis will provide quality data on toxicity in real life situation. It will also support the development of specific trials for those therapies with trends of efficacy and discontinue the usage of those drugs that prove ineffective.

Conclusions: The SACHA study is planned to start recruitment in Q3 2019 in all 31 SFCE centers.

V552 SIOP19-1387 | Innovative Anticancer Therapies Administered Outside Clinical Trials for Children/Adolescents/Young Adults with End-Stage Cancer

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Background/Objectives: To analyze anticancer innovative therapies administered outside their marketing authorization in the last 6 months of life for patients < 25-years-old.

Design/Methods: Retrospective analysis of all patients deceased between 01/01/2016-31/12/2017 in three reference French pediatric departments. The aim of this study was to describe prescription frameworks, type of molecules, and potential benefits and risks of these treatments used outside a clinical study.

Results: Of the 306 patients identified, 43 (14%) received 48 off-label innovative treatments during the previous 6 months before their death. Potential inclusion in an early phase trial was available for 9/43 patients, but off-label treatment was prioritized after by multidisciplinary tumor board discussion. Median age was 10.8 y.o (0-22 y.o) after a median of 2 lines (1-6) of previous anti-cancer treatments. Brain tumors account for 50% of cancers followed by bone tumors in this cohort. Tyrosine kinase inhibitors (TKI) (33/48, mainly mTOR and multi-TKI) were the most frequent molecules prescribed, followed by immunotherapy. For 24 patients, complete molecular profile of their tumor was available, and 15 received matched targeted therapies (62%). Disease evaluation showed 5 objective responses. Median time to progression was 91 days with innovative treatments versus 141 days with the previous line (p=0.24). According to CTCAE v4.0, there were 8 grade 3-4 adverse effects (3 related to immunotherapy), and 20 grade <2. All treatments were administered on an outpatient basis with no difference in hospitalization when compared with patients that did not receive off-target therapies.

Conclusions: Off-label prescription in advanced-stage cancer patients is a reality due to lack of early clinical trials for this population and efficacy/toxicity aren't usually systematically monitored. In our cohort, 5 patients benefited from the use of an innovative molecule, without compromising their end-of-life care. Prospective registration will be organized in all French pediatric oncology centers to monitor precisely this type of drug prescription.

V553 SIOP19-0367 | The 18-Year-Old Trial Inclusion Limit is a Major Barrier in the Access to Clinical Trials for Adolescents and Young Adults (AYAs) With Cancer

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Background/Objectives: The 18-years-old age limit for inclusion in clinical trials constitutes a major hurdle for AYAs with cancer that the main stakeholders are advocating to overthrow. We analyzed the impact of this age barrier on the access of AYAs to cancer trials and novel therapies.

Design/Methods: ClinicalTrials.gov was searched to identify all the trials including patients with ten malignancies particularly relevant for AYAs, starting between Jan/2007-Jul/2018. The trials were categorized as pediatric (including patients <18 years only), adult (≥18 years), and transitional (including both adult and pediatric patients). Transitional trials with a lower limit between 12-18 years and an upper limit <40 years were considered AYA-specific.

Results: Out of 2764 identified trials, 2176 were included: 79% adult, 19% transitional, 2% pediatric. Five trials were AYA-specific. The total number of new trials increased over the years (156 in 2007; 228 in 2017); however, the number of transitional trials remained stable. The availability of trials increased with age, with a major increase at age 18: the number of trials accessible to an AYA patient at age 17 was 20% (442/2176) vs 95% (2075/2176) at age 18. For trials investigating targeted therapies, this increase was 460% (from 197 trials available at age 17 to 901 at age 18); for trials investigating immunotherapies, the increase was 1,200% (from 55 available trials at age 17 to 658 at age 18).

Conclusions: AYAs have limited access to cancer trials and innovative therapies, with no improvement over the last decade. The 18-years-old limit continues to be a major hurdle. The findings of this study support the push of the research

community to change the 18-years-old inclusion criterion in oncological clinical trials and to allow the inclusion of adolescents after first-in-human trials are completed.

V554 SIOP19-1486 | Participation in an Early Phase Trial for an AYA: Is This A Choice?

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Background/Objectives: This study aimed to assess adolescents and young adults (AYA) 15-25 yrs old decision-making process in early phase trials and interaction with their parents and caregivers. In early phase clinical studies, it is essential to draw a distinction between research objectives and personal objectives of patient/parent/caregiver. The research objectives usually are evaluation of toxicity, recommended dose finding (even if now limited to the exploration of dose levels around the adult recommended dose) and preliminary assessment of activity. The personal objectives of the patient/parent/caregiver are mainly related to the hope of at least a tumor response.

Design/Methods: A qualitative study was conducted in four French pediatric or AYA oncology units: a unique psychologist performed audio-recorded semi-structured interview of 21 AYA, 16 parents and 13 caregivers (oncologist, student, nurses). Data were thematically analyzed using coding, drawing upon principles of grounded theory, supported by NVivo 11, qualitative data analysis software.

Results: This number of interviews reaches "saturation" in the context of this qualitative research. AYA and parents were satisfied with the investigator's attitude and explanations. They had a very positive vision of the center, team and investigator's attitude and communication. Although they were not induced by the investigator to consent, they mostly felt like they had no choice because of their medical situation and the proposed "unconvincing" alternatives. They accepted the early phase trial with the hope of cure. The doctors wanted to be transparent, but they could not be completely explicit regarding the context of early phase trial. The majority of nurses had difficulty understanding why an early phase trial was proposed for AYA they felt being in an end of life situation.

Conclusions: AYA were satisfied with consent process and agreed to participate because the early phase trial was considered as the unique option. Hope is maintained by the investigators and the patients.

V555 SIOP19-1499 | Establishment of a Biobank of Patient-Derived Orthoxenografts from Pediatric Solid Tumors Within a Single-Center Precision Medicine Program. Results After 4 Years

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Background/Objectives: Despite improvements in patient survival, 20% of all pediatric cancers remain incurable, and high-risk/metastatic tumors represent the majority of this percentage. Precision oncology can offer novel therapeutic strategies, being already a reality in adult cancer management. As part of our pediatric precision oncology program (Cancer Omics for Kids, Comik) we have developed a biobank of advanced preclinical models, in order to develop real-time treatments and for research purposes. We show our preliminary results developing children-derived orthotopic xenografts (named "Chilodox") from different tumor-types, locations and samples.

Design/Methods: From December 2014 until December 2018, we have orthotopically implanted 95 pediatric tumors. Both primary tumors and metastases from different locations were surgically grafted in their original locations in immunocompromised mice, maintaining their three-dimensional tissue structure. In some cases, Chilodox were used to perform personalized preclinical drug testing and to conduct other research experiments.

Results: To date, we have established 28 children-derived orthoxenografts, including: Rhabdomyosarcomas, Ewing sarcoma, Neuroblastomas, Osteosarcoma, Wilms tumors, Hepatoblastomas, Hepatocellular carcinoma, Malignant rhabdoid tumor, Retinoblastoma and other sarcomas. From 10 patients, local relapse (3 cases) or metastatic models (7 cases) were developed in their original locations (e.g. brain metastasis of neuroblastoma, breast metastasis of alveolar rhabdomyosarcoma, lung metastasis of osteosarcoma). The implantation take rates improved over time, from 14% in 2015 to 33,66% (2.4SD) in the last 3 years. One patient (genitourinary metastatic rhabdomyosarcoma) was treated based on the

drug-response results obtained from his own Chilodox, two patients died before getting results from their Chilodox and one high-risk neuroblastoma model was used to test a new drug.

Conclusions: We have been able to implement a children-derived orthoxenografts biobank. These models may be outstandingly valuable preclinical tools to improve the treatment of bad prognosis/metastatic pediatric tumors and for the development of personalized treatments.

V556 SIOP19-1492 | Hypersensitivity and Silent Inactivation with Generic Pegylated L-Asparaginase in Children with Acute Lymphoblastic Leukemia (ALL)

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Background/Objectives: An integral component of ALL chemotherapy, Pegylated asparaginase (PEG-Asp) is immunogenic and hypersensitivity/silent inactivation are known to be associated with poorer survival. Hence this study was planned to study their incidence.

Design/Methods: This prospective observational study, included 68 patients <18 years of age with ALL treated with generic PEG-Asp (Emcure) as part of our Institutional ALL protocol (BFM-95 based) between January 2016 and December 2018. Two doses of PEG-Asp at 1500 IU/m² were administered as 2-hour infusion intravenously, two weeks apart on days 8 and 22 of induction (Ia) and re-induction (IIa) phase of therapy. Patients were monitored for hypersensitivity and known asparaginase related toxicities and graded as per Common Terminology Criteria for Adverse Events version 4.03. Serum asparaginase activity levels were recorded using medac Asparaginase-Aktivitäts-Test, 0, 7 and 14 days after each dose (day 8,15,22,29,36 of Ia and IIa). Therapeutic level of asparaginase activity was defined as >100 IU/L and silent inactivation as levels <20 IU/L. Study was conducted after appropriate informed consent/assent and approval from the Institutional Ethics committee. The data was analyzed with the software package SPSS, version 20.1 (Chicago, IL).

Results: Serum samples were available for 68 (Ia) and 66 (IIa) of the patients. Therapeutic drug levels (>100IU/L) were achieved among 98%(67/68, Ia) and 93%(62/66, IIa) of patients. Clinical hypersensitivity (>grade 1) occurred in 1/68 and 3/66 patients and silent inactivation among 0/68 and 2/66 patients during Ia and IIa respectively. The incidence of other asparaginase toxicities were similar to those previously reported and there were no toxic deaths. The two-year event free survival was 87%. This study from India reports incidence

of silent inactivation with generic PEG-Asp in a population ethnically different from the west.

Conclusions: During reinduction there was a low (7%) though significant incidence of clinical hypersensitivity or silent inactivation warranting therapeutic drug monitoring during IIa for optimizing therapy.

V557 SIOP19-1597 | Safety and Efficacy of Intraventricular ¹³¹I-Labeled Monoclonal Antibody 8H9 Targeting the Surface Glycoprotein B7-H3

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Background/Objectives: Tumors metastasizing to the CNS are associated with significant mortality. We tested toxicity and dosimetry of intraventricular ¹³¹I-labeled monoclonal antibody 8H9 targeting surface glycoprotein B7-H3 in patients with primary or metastatic CNS tumors.

Design/Methods: Tumor B7-H3 expression was assessed by immunohistochemistry. CSF flow was determined by ¹¹¹Indium-DTPA cisternography. 131 patients received 2mCi tracer of intra-Ommaya ¹²⁴I- or ¹³¹I-8H9 for nuclear imaging followed by therapeutic injection (10-80 mCi, dose levels 1-8 in 10mCi increments for phase I patients; expanded cohort 50mCi/injection) ¹³¹I-8H9. Pharmacokinetics were studied by serial CSF and blood samplings over 48 hours. Dosimetry was based on pharmacokinetics and region of interest analyses on serial PET. Toxicity was defined by CTCAE v.3.0. 8H9 dosimetry and therapy injections were repeated after 1 month if no serious adverse events or progressive disease ensued. Tumor response was determined by clinical, radiographic, cytologic criteria; overall survival was noted.

Results: 57 patients (ages 2-54 years, median age 11.7 years) received 158 injections. Primary CNS diagnoses included medulloblastoma (n=23), ependymoma (N=8), chordoma (n=1), rhabdoid tumor (n=1), choroid plexus carcinoma (n=3), ETMR (n=3), glioblastoma multiforme (n=1), PXA (n=1); metastatic tumors included sarcoma (n=9), melanoma (n=4), retinoblastoma (n=2), and ovarian carcinoma (n=1). Injections were well tolerated and routinely administered in the outpatient setting. Rare self-limited adverse events included grade 1 or 2 fever, headache, vomiting; 3 injections were associated with grade 3 toxicities requiring discontinuation of therapy including chemical meningitis (n=2), and

increasing communicating hydrocephalus (n=1). Although not a dose limiting toxicity, myelosuppression occurred in patients who had received craniospinal radiation and at dose levels 6 and higher (>60mCi). 16 patients remain alive including patients with high-risk malignancies including choroid plexus carcinoma, ETMR, recurrent ependymoma and recurrent medulloblastoma.

Conclusions: We conclude that intraventricular ¹³¹I-8H9 is safe and may have clinical utility in the treatment of primary and metastatic CNS tumors.

V558 SIOP19-0501 | Irinotecan and Temozolamide Treatment -Alone or Combined with Vincristin and/or Bevacizumab- for Relapsed/Refractory Childhood Cancer

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Background/Objectives: Relapse/refractory (RR) disease in childhood cancers (CC) has bad prognosis. We aimed to evaluate the effect of Irinotecan and temozolamide (IT) alone or in combination with vincristine and/or bevacizumab in RRCC.

Design/Methods: Fifty-five patients with RRCC were treated with irinotecan and temozolamide (50mg/m² and 150mg/m², 1-5 days) ± vincristine (1.5mg/m², 1st day) ± bevacizumab (10mg/kg, 1st day). Response to treatment and toxicity were evaluated retrospectively.

Results: There were 34 boys and 21 girls with a median age of 7.6 years. Diagnosis was brain tumor in 21, Ewing sarcoma in 12, soft-tissue sarcoma in 9, neuroblastoma in 7, renal tumors in 5, and other tumors in 6. IT was used alone in 10.9% of cases, was combined with vincristine in 50.9%, with bevacizumab in 18.2%, with both vincristine and bevacizumab in 20%. IT based protocols were used as second, third, fourth and fifth-line treatment in 23.6%, 45.4%, 21.8% and 9% of patients, respectively. Patients received median four (2-16), in total 287 courses. Best response was CR in 10.9%, VGPR in 12.7% and PR in 23.6% of patients. Median duration of responses was 9.6 months. Eight patients had stable and 21 had progressive disease. Following these protocols median follow-up time was 35.6 months. Overall and event-free survival rates at two-years was 23.3% and 11.7%, respectively. Objective response rate was higher in patients who received the protocol as a second line. Addition of vincristine and/or bevacizumab didn't change the response rates. Grade 3-4 diarrhea were observed in nine and neutropenia in six of the 287 courses.

Conclusions: Irinotecan and temozolamide show synergistic effect. Studies have suggested that the activity of IT is enhanced in combination with vincristine or bevacizumab.

We showed that IT is effective and tolerable in patients with RRCC and addition of vincristine and/or bevacizumab did not change the effect of IT.

V559 SIOP19-0853 | Integration of High-Throughput Drug Screening on Patient Derived Organoids into Pediatric Precision Medicine Programs: The Future is Now

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Background/Objectives: One of the most promising option to improve outcomes for pediatric cancer patients with relapsed or refractory disease is through molecular profiling guided treatment approaches. However, only 50% of these tumors harbor actionable events according to the first results from precision medicine programs in paediatric cancer. Therefore, compound screening on organoids grown from tumor tissue might reveal additional treatment options.

Design/Methods: The Princess Maxima Center, individualised THERapies program (PMC-iTHER) performs Whole Exome Sequencing (WES), low coverage Whole Genome Sequencing (WGS), RNA profiling using RNAseq and Affymetrix microarrays, and a methylation array on biopsy samples of relapsed or refractory patients. Data are analyzed using the Dutch R2 bioinformatic platform. In addition, tumor derived organoids are cultured profiled through the same pipeline. Semi-high-throughput screening of a 170-compound library is performed and effect on cell viability using the CellTiter-Glo® 3D cell viability assay is assessed.

Results: To date, 106 patients with relapsed/refractory pediatric malignancies have been enrolled and analysis has been completed of 80 study subjects. In 47 patients, a total of 128 molecular targets were identified and 29 patients harbored an actionable event with priority score $\geq$ moderate (46%). In 14% a matched targeted therapy was initiated and one-third of these patients achieved complete remission.

Simultaneously, 6 tumor organoids have been cultured of neuroblastoma PMC-iTHER patients and molecular profiling was performed to confirm they reflect the patient's tumor biology. High-throughput drug screening confirmed sensitivity to drugs targeting known driving molecular events such as ALK and NRAS. In addition, treatment options could be identified for patients without high priority molecular targets.

Conclusions: Our proof-of concept of patient-specific drug testing on tumor organoids within our pediatric precision medicine program might reveal additional treatment options for children who currently have none. Clinical benefit will be evaluated in our upcoming clinical trial iTHER 2.0.

V560 SIOP19-1470 | Apatinib as a Single Agent or Combined with Chemotherapy in Recurrent or Refractory Childhood Solid Tumor Patients

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Background/Objectives: The prognosis of recurrent or refractory childhood solid tumor patients is very poor. We assessed the efficacy and safety of apatinib, a specific vascular endothelial growth factor receptor 2 inhibitor in these patients.

Design/Methods: This retrospective analysis involved 64 recurrent or refractory solid tumor patients younger than 18 years old at Sun Yat-sen University Cancer Center, with at least one measurable lesion according to RECIST 1.1 from October 2015 to February 2019. All patients failed after at least 2 lines of chemotherapy regimens. Oral apatinib was given at a dose of 250 mg (< 25 kg) and 500 mg ($\geq$ 25 kg) once daily. Treatment was continued until disease progression, patient withdrawal, or unacceptable toxic effects.

Results: The main subtypes eligible were neuroblastoma (n = 25), rhabdomyosarcoma (n = 15), ewing's sarcoma (n = 7), wilms tumor (n = 4), and others (n = 13). Treatment regimens included apatinib monotherapy and apatinib combined with chemotherapy: apatinib monotherapy (n = 14), VIT (vincristine, irinotecan and temozolomide) (n = 17), oral cyclophosphamide + oral vinorelbine (n = 14), oral etoposide (n = 9), and other regimens (n = 10). Fifty-six patients were able to evaluate the efficacy. The objective responses rate (ORR) for all patients was 75%, including PR(16 [28.6%]) and SD(26 [46.4%]). For patients with apatinib monotherapy, the ORR was 66.7%: PR(4 [33.3%]), SD(4 [33.3%]). The most common grade 3 or 4 adverse events were hand-foot syndrome (11 [17.2%]), hypertension (6 [9.4%]), mucositis (5 [7.8%]), grey hair (5 [7.8%]), and active bleeding (5 [7.8%]). One treatment-related death was recorded, who died of intracranial hemorrhage. Seven patients discontinued apatinib due to intolerable toxicities.

Conclusions: For recurrent or refractory childhood solid tumor patients, apatinib as a single agent or combined with chemotherapy shows promising efficacy and manageable toxicities. Prospective randomized controlled clinical trial is warranted.

V561 SIOP19-0955 | Revisiting the Ethics of Phase 1 Oncology Trials in the Era of Precision Medicine: A Systematic Review

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Background/Objectives: Phase 1 clinical trials are a crucial step in the evaluation of new cancer therapies. However, critics cite a low rate of response to therapy (5%), together with a not insignificant risk of death from toxicities (0.5%), suggesting a risk-benefit ratio that may limit the ethics of inviting patients to participate. With the introduction of novel targeted therapies, a contemporary estimate of risks and benefits is needed.

Design/Methods: A systematic review was conducted. Eligible for inclusion were phase 1 trials in pediatric and adult populations published between Jan 2015 and July 2018 of targeted immunomodulators, molecularly targeted therapies, and antiangiogenic agents for solid and hematological malignancies. We searched PubMed and Embase. Rates of objective response (complete and partial), stable disease, and Grades 3, 4 and 5 treatment-related adverse events were extracted and pooled. The protocol was prospectively registered in PROSPERO (CRD42018100386).

Results: 116 trials (109 adult, 6 pediatric, 1 mixed) met inclusion criteria. The studies reported on over 4400 patients (52% male, 48% female). Most trials reported on molecularly targeted therapies (53%), followed by immunomodulators (35%). The combined overall objective response rate was 6% (95% CI 4% to 8%). The rate of stable disease was 34% (30% to 38%). Of the types of therapy, the response rate appeared highest in the molecularly targeted therapies, at 8% (5% to 11%). Overall, the rate of treatment-related deaths was 0.02% (0% to 0.2%).

Conclusions: Our results suggest that rates of treatment-related deaths for single agent, targeted phase I anti-cancer therapies are lower than estimates derived in the conventional chemotherapy setting. This weakens criticism that participation puts patients at great risk. Response rates, however, are not materially different. In an era where providers tout the benefits of precision medicine, this is an important consideration when counselling patients considering participation in phase I trials.

V562 SIOP19-0313 | Inhibitors of the Notch Pathway, RO4929097 and DAPT, Have Limited Effects on Pediatric Ependymoma Cell Line from the RELA Subgroup

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Background/Objectives: RELA ependymoma (EPN) subgroup accounting for approximately 70% of all childhood supratentorial (ST) and shows the worst prognosis among the ST-EPNs subgroups. Due to the low efficacy of the chemotherapy the treatment options for this tumor are limited. Considering the role of γ -secretase inhibitors (GSI), which inhibit Notch activation, as one of the most potentially therapeutic targets in brain tumors, we evaluated the effect of GSI inhibitors, DAPT and RO4929097 in cell proliferation, apoptosis and cancer stem cells (CSCs) markers expression on pediatric EPN cell line from RELA subgroup.

Design/Methods: Gene expression data was downloaded from R2: Genomics Analysis and Visualization Platform (<http://r2.amc.nl>) and analyzed using GSE64415 data set of ST-EPN subgroups. Cell proliferation in the RELA cell line of EPN (BXD-1425) was analyzed by resazurin and cell apoptosis was detected by flow cytometry. Gene expression after treatment was assessed by RT-qPCR using TaqMan probes. GUS and HPRT were used as endogenous control and untreated cells as a calibrator. Protein expression was investigated by western blot analysis.

Results: RELA subgroup patients appear to have upregulation of Notch genes (*NOTCH1*, *JAG1*, *JAG2*, *HES4*) among ST subgroups. The inhibition by DAPT and RO4929097 showed efficacy in depleting Notch expression in RELA positive cell line. However, there was no effect on cell proliferation and apoptosis in BXD-1425 cells were treated with both GSI inhibitors. Additionally, we find overexpression of CSCs markers (*VEGFA*, *LICAM*, *MYC*, *CCND1* and *CDK6*) and GSI inhibitors also lead to reduction of *VEGFA*, *MYC*, *CCND1* and *CDK6* expression in RELA cell line.

Conclusions: Our data suggest that NOTCH inhibition could act in the maintenance of CSCs in RELA, whereas EPN growth could be completely independent of these mechanisms. Notch activation may have a potential implication to poor outcome of ST-EPN-RELA and a valuable meaning for further investigation of new therapies for EPN.

V563 SIOP19-1083 | A Phase 1 Trial of Olaratumab as Monotherapy and in Combination with Doxorubicin, Vincristine/Irinotecan, or High-Dose Ifosfamide in Pediatric Patients with Relapsed/Refractory Solid Tumors

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Background/Objectives: Olaratumab is a targeted human IgG1 monoclonal antibody that specifically binds to PDGFRA, blocking PDGF-AA, -BB, and -CC receptor activation. We conducted a Phase 1 trial (NCT02677116) to evaluate the safety of olaratumab in children and determine a recommended dose of olaratumab in combination with 3 different chemotherapy regimens.

Design/Methods: Patients <18 years with a diagnosis of relapsed/refractory solid tumors (including CNS tumors) were enrolled to 2 dose levels of intravenous olaratumab. Patients received olaratumab monotherapy at 15mg/kg (Part A) or 20mg/kg (Part B) on Days 1 and 8 of the first 21-day cycle, followed by olaratumab combined with fixed doses of standard chemotherapy with doxorubicin, or vincristine/irinotecan, or high-dose ifosfamide for subsequent 21-day cycles. Patients in Part C received olaratumab 20mg/kg plus assigned chemotherapy for all cycles.

Results: Sixty-one patients across Parts A-C were enrolled to receive olaratumab plus doxorubicin (n=14), vincristine/irinotecan (n=23), or ifosfamide (n=24). Three dose-limiting toxicities (DLTs) occurred during olaratumab monotherapy (at 15mg/kg, grade [G] 4 elevated alanine aminotransferase [ALT]; at 20mg/kg, G3 lung infection and G3 elevated gamma-glutamyl transferase [GGT]). One DLT occurred in a patient who received vincristine/irinotecan with olaratumab 20mg/kg (G2 elevated ALT). Any treatment-emergent adverse event reported in >25% of patients across Parts A-C included $\geq$ G1 anemia, fatigue, leukopenia, lymphopenia, musculoskeletal pain, neutropenia, and thrombocytopenia and $\geq$ G3 anemia, leukopenia, neutropenia, and thrombocytopenia. Pharmacokinetic profiles of olaratumab in combination with the analyzed chemotherapy regimens were within projected range based on adult data. There were 2 complete responses (pineoblastoma and rhabdomyosarcoma) in the vincristine/irinotecan arm (Part B) and 1 partial response (rhabdomyosarcoma) in the doxorubicin arm (Part A). Twenty-one (34%) patients received 3 or more cycles of treatment.

Conclusions: Olaratumab was tolerable and safely administered in combination with common pediatric chemotherapy regimens in children and adolescents. Serum concentrations of olaratumab were within expected range.

V564 SIOP19-0915 | Encouraging Early Outcome of Combined Chemotherapy with Arsenic Trioxide for Alveolar Rhabdomyosarcoma in Children

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Background/Objectives: Alveolar rhabdomyosarcoma (ARMS) is a subtype of rhabdomyosarcoma characterized by its aggressive behavior and poor prognosis. Frequent cases of recurrent or refractory ARMS highlights the need of new treatment options. Recently, arsenic trioxide (ATO) has been shown to specifically inhibit tumor growth and invasion of ARMS in vitro by acting on the hedgehog (Hh) pathway. It's necessary to evaluate the efficacy of ATO in ARMS patients from bench to bedside.

Design/Methods: Three ARMS patients, all males with a median age of 5.8 years (range, 5.1 to 12.5 years), were enrolled in the pilot study of combined chemotherapy with ATO based on comprehensive management in line with the Intergroup Rhabdomyosarcoma Study Group (IRSG) protocol. Except for one patient, the other two were either refractory with distant metastasis or relapsed after standard treatment at initiation of ATO. ATO was administered 0.16mg/kg per day over eight hours IV daily for ten days with combined chemotherapy of vincristine, dactinomycin, and cyclophosphamide (VAC regimen) on the third day, repeated every 21 days.

Results: All patients were sensitive to ATO combined chemotherapy and achieved partial remission (PR) or complete remission (CR) during 7-8 cycles of treatment. More specifically, one patient with multiple systemic metastasis at diagnosis achieved CR after 8 cycles of combined therapy but underwent relapse of brain lesions in subsequent therapy without ATO and died after giving up treatment. The other two are under treatment with PR status at present, and it's noteworthy that one of them showed continuous good responses to ATO combined chemotherapy in condition of multiple relapse partly because he suspended the course of treatment. No significant extra toxicity of ATO was observed during the period of treatment.

Conclusions: ATO combined with VAC regimen has activity against ARMS in children, but prospective large-scale clinical trials are warranted to determine long-term efficacy, optimal courses, and late toxicity in this population.

V565 SIOP19-1252 | Repositioning ER005 for the Treatment of Rare and Pediatric Cancers

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Background/Objectives: ER005, an oral small molecule has been clinically developed up to Phase II between 2005-2013 for fibrotic and inflammatory diseases but was then discontinued by the pharmaceutical industry for strategic reasons. EspeRare obtained the rights for the development and strives to reposition ER005 for rare cancer therapy. Its good safety profile in humans compared to other JNK inhibitors is a big asset of ER005 and enables EspeRare, after completion of positive preclinical studies, to take ER005 to Clinical Phase Ib/II building on previous pharmacology, toxicology and safety studies. ER005 selectively targets the c-Jun N-terminal kinases (JNKs 1, 2 and 3), protein kinases implicated in tumorigenesis and cancer development. We analyzed the activation of JNK in rare and pediatric cancer cell types and demonstrate that ER005 inhibits cancer cell growth.

Design/Methods: The cytotoxicity of ER005 on a panel of 20 human cancer cell lines (neuroendocrine tumor (NET), neuroblastoma, sarcoma, T lymphoma) and non-cancer cells was determined. JNK activation was analyzed by quantifying the phosphorylation of c-Jun using Western Blot analysis.

Results: Western blot analysis revealed a consistent activation of JNKs in all cancer cells, but not in normal human fibroblasts. ER005 effectively inhibited tumor cell growth at a low micromolar range, whereas normal cells remained unaffected.

Conclusions: ER005 displayed encouraging cytotoxicity against rare and pediatric cancer cell types at low micromolar concentrations. Previous pharmacokinetic data showed that such concentrations can be safely reached in humans, thus warranting further efficacy studies in vivo.

V566 SIOP19-0382 | Precision Medicine Program for Hard-to-Treat and Relapsed/Refractory Childhood Cancers: A Report from the TRICEPS Study

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Background/Objectives: Despite survival improvement in childhood cancers with modern intensive chemotherapy regimens, around 20% of patients do not respond to conventional therapies and ultimately succumb to their disease, urging the need for novel therapeutic avenues. Personalized targeted therapy based on comprehensive molecular profiling may identify novel therapeutic targets to improve survival rates and decrease treatment-related mortality for this vulnerable patient population. The CHU Sainte-Justine (CHUSJ) launched a Childhood Cancer Precision Medicine program called TRICEPS for hard-to-treat and relapsed/refractory childhood cancers. The objectives were to 1) determine the feasibility of using next-generation sequencing (NGS) technologies in a clinically-sensitive timeline and 2) determine the frequency of actionable alterations through NGS.

Design/Methods: TRICEPS, initiated in April 2014 at CHUSJ, offers in-depth genomic and transcriptomic analysis (WES and RNA-seq) of patient's tumor to identify patient-specific alterations within a clinically reasonable timeframe. Hard-to-treat (≤ 18 years old at diagnosis) and relapsed/refractory cancers (≤ 21 years at relapse) are eligible.

Results: Over a period of 59 months (April 2014-March 2019), 133 eligible patients were enrolled in TRICEPS. The mean age was 12.85 years [1-21 years] with a similar male to female ratio [67 vs 66]. One hundred and four patients (78%) had sufficient material for multimodal molecular profiling. The process from nucleic acid isolation to genomic sequencing and data analysis took a median of 26 days [6-63] and the complete process from patient consent to report delivery took a median of 8.6 weeks [3.9-17.1]. Potentially actionable alterations were identified in 88/104 patients (85%). The most frequently altered signaling pathways were TP53, Ras-MAPK, PI3K-AKT-mTOR, and JAK-STAT. Therapeutic actions have been taken in 32/88 patients (36%).

Conclusions: Our study demonstrates the feasibility of incorporating NGS in the clinical management of hard-to-treat pediatric cancers. The molecular profiling led to the identification of therapeutically actionable alterations and/or clinically relevant information of diagnostic and prognostic significance.

Treatment and Care - Nursing

V567 SIOP19-0701 | The Factors Affecting the Sleep in Hospitalized Pediatric Cancer Patients

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Background/Objectives: Children diagnosed with cancer may have sleep problems. There are environmental and patient/disease related factors affecting the sleep of the child with cancer. Studies regarding sleep disturbances in children with cancer in developing countries are scarce. This study aims to evaluate the frequency of sleep disturbances in children with cancer and factors that effect sleep in a center in a developing country.

Design/Methods: The study was planned as a descriptive study in order to determine the factors affecting sleep status of cancer children treated in the Pediatric Hematology-Oncology Unit of the Istanbul University, Oncology Institute. The data of the study were collected by using "The Factors Affecting the Sleep of Children with Cancer Survey". The sample included 75 children (42 boys, 33 girls) with cancer, with an age range of 7 to 18 years; and their caregivers (75 mothers).

Results: Sixty eight percent of the children stated that sleep was "bad" and six percent as "very bad" in the hospital, 86% of the mothers said that their sleep was "bad/very bad" in the hospital. Hospital environment such as crowded rooms, frequent visits of the nurses for treatment at night, noise and light in the room, odors in the room were the mostly reported environmental factors associated with sleep problems in children. Excessive urination, nausea and vomiting, pain, nightmares were the mostly reported symptoms disturbing the sleep of the children.

Conclusions: The hospital environment, including noise and light levels, as well as room interruptions, may play a role in disrupting sleep. Sleep should be assessed regularly by nurses and doctors in all children hospitalized in the pediatric oncology ward. Nurses may be able to control some of the factors that affect sleep duration in hospitalized pediatric patients with cancer.

V568 SIOP19-0801 | The Development and Validation of a Knowledge Test for Nurses on Long-Term Central Venous Catheters of the Type Tunneled Catheter and Totally Implanted Ports

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Background/Objectives: Although there are a lot of evidence-based guidelines available concerning long-term central venous catheters, applying them to the clinical setting on a broad range of patients is challenging. Research showed that the management of these catheters is very different. A knowledge deficit can lead to ineffective and inappropriate care. No valid and reliable instruments are available to assess the full domain of knowledge concerning these catheters.

To develop a valid and reliable Dutch questionnaire to assess the knowledge of nurses on long-term central venous catheters, more exactly of the type tunneled catheter and totally implanted port.

Design/Methods: A prospective psychometric instrument validation study.

The questionnaire was developed based on the international guidelines of the Centre for Disease control, literature, information and product booklet. Content validity was evaluated by a team of experts. Item-analysis, construct validity and stability were assessed. A sample of 380 graduated nurses participated. Data collection took place between May and July 2017.

Results: A 32-item questionnaire was developed, including four themes: (1) characteristics, (2) insertion and first days after insertion, (3) standard care and (4) complications. Multiple-choice questions and true-false questions were developed. Content validity was established. The mean test score was 18,95/32 (59,2%). Difficulty-index for the questions ranged from 0,19 to 0,99. Quality of the response alternatives varied between 0,00 and 0,54. Discrimination-index ranged from 0,01 to 0,80. The score of participants with (theoretically expected) more expertise was significantly higher than the score of participants with (theoretically expected) less expertise. The stability of the instrument was found good with an intracorelation coefficient of 0,812. Kappa-values had a minimum value of -0,03 and a maximum value of 0,74.

Conclusions: A questionnaire was developed with an acceptable content, construct and item validity. It can be applied in both research and practice for evaluating knowledge. Findings can be used to develop educational programs.

V569 SIOP19-0220 | Virtual Reality and Invasive Procedures in a Pediatric Oncology and Hematology Department

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Background/Objectives: To evaluate the efficacy of using clinical hypnosis with virtual reality headset during invasive procedures in a pediatric oncology and hematology department.

Design/Methods: Use of a virtual reality headset during invasive procedures for patients over 5 years-old. Questionnaires for children, their family and nurses were used to evaluate the procedure easy-going, the patient tolerance, the pain and the felt effects after the procedure.

Results: Twenty-eight procedures carried out in 23 patients aged 5 to 19 years-old were analyzed: 9 bone marrow aspi-

rations, 7 lumbar punctures, 5 nasogastric tube insertions, 2 venous catheter insertions, 5 others. The median pain score during and after the procedure was respectively of 10/100 and 0/100. Pain score over 40/100 was reported for only 33% of the patients during the procedure and 4% after the procedure. For most of the patients, there were a benefit of using clinical hypnosis in terms of relaxation (86%), procedure easy-goingness (71%) and decreased restraint (54%).

Conclusions: Clinical hypnosis using a virtual reality headset is associated with fewer pain during and after invasive procedures in pediatric onco-hematology. Furthermore, a relaxation during and after the procedure is observed that facilitate its achievement.

V570 SIOP19-1196 | The Documentation of Everyday Functioning in Children with Brain Tumors in Medical Care, Habilitation Services and School – is There a Coherent Description?

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Background/Objectives: Many children diagnosed with a brain tumor experience long-term difficulty in physical, psychosocial and cognitive areas that may affect their function, and participation in everyday life. The follow-up program after childhood cancer in Sweden, has mainly focused on the child's physical functioning with less focus on a holistic view of the child's health, notably psychosocial functioning. The aim of this study is to explore participation of children with brain tumors in the full range of everyday school activities by linking professionals' descriptions of the child's functioning as captured in health care records, habilitation documentation and school records to body, activity/ participation and environment codes in the World Health Organization's International Classification of Functioning, disability and health: Children & Youth version (ICF-CY).

Design/Methods: Retrospective data from 9 children who had completed treatment for a brain tumor were extracted from health care, habilitation services, and school records regarding the child's problems and recommended support. The first researcher was supervised by the other authors familiar with linking extracted text to ICF-CY codes. Data were then analyzed deductively by linking meaning units to ICF-CY codes.

Results: Preliminary results reveal that the most frequently used codes were linked to the ICF-CY domain of body functions, independent of documentation source, whereas documentation linked to the ICF-CY domains of activity/ participation or environmental factors were less frequent.

Conclusions: Code prevalence likely reflects where health-care professionals and educators focus attention in meeting the needs of children who have been treated for brain tumors. To maximize the children's function and participation in everyday life, the effects of the full range of their impairments- body, cognitive, and psychosocial- on children's activity, participation and environment must receive more focus by healthcare professionals and educators in practice and thus in the child's records.

V571 SIOP19-0916 | Improving Access to Fertility Preservation in Pediatric Oncology: The Impact of an Oncofertility Program

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Background/Objectives: Treatment for childhood cancer may increase the risk of infertility. At our institution, we have developed a program that offers consultation to all newly diagnosed patients, provides an estimate of risk of infertility, and, if a family chooses, facilitates fertility preservation prior to the initiation of treatment. The fertility preservation options offered include oocyte or embryo cryopreservation, ovarian tissue cryopreservation (OTC), semen cryopreservation, testicular sperm extraction (TESE), and testicular tissue cryopreservation (TTC).

Design/Methods: In 2018, a nurse practitioner was hired to develop a pediatric oncofertility program. A multidisciplinary team including specialists from oncology, urology, gynecology, and reproductive endocrinology was identified. Educational materials on fertility preservation options were developed for patients and families. A database was created to track all new patients, whether a fertility consult was provided, and outcomes. The proportion of patients for which infertility risk and fertility preservation were discussed pre- and post-intervention were compared.

Results: In the six months prior to launching the oncofertility program, 24% of patients (total N eligible = 124) were counseled about the risk of treatment-related infertility and options for fertility preservation. Of those patients, 20% (5% of total eligible) elected to pursue fertility preservation (3 oocyte cryopreservation, 2 semen cryopreservation, and 1 TTC). In the six months following the development of the program, 61% of patients (total N eligible = 133) were consulted and 40% of those patients (24% of total eligible) pursued a fertility preservation option (2 oocyte cryopreservation, 8 OTC, 14 semen cryopreservation, 7 TTC, and 1 TESE).

Conclusions: A program dedicated to fertility preservation improves patient understanding of treatment related fertility risks and has increased the election of preservation treatment. Future directions include improving financial assistance for fertility preserving procedures, expanding services for cancer survivors, and assessing the psychosocial impact of fertility preservation in pediatric patients.

V572 SIOP19-0961 | Development of a Process for Comprehensive Assessment of Pediatric Oncology Nursing Practices in Low-and-Middle-Income Countries: A Pilot Application in Harare, Zimbabwe

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Background/Objectives: A baseline understanding of local nursing capacity is vital to identifying and prioritizing areas for improving childhood cancer care. As part of the St. Jude Global-Parirenyatwa Hospital collaboration, we developed and pilot tested a comprehensive nursing assessment process in the pediatric oncology inpatient ward in Harare, Zimbabwe.

Design/Methods: To assess baseline clinical practice, our team used existing tools to develop a mixed method qualitative and quantitative assessment of nursing processes. In-person assessments with nurses from St. Jude Global and Parirenyatwa Hospital were conducted over six days in November 2018 and included quantitative metrics derived from chart audits and observations. Additionally, the nurse in charge was interviewed using a structured instrument from the International Society of Pediatric Oncology (SIOP) Baseline Nursing Standards survey. Assessment components were classified into five domains, inspired by The Joint Commission International Accreditation Standards (JCI): 1. Assessment of patient; 2. Care of patient; 3. Medication management and use; 4. Prevention and Control of infection; 5. Patient safety. Results were categorized according to established criteria of met, partially met or did not meet, based on how often observed nursing practices met expected measures.

Results: Based on our initial assessment, no nursing standards were fully met in the inpatient pediatric oncology ward. Using these data, hospital administration established a local nursing working group to implement quality improvement (QI) projects and education initiatives to address pediatric oncology nursing specific needs. Top priorities included positive patient identification (PPI), pain management, hand hygiene,

and safe chemotherapy administration with the PPI program now already implemented.

Conclusions: Our assessment process evaluated current nursing practices and provided hospital administration with relevant data to identify and prioritize QI opportunities. Next steps include re-evaluation in Harare following implementation of planned projects and assessing reproducibility of this approach through nursing assessments at other centers in Sub-Saharan Africa.

V573 SIOP19-1191 | A Follow-up Program to Create Comfort and Security for Children Newly Diagnosed with Cancer and Their Parents

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Background/Objectives: We developed a systematic follow-up program after the first discharge at home to ensure that families got the information, guidance and training they needed to handle care and treatment tasks. The aim of the study was to describe characteristics and assess usability and safety of the program.

Design/Methods: It is an observational intervention study from February 2017 to February 2019. Families were included if they spoke and understood Danish and lived within approx. 50 km from the hospital. The intervention consisted of a systematic pedagogical follow-up visit at home by a nurse. Socio-demographic data and data related to the follow-up visit were registered including a web-based parental questionnaire about treatment and care tasks, and their sense of security directly after the follow-up visit. Data was collected and analyzed with descriptive statistics.

Results: There were 48 newly diagnosed children and adolescents with different diagnosis, who received a follow-up visit. The average age was 6.4 years (range 0 - 17). Of the 48 families, 32 answered the questionnaire, 75% by mothers and 25% by fathers. The majority (91%) found the follow-up visit usable "to a very high degree" and 9% "to a high degree. 22% were "very much" safe at home before the follow-up visit, 53% "to a great extent", 19% "to some extent" and 6% a little. After the follow-up visit, 72% were "very much" safe, 25% "much" safe, and 3% "to some extent" safe. Everyone reported that their concerns and questions were answered "to a great extent" and 60% wanted a visit more and 28% maybe.

Conclusions: A follow-up program can enhance the parents' knowledge and training and increase sense of safety after the first discharge. It is now an integrated part of the department's treatment options due to the positive results.

V574 SIOP19-0750 | Emotions of Children with Cancer During Hospitalization - A Qualitative Study

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Background/Objectives: Children diagnosed with cancer spend a considerable amount of time in the hospital during their treatment. It is important to note the emotions or stressors they go through. Children may have a difficult time expressing feelings or emotions to the medical team and sometimes parents. Understanding emotions of children during hospitalization is crucial to promoting their recovery. The aim of this study is to understand the mental and emotional stressors the children go through during their long stay in the hospitals when undergoing their cancer treatments.

Design/Methods: The study was conducted on the pediatric oncology unit in a teaching hospital in Ghana. A qualitative sampling was used. Fifty children (20 males and 30 females) within the ages of 10 to 15 years participated in the face-to-face interview using a structured questionnaire. The children included had been hospitalized for between 1 to 4 weeks or had been discharged home after hospitalization.

Results: Majority (70%) had siblings at home who they had been away from. Eighteen children interviewed (24%) had been on admission for 1 -2 weeks. Twelve children (36%) had spent a month or more on the ward. The majority hospitalized within a period of one week to one month (60%) found themselves feeling sad because they missed their siblings at home. They recalled feeling scared whenever people around them died. They felt angry whenever they were not attended to promptly when they called for medical attention. Some were anxious on account of painful procedures. However, they were excited that the medical team on the ward are very friendly. Recommendations they gave for improvement included increase in the number of medical staff.

Conclusions: When the emotions of these children are understood specific interventions can be put in place to address their fears and anxiety as well as encourage resilience to promote recovery.

V575 SIOP19-0069 | What are Children's Nurses' Perceptions of the Effectiveness of Foundation Education Compared to Formal Education?

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Background/Objectives: **Background:** Children with cancer in the United Kingdom receive care from both a Principle Treatment Centre (PTC) and a Paediatric Oncology Shared Care Unit (POSCU). Nurses must be adequately educated to

provide safe care in the POSCU setting. There are two levels of oncology education that NHS England (2014) deem to be adequate for POSCU nurses: foundation and formal education. There is a considerable variance between these two levels of education.

Aim: The aim of this Service Evaluation was to explore POSCU nurses' perceptions of the effectiveness and impact on clinical practice of foundation education compared to formal education, and to identify if a more effective approach to the provision of oncology education was necessary.

Design/Methods: Methods: A qualitative approach was used to explore POSCU nurses' lived experiences of oncology education. A purposive sample was invited to participate in semi-structured interviews within the work place. Data was analysed using thematic analysis.

Results: Foundation education alone can reduce nurses' anxiety associated with caring for paediatric oncology patients and is sufficient to provide the skills to provide competent care. Formal education did not provide any additional clinical skills although did increase nurses' knowledge and confidence. Nurses did not feel that their level of competence increased after formal education. Both levels of education resulted in nurses still seeking additional knowledge regarding malignancies and treatment. All participants felt that face-to-face learning was most beneficial and that ongoing support from more experienced staff essential. Frequency of clinical updates depended upon exposure to paediatric oncology patients. Nurses reported that foundation education made them more proficient with non-oncology patients.

Conclusions: Discussion: A more concise and tailored approach to oncology education is required and would be more cost effective for both POSCU staff and NHS Trusts.

V576 SIOP19-0170 | Unique Staffing Model for Nurse Practitioners at an Outpatient Pediatric Ambulatory Care Center

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Background/Objectives: The pediatric program at Memorial Sloan Kettering Cancer Center (MSKCC) is the largest outpatient pediatric hematology oncology program in the United States. The Pediatric Ambulatory Care Center (PACC) serves a wide array of patients, averaging one hundred and fifty visits each day. The PACC is comprised of multiple specialty teams including: Leukemia/Lymphoma, Sarcoma, Neuro-oncology, Neuroblastoma, Long Term Follow Up, Surgery, Neurosurgery, and Bone Marrow Transplant. Within such a large program, Nurse Practitioners play an integral role in the care and management of the complex pediatric patients and thus creates a need for a unique staffing model.

Design/Methods: To provide consistent quality of care within a high-volume clinic and in order to account for flexibility in staffing and coverage for all services, the role of the float nurse practitioner was created. Float Nurse Practitioners are trained in a primary specialty and are cross trained to cover all disease services. Fifty percent of clinical hours are spent at their primary specialty and fifty percent are spent “floating”. While the role of Float Registered Nurse is common and well defined, the role of float nurse practitioner has not previously been defined.

Results: In addition to providing planned coverage for medical leaves, maternity leaves, vacant positions, and vacations the float nurse practitioner has been able to provide coverage for unplanned sick days as well as high volume clinics. The ability to cross over between different services has increased communication and collaboration amongst different care teams.

Conclusions: The role of the float nurse practitioner amongst different specialties has been well received by all members of the multidisciplinary team as well as patients and family members. The role of the float nurse practitioner is both feasible and extremely beneficial in a high volume, fast paced, outpatient ambulatory clinic.

V577 SIOP19-0511 | Indonesian Basic Pediatric Oncology Nursing Training Course and Evaluation Yuliana Hanaratri Indonesia Pediatric Nurses Association, Jakarta

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Background/Objectives: Pediatric oncology nurses are responsible for their own ongoing and professional growth. The science of cancer care is constantly evolving with new treatments and protocols, administration guidelines symptoms management, and safety issues that challenge nurses to stay up to date. In 2018, the Indonesia Pediatric Nurses Association (IPNA) implemented the first national training course in Basic Pediatric Oncology Nursing in Jakarta.

Design/Methods: The course was given over five days (classroom instruction) and two days of group case presentations. Quantitative evaluations (20 multiple-choice questions) were given over 50 minutes. Half of the questions were nursing case studies, e.g., nursing diagnosis, pain management, nutrition and toxicity management. Question variation was performed according to Revised Bloom’s Taxonomy for the level of *understanding* (C2) 30% questions, *applying* (C3) 60% questions, and *analyzing* (C4) 10% questions. Qualitative evaluation measured the participants’ ability to apply knowledge by instructor observation of nursing care in the clinic area

and parent teaching in the “shelter house”. Participants were divided into six groups, and each group was expected to write a nursing care plan and do a group case presentation.

Results: Forty-nine nurses participated (education nursing diploma to undergraduate nursing degree and clinical experience <1 to 5 years). Pre-test scores ranged from 1.5 - 6.5/10 and post-test scores 5 - 10/10. Mean score in the pre-test was 4.7/10 and the post test was 8.6/10.

Conclusions: Quantitative evaluation is more reliable and valid than qualitative, and easier to replicate and administer, but does not provide a holistic overview of a participant’s learning and thinking. This training program implemented qualitative methods as well to evaluate the application of the participant’s practice knowledge by instructor observation in clinical settings. There is still a need to refine the IPNA program evaluation for pediatric oncology nursing training, which will be a regular program implemented yearly.

V578 SIOP19-0708 | Life Experiences of Cancer Patients in the AYA Age Group in Japan - A Study Based on Analysis of Experience Notes Using Text Mining

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Background/Objectives: In Japan, there are only a few specialists who specialize in cancer treatment for the AYA age group, and it is considered urgent to understand the current status of cancers that occur in AYAs. Also, for nursing, it is considered an issue to grasp the characteristics of AYA patients and how to support them. Therefore, this study aimed to clarify life experiences of cancer patients in the AYA age group in Japan, by analyzing experience notes using a text mining technique.

Design/Methods: Experience notes written by AYA cancer patients were analyzed using a text mining technique.

Results: Results of the analysis showed that words which appeared frequently in the word frequency analysis were “Cancer”, “Treatment”, “Patient”, “Disease”, and “Feeling”. As a result of cluster analysis, the described contents of the experience notes were typified into 5 clusters. These clusters were interpreted as “The life I have built so far being thrown away,” “Distress that I got cancer,” “Anxiety about treatments with uncertain outcomes,” “Treatment being life’s highest priority,” and “Living as a cancer patient”.

Conclusions: Results of analysis of the experience notes clarified that AYA age patients experienced suffering from the onset of cancer at a young age and having to prioritize treatment every day of their lives, typically abandoning the lives that they had formerly established. AYAs are young and are in

the age groups that are progressing toward the future through several of life's turning points, such as going to school, getting jobs and getting married. It was suggested that the interruption of such progress, and cancer's prevention of their defining a picture of their futures, caused patients great distress. It is necessary for nurses to understand the suffering such AYAs experience, and to think about types of support for them, to help them overcome their distress and return to society.

V579 SIOP19-0753 | Study of Nutritional Problems and Coping Strategies of Mothers and its Impact on Nutritional Status of Children Receiving Chemotherapy for Hematological Malignancies

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Background/Objectives: Malnutrition is a negative prognostic factor in children with hematological malignancies.

OBJECTIVES: 1. Assess the nutritional problems faced by mothers.

2. Identify coping strategies adopted by mothers.

Examine the impact of nutritional problems and coping strategies

Design/Methods: Descriptive survey.

- Structured questionnaire was introduced to 100 subjects

Results: Age: Mothers (56%) 26-30 years Education: (37%) secondary school Age: Children 33%(33) 2-4yr, 32% (4.1-7yrs and 35% 7.1yrs. **PROBLEMS:** Loss of appetite.(98%). inadequate amount of meal- 95% Weight loss: 73% 59% had no taste and, 45%, Mouth sores, 39%.had difficulty in swallowing 35% Diarrhoea. 87% Fatigue 97% soft and clear liquids. Medication: 93% Diarrhea: 33%-plenty of fluids, 29%-medications. 72% drink fluids and rinse mouth (64%) 93% followed the diet plan. 67%children enjoyed playing with a toy. 69% normal nutritional status (between -1 and 0 SD). moderate wasting (-2SD) were 24%,7% severe wasting (<-3SD). No significant association association selected demographic variables and coping strategies. statistical significance: education of mother (p=0.01) And Father. with the weight of the child. The mothers with higher educational background had understanding regarding of food and concept of balanced diet. statistical significance between the education of the father p=0.02 and occupation of the father p=0.003 with the weight of the child.

Conclusions: This study showed that the demographic variables of the parents have an impact on the nutritional status of the child. The problems that the mothers face during the therapy may be influenced by the other mothers they communicate with. The coping strategies that have been said to adopted in reality might have had not been adopted by the mothers.

Hence nutritional assessment along with proper history collection can be a good tool for screening malnourishment at early stage during the therapy.

V580 SIOP19-1505 | Children's Participation in the Decision-Making Process During Hospitalization: An Observational Study

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Background/Objectives: In 2015, a new Patient law reinforcing the rights of the child as stated in the United Nations Convention on the Rights of the Child was enacted in Sweden. The law stresses the importance of clarifying a child's reaction to the current treatment, while taking into consideration the child's age and maturity. An evaluation of the implementation of the Patient law in 2017 showed no improvements for adults and for parents. Absent is an evaluation of children's experiences, which is a serious omission. The aim of this study was to identify everyday situations in medical and nursing care that illustrate children's participation in decision-making.

Design/Methods: A qualitative approach with non-participant observations of 32 children with different diagnoses including paediatric cancer (2-18 years), their parents, and healthcare personnel was conducted at three paediatric settings in Sweden during six months in 2018. Analysis followed the identification and grading of situations related to children's participation in decision-making processes, using the five levels Scale of Degrees of Self Determination of attending to people's opinions, wishes, and values.

Results: Most children took part in decision-making processes and expressed wishes that was respected by healthcare personnel. There were also instances where the integrity of children was not respected. When information was given to a child, it was not always checked if the child understood what was communicated. Despite healthcare personnel's efforts to motivate the children to take part in a planned procedure, the protests of the child against taking part in the procedure did not affect the initial planning.

Conclusions: In order to influence clinical practice children's experiences during hospital stay needs to be evaluated and relevant actions taken to get a more robust implementation of the patient law.

V581 SIOP19-0027 | A Study of Discomfort and Bleeding According to Bedrest Time After Bone Marrow Examination in Pediatric Hemato-Oncologic Patient

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Background/Objectives: The purpose of this study is to investigate hemato-oncologic patient's discomfort and bleeding according to the bedrest time after bone marrow examination.

Design/Methods: The data was collected using self-report questionnaire from total of 60 patients who underwent bone marrow examination from January 2017 to September 2017. The study was done after 2 hours of bed rest and again at 4 hours of bed rest checking the patient's discomfort and bleeding. Additional investigation was done to check the patient's PT, aPTT, the number of bone marrow examination, the bone marrow examination site and whether the patient had platelet transfusion or sedation that can affect the results. Data were analyzed with descriptive statistics, t-test, Pearson's correlation coefficients, McNemar's test and logistic regression. The significance level (α) was set at 0.05.

Results: The discomfort rate after 4 hours of bed rest increased significantly ($p < .001$) than the discomfort rate after 2 hours of bed rest. There was a correlation between the two discomfort rates. ($r = .59$, $p < .001$). There was a significant difference in bleeding between 2 and 4 hours of bed rest after the bone marrow aspiration and biopsy ($p < .001$), but all bleeding was mild. And 82% of the patients showed no bleeding after 2 hours of bed rest when the gauze was removed.

Conclusions: The bed rest time after bone marrow aspiration and biopsy was helpful in improving the patient's well-being, and it showed the possibility of reducing the bed rest time according to the bone marrow examination site and the patient's condition.

V582 SIOP19-0662 | The Processes of Parents' Support to Develop Independent Living and Health Management–Social Life Balance in Adolescent and Young Adult Childhood Cancer Survivors

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Background/Objectives: This study aimed to elucidate how parents support adolescent and young adult childhood cancer survivors to develop long-term independence and balance between health management and their social life.

Design/Methods: We interviewed 19 parents of childhood cancer survivors aged 16–25 years and performed analyses using the modified grounded theory approach.

Results: Three [categories] and twenty “concepts” were generated. Parents of childhood cancer survivors [supported careful behaviors] during chemotherapy in the outpatient clinic or

shortly after discharge, which included “worry about absence from school because of their physical condition and change in appearance”, “concern about overexertion”, “help with managing their physical condition and going to school”, and “advice to be careful in daily activities and selecting a life path”. Then, the parents “felt relief about recovery of their physical condition and daily life”, and “watched over their children's lifestyle and physical management by themselves”. On the other hand, they had “ongoing anxieties about late effects of therapy and recurrence”, “expectations to acquire abilities for living independently”, and “conflicts between protecting and letting go of their children”. That is, parents [watched over but were conflicted]. They “understood their children's anxiety about recurrence and death”, which continued even after recovery of their physical condition, and they “felt the weight of living and shifted their values”. Then, they “supported their children's aspirations”. As their children grew up, they [recognized positive development in their children], which included “recognition of their children's development and effort”, “awareness of positive effects the illness experience had on their children”, and “entrusting their children with preparing for and visiting the hospital”.

Conclusions: These findings suggest the necessity of accepting parents' feelings, which include conflicts in dealing with adolescent children. It is also necessary to promote parent–child mutual understanding, which includes parents' recognition of children's development and parents' reflection of their values.

V583 SIOP19-1601 | Development and Validation of a Knowledge Test for Nurses Regarding Antineoplastic Drugs

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Background/Objectives: Chemotherapy is an important compound of cancer treatment. Because of the severe toxicity of neoplastic drugs, it is important nurses have sufficient knowledge on their use and adverse events. A literature review shows that a knowledge test for nurses regarding antineoplastic drugs with good psychometric properties is not yet available. The development of this kind of test was the objective of this study.

Design/Methods: A prospective psychometric instrument validation study was used. The knowledge test was developed in four stages: (1) determination of the structure of the knowledge test, (2) development of the knowledge test, (3) evaluation of the content validity and (4) psychometric evaluation of the knowledge test.

Results: Double Delphi round (16 participants), a Delphi round with methodological experts (n=3) and a pilot study (n=10), served as a base for the knowledge test with 3 themes and 31 questions. After the item analysis, three questions fell short of which two questions were deleted. One question was retained for the sake of relevance. The known groups technique was used to test the construct validity (439 respondents). The scores of respondents with a theoretically expected higher level of knowledge are significantly higher. The reliability was determined with the intraclass correlation coefficient for the test-retest on 38 respondents and was 0.93. Training and experience are two associated factors that greatly contribute to an adequate knowledge score. Based on this, 29 knowledge questions were divided into a theory-oriented part and a practical part.

Conclusions: Based on the psychometric evaluation, we can conclude that the knowledge test has a good content validity and construct validity. It is recommended to test the reliability of the knowledge test at a larger study population with a more consistent knowledge of antineoplastic drugs.

V584 SIOP19-0572 | A Study on the Children's Coping Ability at Hospitalization: For Patients of 3-10 Years Old

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Background/Objectives: Hospitalized children hold great psychological confusion in changes of the environment. **Objectives:** The purpose of this study is to make clear how preparation influenced the children's coping ability when being admitted to a hospital.

Design/Methods: The subjects of this study were eight children of 3-10 years old with leukaemia. During the children's hospitalization, nurses explained children the necessity of their hospitalization, visiting hour, hospital life and various staff using a picture book. Time of the explanation was 20-30 minutes. They were hospitalized for the first time in a B ward for a hospitalization period of 3-7 days. Data was collected by means of participation observational method. The children's reaction toward hospitalization were observed. We analyzed and coded the children's reaction focusing on the state of their hospital life. The coded results were classified to subcategories, categories and then core categories.

Results: The derived 7 core categories are as follows: [Children made up their mind to be staying in the hospital by joining preparation during hospitalization.] [They made an effort in order to get over loneliness staying away from their family.] [They could spend their hospital life depending on nurses.] [They spent the hospitalization with the relaxed feelings] [They had positive feelings toward the hos-

pital life] [They could positively receive medical practice.] [They persevered in the hospitalization and had the feeling of achievement.]

Conclusions: Children became able to imagine a hospitalization life somehow because they received preparation with their family's cooperation. Children were able to communicate with a nurse by sharing a picture book in preparation for hospitalization. Therefore children could build mutual trust relationship with a nurse and entrust a nurse with their hospital life. We consider children can evade prospective critical situation in hospitalization by receiving preparation utilizing a picture book.

V585 SIOP19-0124 | The Children's Action-Reaction Assessment Tool (CARAT) as an Observational Tool for Assessing Pain Management: An Initial Validation Study with Children Undergoing Needle Procedures

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Background/Objectives: *Aim:* The aim of this study was to determine sensitivity and inter-rater reliability of the CARAT.

Background: In the "Knowing-Doing" conceptual framework, Knowing is based on availability and accessibility, i.e., the health care professionals (HCPs) need knowledge and access to a range pain management strategies. Doing is based on affordability and acceptability, i.e., the HCPs have to believe pain management strategies are valuable to use in clinical practice. Doing is divided in actions (strategies to prevent children's pain) and reactions (strategies to intervene when children already experiencing pain) (1). There is a need to develop an observational tool to evaluate HCPs action-reaction strategies when working with children with cancer undergoing needle procedures.

¹Adolfsson, M, Johnson, E, & Nilsson, S (2018) Pain management for children with cerebral palsy in school settings in two cultures: Action and reaction approaches. *Disabil Rehabil*, 40, 2152-62.

Design/Methods: *Methods:* The CARAT consists of 20 items of action-reaction strategies. The scores are graded "1=Not at all", "2= To a small extent", "3= To a large extent", and "4=Completely" or "0=Not Applicable".

Sensitivity of the Scale: The first and last authors individually analysed video recordings of 3-to-7-year-old children (n=21) receiving needle procedures to observe and evaluate HCPs action-reaction strategies using the CARAT as an observation tool. The differences of HCPs' action-reaction strategies

before, during and after each child's needle procedures were calculated.

Inter-rater-reliability: The observation scores from the first and last authors were calculated with a correlation test.

Results: Differences were observed between HCPs' use of action and reaction strategies during needle procedures. The authors' scores also correlated, which showed a sufficient interrater-reliability.

Conclusions: This initial validation study showed promising results of sensitivity and inter-rater reliability of the CARAT, which can be used to facilitate the care for children with cancer.

V586 SIOP19-0171 | Relationship Between Nurses' Awareness of Support for Siblings with Pediatric Cancer and the Provision of Care - Based on the Results of a Questionnaire Survey

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Background/Objectives: I. The objective of the present study was to examine the relationship between hospital nurses' views of support for patients who are siblings and its provision to develop specific methods for supporting siblings in clinical settings.

Design/Methods: II. Research Methods

1. Design: A questionnaire survey
2. Subjects: 300 nurses and managers of hospital wards involved in pediatric sibling cases receiving treatment and long-term outpatient care in pediatric hospitals across Japan
3. Period of Data Collection: June to August 2016
4. Data Collection and Analysis: A questionnaire survey form was sent to ten hospitals that had consented to the survey. The question items included ten items associated with the attributes of the patients, the status of support for the siblings provided by the hospitals, and hospitals' awareness of support for the siblings, as well as nine items associated with the provision of support. The survey was based on the 4-grade Likert and descriptive statistics methods, and correlation coefficients were calculated.

Results: III. Results: Responses were collected from 123 people (response rate: 72%). The mean values and standard deviations of the awareness of support for the siblings and each assessment item associated with the provision of support were compared, and the mean values of awareness-related items (2.76 to 3.67) were higher than those of care provision-related items. The mean values of no care provision-related items were three points or higher.

Conclusions: IV. Discussion: Although nurses' awareness of support for pediatric patients in sibling relationships was high, the rate of nurses who had provided appropriate care for them was low; nurses with high-level awareness provided relatively high-quality care. There were significant correlations among three items associated with the awareness of support and provision of care in particular. It is necessary to raise the awareness of incumbent nurses, so that they will be able to improve their nursing care.

V587 SIOP19-1462 | Designing an Application to Promote Physical Activity for Adolescents with Cancer During Treatment

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Background/Objectives: In Japan, almost all children/adolescents with cancer are hospitalized over several months for undergoing treatments, and they have to live in a narrow area around their room to prevent infection. Therefore, children/adolescents cannot take enough exercise to keep up their strength during hospitalization. As a result, it is difficult for them to return to their school after treatment by loss of physical strength. To objective of this study was to develop an application for smartphone to promote physical activity of hospitalized adolescents with cancer.

Design/Methods: First, five nurses familiar with pediatric cancer nursing considered the contents of the application. Next, we got some advices on the contents of our application from a pediatric oncologist, a rehabilitation department doctor, and a physical therapist. In addition, members of creation of this application included a digital contents professional.

Results: Age: this application was aimed at children > 10 years old, as children at this age can "understand and accept their own disease and treatment" and "make their own rules and keep the rules".

This application Contents: This application was a system that allows patients to record their activities and compete with adolescents in other hospitals for cancer treatment. Regarding physical activity: the number of steps can be registered automatically if you walk carrying a smartphone. On the other hand exercises such as abdominal muscles and foot lifting should be registered by themselves. Further more, in order to increase the motivation to exercise of the adolescent, they acquired monsters according to the amount of activity, and adopted them as they grew up.

Conclusions: From now on, based on the result of investigation about the physical stress by the activity in hospital, we will decide the exercise level that adolescents can use this application safely and plan the intervention research.

V588 SIOP19-0218 | A Literature Review on Cancer Treatment Decision-Making by Pediatric Patients and Their Parents

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Background/Objectives: Objective: The present study involved pediatric patients with incurable cancer and their parents, and aimed to examine methods for supporting their decision-making on a transition to home medical care by reviewing literature on decision-making by pediatric cancer patients and their parents in various situations.

Design/Methods: Methods: A search of papers published between 1985 and 2017 was conducted using Ichushi-Web with keywords of “infants”, “decision-making”, and “nursing”, and 136 papers were extracted. Among them, 51 papers were selected, and 20 were on pediatric cancer.

Results: Among the 20 studies, there was one case study on a transition to home medical care in the end-of-life phase. The following four subjects were extracted: [selection of therapeutic methods], [notification of the name of the disease to pediatric patients], [anxiety of the families of pediatric patients with incurable diseases and support provided by health care professionals], and [a transition to home health care in the end-of-life phase]. Although no previous papers written in Japan clearly defined or conceptualized “decision-making”, importance was placed on the relationships among health care professionals, patients, and their families. There were few studies that involved pediatric cancer patients and focused on decision-making related to cancer and their transition to end-of-life care at home. No studies have been conducted to discuss pediatric patients’ decision-making supported by their families and the process of decision-making including pediatric patients.

Conclusions: Discussion: It is necessary to examine the process of decision-making on treatment involving pediatric patients to provide them with specific support.

V589 SIOP19-0330 | Success of Time Out Form in Reducing Procedure Related Incidents at Pediatric Oncology Unit of the Indus Hospital Karachi Pakistan

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Background/Objectives: Bone marrow aspiration, Trephe and administration of intrathecal chemotherapy are part of treatment in most of childhood Cancer treatment plan. In our oncology daycare setup at Indus Hospital the number of new registered cases each year is more than nine hundred patients. The flow rate of such procedures are seven hundred to seven

hundred and fifty per month that is twenty to twenty five procedures per day. The procedures are carried out under conscious sedation. These procedures are of high importance in cancer treatment requiring precise focus and accuracy. We confronted three incidents (0.4%) in a period of three months related to procedures that could have led to sentinel events bringing attention towards defining strategies to reduce them. The objective of this project was to introduce a tool/SOP to reduce procedure related errors ensuring patient safety.

Design/Methods: Literature review was done. Guideline from WHO and JCIA were studied and from their recommendation of IPSG Time Out Form was identified and deliberated. After approval from multidisciplinary team Guidelines were developed then communicated to the team. The procedural team were oriented and trained through sessions before initiation of pilot. Documentation of all procedures and events were closely monitored to evaluate outcome.

Results: After three months of pilot study it was observed that we had reduced number of incidence to zero which was a great success by timely identifying the potential error as near miss hence preventing errors of major or sentinel category.

Conclusions: The implementation of time out form has proved to be effective in reducing the number of errors occurring during procedures. Although it’s not a major operative procedure but consequences of errors could lead to sentinel events. It is essential to develop system and procedure to reduce or minimize such errors. Procedural errors are included in our monthly indicator for continues record keeping.

V590 SIOP19-1197 | To Audit the Compliance of Mouthwash Among Children Receiving Chemotherapy

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Background/Objectives: Tata Memorial hospital is the biggest tertiary care oncology hospital in India, where the number of pediatric patients getting admitted with chemotherapy is increasing every year. Children receiving chemotherapy are at risk of oral complications which may cause significant morbidity and a potential risk of mortality. Hence it is crucial to prevent morbidity related to side effects of chemotherapy for better outcome of care.

To find out the compliance of mouthwash among children receiving chemotherapy.

Design/Methods: Quantitative research with survey and observation to assess the compliance of mouthwash among 50 children receiving chemotherapy in pediatric oncology ward. Children were selected using convenient sampling. The tools used were Observation checklist to collect data regard-

ing mouthwash practices, oral mucositis scale and opinion scale to find the barriers for noncompliance to mouthwash practices.

Results: Compliance of mouthwash practices was much better among the age group of 10-15 years. The agent used for mouthwash is chlorhexidine with 1:1 ratio. Compliance to the following practices: ratio of dilution, frequency and 1 minute swish was better in this age group as compared to children below 10 years. Children below 10 years were more dependent on parents for the compliance of mouthwash practices. Children of parents with low socioeconomic background and below secondary education showed poor compliance. Incidences of mucositis were lesser in children above 10 years of age group. The common barrier for non compliance to mouthwash with chlorhexidine is awful taste.

Conclusions: Educating and empowering parents with oral care protocol is essential to improve oral care among children receiving chemotherapy.

V591 SIOP19-0429 | The Importance of Place During Sedation for Intrathecal Chemotherapy in Pediatric Oncology Care

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Background/Objectives: Children who are treated for childhood cancer are exposed to hospitalization, interaction with unfamiliar people in strange environments, and unpleasant, and sometimes, procedures. Having to wait for procedures is one of the worst situations, experienced by child patients. It is therefore important that hospitals provide environments that are non-stressful and safe for children in conjunction with procedures. Especially important, is the possibility for children who are hospitalized to sustain everyday activities, such as play, irrespective of their age and severity of illness.

Objective: To assess differences in expenditure of time and dose of anesthetic drugs during sedation for intrathecal chemotherapy in two different environments- the children's ward, where the child was hospitalized, and the operation theatre.

Design/Methods: The study is based on retrospective data from repeated treatment sessions recorded in operation planning programs and journals during 2011-2018 (n=164). Children of the ages 1-12 years (n=22) with varying number of treatments were included in the study. Data was analyzed with the Kruskal-Wallis test and post-hoc analyses included the Mann-Whitney Test with Bonferroni correction.

Results: The time from the start of the procedure until the start of sedation was significantly lower at the children's ward, which was also the case if including the waiting time before

the start of the procedure. No significant differences could be found regarding the dose of anesthetic drugs used.

Conclusions: Sedation for intrathecal chemotherapy at the children's ward provides care to a higher extent in accordance with the needs of the child, by reducing the time for the procedure and thus the interference with the child's everyday life at the hospital.

V592 SIOP19-0262 | Advanced Nurse Practitioners (ANPS) – A Survey of Services Provided in Tertiary Paediatric Oncology Centres in the UK - A 2019 Update

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Background/Objectives: "Advanced practice is a level of practice, rather than a type of practice. Advanced Nurse Practitioners are educated at Masters Level in clinical practice and have been assessed as competent in practice using their expert clinical knowledge and skills." (Royal College of Nursing Advisory Group, 2018).

Within the field of paediatric oncology in the UK numbers of ANP's have increased but little research has been done to establish the numbers and the services they provide.

Design/Methods: A survey was devised 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 the role. The survey was sent to all 21 tertiary centres in the UK and Ireland using a well established 'link member' network within the CCLG paediatric cancer centres. The survey focussed on several areas of the ANP role in paediatric oncology; service provision, clinical roles, responsibilities and skills practiced and non-clinical responsibilities.

In March 2019 a further audit was undertaken with a few modifications of the original questionnaire, based on the answers provided in the original survey.

Results: Of the 21 centres contacted 19 responded. 9 (45%) had a comprehensive ANP service while around 30% of the centres who did not recognised the value of the role and were implementing, or aiming to implement it. The role of ANP is fairly standardised in paediatric oncology units within the UK. There is, however, a great deal of variation within the 4 pillars of nursing and barriers faced by ANP's.

Conclusions: The last few years has seen an increase in ANP's within paediatric oncology and a development of the services provided.

It is hoped that these results will be used to guide units developing ANP roles, allow bench-marking and move towards creating a national network for ANP's.

V593 SIOP19-0155 | The Development of E-Healthcare Services System for Children with Cancer and Their Families: KMH Experience

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Background/Objectives: The mobile device for healthcare applications has become popular and efficient. Hence, E-Health mobile healthcare have gradually become a trend to monitor cancer patients health status. The study was to (1) Establish the Healthcare services system to analysis personal health records, and patients' self-care management behaviors. (2) Provide the E-medical care information for pediatric cancer patients and their families.

Design/Methods: Our team reviewed the literature on related iHealth mobile healthcare on pediatric cancer care. Three key aspects associated with technology, information, and evaluations were identified. Meanwhile, the multi-disciplines club was set up to regular discuss and develop self-learning e-books for pediatric cancer patients and their families.

Results: The cloud-service platforms have been set to test the service stability and performance. Our study not only provides the information for patients and their families but also provides the healthcare providers a reference to monitor their patients' health conditions.

Conclusions: The Healthcare services system provide integrated, appropriate, and efficient medical care information, and help the patients and their families to keep track of their health conditions. The results could make reference for other settings in the future.

V594 SIOP19-1288 | Predicting Quality of Life with Clustered Health Status for Children with Cancer in Taiwan

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Background/Objectives: Fatigue and poor sleep, two of the most often reported symptoms, trigger a vicious cycle among

reduction of physical activity, deterioration of fatigue and sleep problems, and lower quality of life. Enhancing physical fitness (through increasing exercise participation and achieving appropriate exercise intensity) may break this cycle and eventually alleviate fatigue and sleep problems and enhance quality of life. The purposes of this study were to (1) classify patients into health status based on level of symptoms of fatigue and sleep problem and physical fitness (exercise participation and exercise intensity), and (2) examine the association between quality of life and health status and demographics.

Design/Methods: A hundred 7-12-year-old children with cancer were recruited into the cross-sectional study. The K-means cluster algorithm was employed to classify patient's health status based on symptoms (fatigue and sleep problem) and physical fitness (exercise participation and exercise intensity). Multivariate regression analysis was then employed to examine the association between health status and quality of life after controlling for demographic characteristics.

Results: Children with cancer were classified into three levels of health status: (1) better health (less symptoms and better physical fitness) (n = 10), (2) in between (n = 61), and (3) worse health (more symptoms and less physical fitness) (n = 29). Problems in quality of life were significantly fewer among participants who were older (p = .037), off-treatment (p = .005), and in better health status (p = .011).

Conclusions: Classifying children with cancer into three levels of health status helps healthcare professionals provide personalized care including suggesting appropriate exercise programs based on their health status. This study informs clinical practice by providing a way to manage symptoms and enhance children's quality of life.

Treatment and Care - Palliative Care

V595 SIOP19-1025 | Radiotherapy Improves Pain Control in Pediatric Cancer Patients Receiving Palliative Care

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Background/Objectives: Pain control can be challenging for children with advanced cancer. We implemented a multidisciplinary approach to manage our patients where decisions are shared by the palliative care team, primary oncologists and radiation oncologists.

Design/Methods: We retrospectively studied patients who received palliative radiotherapy from Jan2014 and Dec2018

at our center. Pain scores are recorded regularly at each clinic encounter and during hospital stay. Narcotics doses were all converted to daily morphine PO equivalent for further analysis. Wilcoxon test was used to compare paired samples.

Results: Forty-one patients (16 females) were included in this analysis. The median age at diagnosis was 9.8 years (range, 0.56-20). Patients relapsed/progressed after a median of 11 months following diagnosis (range, 0.4-141). They received radiation after a median of 27 weeks following relapse (range, 0.56-144). The median dose of radiation was 30Gy (range, 12-55) and the median dose per fraction was 1.8Gy (range, 1.3-3). The majority of patients (N=40) had decrease in their pain score following radiation. There was no significant decrease in daily narcotics requirement following radiation ($P=0.44$); however, a statistically significant drop in pain score from a median of 7 before radiation to a median of 2 following radiation was identified ($p<0.001$). The median duration to best response was 3.5 weeks (range, 0.3-55). Pain progressed later at the site of radiation in 29 patients (71%) after a median of 12 weeks following radiation (range, 2-105). All patients in this study died after a median of 34 weeks following radiation (range, 1.1 to 118).

Conclusions: Radiotherapy was effective in controlling pain in our patients with best responses typically seen after a month of radiation and lasting for 3 months in average. Concerns for long-term toxicity are not valid for children with advanced cancer so we advocate the use of radiotherapy as an adjuvant in pain control for these patients.

V596 SIOP19-0707 | Establishing Hospital Based Childhood Cancer Registry in a Low Middle Income Country (LMIC)

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Background/Objectives: There is no national childhood cancer registry in Pakistan. Estimation of childhood cancer is important for priority setting and planning. With the help of grant from My Child Matters, The Indus Hospital launched a project for holistic improvement in Pediatric Oncology Units in public sector hospitals. To collect statistics of childhood cancers in these centers, a web-based childhood cancer registry software was developed. Aim of study is to collect and analyze childhood cancer data from hospital based cancer registry of these centers.

Design/Methods: This is a retrospective study. Data was collected on web based database from January 2016 to December 2018 from 3 centers. We followed the following steps; developed tumor registry software, training of data operators was done, data entered into software. Data from all centers was updated, audited and analyzed on monthly basis.

Results: Total 722 patients were registered during study period. Male to female ratio was 2: 1, mean age was 7.4 ± 3.6 . Frequency of Leukemia (58%), Lymphoma (19%), Retinoblastoma (9%), Renal tumors (4%), Soft tissue sarcomas and Neuroblastoma were observed in 2% of patients while CNS and Intraspinal tumors, Bone tumors, Epithelial Neoplasms and Melanomas, Germ cell tumor, Hepatic tumors and LCH tumors were observed in 1% of patients. Stage IV tumor was observed in 34.2% of patients. 14% of patients left before treatment, 10% left during treatment. 29% were on palliative treatment while 71% were on curative treatment. Treatment related mortality was 16%.

Conclusions: In absence of national cancer registry, hospital based cancer registry from multiple centers can give good estimation of prevalence of different types of childhood cancer in LMIC. Our study shows advanced disease at presentation, high rate of abandonment and treatment related mortality as major determinant of survival.

V597 SIOP19-0930 | Integrating Palliative Care Into A Sub-Saharan Africa Pediatric Oncology Program

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Background/Objectives: The World Health Organization has declared that access to pediatric palliative care is a basic human right. We have developed a three-tier approach to addressing the need for sustainable Pediatric Palliative Care integration in low- and middle-income countries: 1. Education for bedside nursing staff and prescriber, 2. development of palliative care policies, and 3. early integration of palliative care teams into clinical (oncologic) pathways. We have begun assessment of this approach as part of the St. Jude Global-Parirenyatwa Hospital collaboration in Harare, Zimbabwe.

Design/Methods: Palliative care elements were assessed through four primary domains (Joint Commission International Accreditation Standards): 1) Assessment of Patient; 2) Care of Patient; 3) Medication Management and Use; 4) Patient Safety. Results were categorized according to

established criteria of met, partially met or not met, based on how often observed nursing practices met each measure.

Results: Based on our initial assessment, no palliative care-related nursing standards were fully met in the inpatient pediatric oncology ward. A local nursing working group to implement quality improvement (QI) projects and education initiatives to address pediatric oncology nursing palliative care-related needs. Top priorities included creation of pain policy and pain-related educational resources, addressing procedural pain (pharmacologic and non-pharmacologic strategies) and creation of a more standardized approach to end-of-life care. Additionally, a Zimbabwe-based nurse educator was identified and trained in utilization of these educational materials.

Conclusions: In response to findings from the palliative care assessments, an educational program utilizing a Nursing Pain Education Workbook and pocket card pain reference guide was created. This initiative will be integrated into annual competencies for nursing staff. In the future, specified pain and procedure-related policies as well as end-of-life care policies will be developed and implemented. Finally, palliative care pathways are being developed and integrated into the overall clinical pathways of oncologic treatment guidelines.

V598 SIOP19-0039 | Palliative and End of Life Care in Children, Adolescent and Young Adults with Cancer: A French Retrospective Multicentric Regional Study (PALLIFHOP)

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Background/Objectives: In France, cancer remains the main cause of paediatric death from illness, after the neonatal period. The PALLIFHOP study aimed to describe the care trajectories of children, adolescents and young adults (CAYA) with solid tumours (ST) or haematological malignancies (HM) at the end of life.

Design/Methods: We performed a multicentric retrospective review of medical files of all CAYA who died from tumour progression in 2016, in the Île-de-France area that surrounds and encompasses Paris. Extensive data from the last three

months of life were collected, analysed and compared to French historical cohorts.

Results: A total of 99 CAYA were eligible with a median age at death of 9.8 years (range 0.3-24 yo). Decision for palliative care was found in all files. Do-not-resuscitate orders (DNRO) were present in 90/99 files. CAYA were out of hospital for 70 days during the last three months of life. Most frequent terminal symptoms were pain (n=86), asthenia (n=84), dyspnoea (n=49) and anorexia (n=41), with a similar prevalence between ST and HM. Median number of medications per patient was 8 (range 3-18). CAYA frequently required administration of opioids (n=91), oxygen (n=36) and/or sedation (n=61). CAYA with HM received significantly more transfusions (p<0.001) and antibiotics (p=0.023) than those with ST. Trajectories of care were mostly similar between children and AYA. A wish regarding the place of death was expressed for 64 patients and could be respected in 42 instances. Seventy-five CAYA died in hospital. Comparison to French historical data showed that DNRO were more frequently reported in the PALLIFHOP study. The overall rates of in-hospital deaths were similar.

Conclusions: PALLIFHOP represents a large and informative cohort, illustrating our current palliative care approaches in pediatric hemato-oncology. End-of-life remains an active period of care that requires the fine coordination of multidisciplinary teams.

V599 SIOP19-0823 | Assessing Doctors' Attitudes on Palliative Treatment (ADAPT): Development of a Standardized Tool to Evaluate Palliative Care Integration within Pediatric Oncology in the Eurasian Region

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Background/Objectives: The World Health Organization (WHO) advocates for early integration of palliative care for all children with high-risk cancer. Lack of provider education and misperceptions about the purpose and delivery of palliative care can impede this imperative. In 11 countries of the Eurasian Region, little is known about physician knowledge and perspectives on palliative care. The Assessing Doctors' Attitudes on Palliative Treatment (ADAPT) survey was developed as an evidence-based, comprehensive, and culturally relevant assessment of physician perceptions in the region.

Design/Methods: Developed in line with WHO guidelines and review of published literature, the ADAPT survey

evaluates perceptions of physicians caring for children with cancer on palliative care integration. To enhance face and content validity, two panels of US and Eurasian palliative care experts serial tested survey items in English until final consensus was achieved. The survey was then translated to Russian and reviewed for colloquial syntax, comprehension, and cultural relevance. Back-translation to English ensured item construct consistency. The survey was pilot tested on an electronic platform (Qualtrics) by 12 English-speaking and 12 Russian-speaking physicians, representative of the diversity of specialties in the target population, with adjustments made based on feedback.

Results: After iterative rounds of pilot testing and review, the final survey consists of 61 questions comprising the following domains: timing of palliative care integration, scope of palliative treatment, physician responsibility, and ethical considerations. ADAPT utilizes a mixed-methods approach, with 55 Likert-scale, 2 multiple-choice, and 4 open-ended questions to enrich data interpretation.

Conclusions: We describe the development of an evidence-based, culturally relevant survey to evaluate provider attitudes of palliative care integration in pediatric oncology in the Eurasian region. We plan to disseminate ADAPT to inform improvements in access and quality of care for children with cancer in the region. In the future, ADAPT can also be modified to assess childhood cancer provider perspectives globally.

V600 SIOP19-1106 | Metronomic Chemotherapy as an Approach to Children with Advance Cancer in Resource-Limited Countries

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Background/Objectives: Children in resource-limited countries present late at diagnosis with very advance disease, poor prognosis even with standard therapy and inevitable demise. With the aim to provide therapy and relief of suffering to these children from Honduras, Nicaragua and Dominican Republic was designed a simple metronomic therapy, in association with palliative care.

Design/Methods: Honduras, Nicaragua and Dominican Republic enrolled 271 patients. Children with advance cancer with a survival in high income counties less than 20%, and relapse patients were diagnosed, staged and counseled. All patients were provided concomitant Palliative Care. Treatment consisted of oral biweekly methotrexate (15mg/m2) for

21 days, alternating with daily cyclophosphamide (25mg/m2) for 21 days, with twice daily ibuprofen (20mg/kg) in cycles of 42 weeks for 9-23 cycles. All patients received care for pain, and improvement of symptoms. No transfusions, antimicrobials or growth factors were administered.

Results: Of 271 patients were treated over 3 years. Age 1-18 years, 58% male. Ninety-four (35%) were relapse leukemia, 44 (16%) bone tumors, 32 (12%) CNS tumors, 19 (7%) neuroblastoma, 18 (7%) sarcoma, 14 (5%) lymphoma, 10 (4%) Wilms and 5 (2%) retinoblastoma and 34 (13%) other. Toxicity was minimal (mostly gastritis), never requiring admission to hospital. All patients were able to go and remain home. One hundred and ninety-six (72%) died, 5 (2%) lost of follow up and 70 (23%) were alive after 9-23 cycles (2.7 years).

Conclusions: This metronomic therapy provided prolongation of life with minimal side effects, cost and suffering. Children were able to go home and mostly pain controlled. Most of them died with dignity and close to family at home, 23% remain alive in follow up. This is an acceptable approach to those populations that do not have a curative option of care.

Body Words: 286 Title: 13

V601 SIOP19-1151 | Enhancing Palliative Care Training in Canadian Paediatric Haematology/Oncology Fellowship Programs: A Quality Improvement Project

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Background/Objectives: **Background:** Children with cancer benefit when their oncologists are skilled in delivering Palliative Care, regardless of the outcome of cancer therapy. It is vital that Paediatric Haematology/Oncology trainees receive high quality palliative care training in order to adequately care for their patients, as a lack of training may prevent the delivery of high quality palliative care. We introduced a palliative care curriculum for Haematology/Oncology fellows at SickKids in 2015. In 2017 we carried out a Quality Improvement project to inform curriculum development.

Objectives: We sought to understand the needs of trainees regarding palliative care education, and the program directors' and trainees' experiences in providing palliative care.

Design/Methods: Online surveys were sent to all program directors and trainees in Canadian Paediatric Haematology/Oncology Fellowship Programs in 2017 as part of our quality improvement project.

Results: Our survey provides the first description of palliative care education for Canadian Paediatric Haematol-

ogy/Oncology fellows. Our participants valued palliative care education and believed it should be provided for all trainees. All Canadian Haematology/Oncology training programs provided some training in palliative care. However, we identified deficiencies in the training with little time allotted to training, a failure to teach critical skills and a lack of opportunities for trainees to practice their practical skills. Seventy-five percent of fellows had experienced palliative care situations where they felt they lacked the necessary skills and 60% had experienced distress as a result of managing palliative care situations. Only 55% of program directors thought their fellows were adequately trained in palliative care on completing oncology training.

Conclusions: Despite increasing awareness of the value of palliative care for children with cancer, this subject does not receive appropriate attention in training curricula. We hope to continue to work with our colleagues to build on the foundation previously created and develop a national curriculum that addresses this training gap.

V602 SIOP19-0176 | Management of Patients Followed in Home Hospitalization in a Palliative Context: Family Experience

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Background/Objectives: Palliative care is a complex situation and this complexity is increased in a pediatric population. Indeed, the direct environment of the child involves his parents and his siblings. The expectations of families in these difficult times are not always met. This study describes the experience of the entourage of children with cancer followed by Home Hospitalization in a palliative context. Their satisfaction with Home Hospitalization was also assessed.

Design/Methods: We conducted a monocentric prospective interventional study and assessed the experiences of parents and siblings using self-questionnaires that were sent home one month after the child's death.

Results: 46 children were included. The response rate was 41.3%. In 94.4% of cases, the choice of the end-of-life location was "completely respected". According to our study, Home Hospitalization improves the relationship of the family with the sick child, as well as the behavior of other children and their fatigue. There is no negative impact on parents' exhaustion. This mode of hospitalization in this context, largely meets their expectations.

Conclusions: Home-based care in a palliative context of children with cancer does not have a negative impact on the family of the patient but has advantages.

V603 SIOP19-1130 | Global Impact of Education in Palliative and End-of-Life Care for Pediatrics (EPEC-PEDS): Dissemination of Palliative Care Principles to Pediatric Oncology Providers on an International Scale

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Background/Objectives: Worldwide, over 80% of children diagnosed with cancer live in low- and middle-income countries with the majority eventually dying of their disease. The World Health Organization states that access to palliative care for children is an ethical responsibility. Limited access to pediatric palliative care training prevents successful integration of palliative care principles into pediatric oncology practice.

Design/Methods: In September of 2018, St. Jude Global Academy selected health professionals from 23 countries across 5 continents to participate in an online plus two-day face-to-face training in the Education in Palliative and End-of-Life Care for Pediatrics (EPEC-Peds) curriculum. The participants consisted of physicians and nurses in the fields of pediatric oncology and palliative care. These individuals were certified as EPEC-Peds Trainers and encouraged to teach the curriculum in their respective countries. Baseline and follow up surveys were conducted to assess current and future educational experiences across each global site.

Results: Twenty-seven individuals were trained over the 2-day educational curriculum. Sixty-five percent of participants had a pediatric palliative care team at their home institution, but 69% (18/26) lacked a pediatric palliative care training program in their country. Upon returning to their countries of origin, Trainers provided 53 educational sessions over a 4-month period, with more than 2,000 health professionals and medical students participating in these sessions. Nineteen different modules were taught, with frequently taught topics including: "What is Pediatric Palliative Care and Why Does it Matter?"; "Multimodal Analgesia"; "Opioid Selection and Opioid Rotation"; and "Preparation for Imminent Death", among others.

Conclusions: Dissemination of EPEC-Pediatrics is feasible, and the use of standardized training modules can increase exposure to palliative care principles to pediatric oncology providers on a global scale. Further investigation is needed to understand the impact of global palliative care education on end-user knowledge, comfort, and competency.

V604 SIOP19-0910 | Management of Moderate-Severe Pain in Children with Advanced Cancer from a Tertiary Hospital in a Developing Country: Barriers in Opioid Treatment

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Background/Objectives: Children with advanced cancer have chronic, moderate-severe pain, whose treatment of choice is morphine: potent opioid analgesic, however in Mexico, 80% of the population does not have access to it.

Objective: To demonstrate pain control with a semisynthetic opioid: transdermal buprenorphine, in the absence of morphine in a mexican tertiary hospital.

Design/Methods: We conducted a literature review of the policies related to the prescription of opioids in Mexico as a developing country. We extracted the data of advanced stage and/or metastatic patients treated with transdermal buprenorphine from January to December 2018.

Results: The main barriers identified for the prescription of morphine were: complexity in requirements to obtain the corresponding license, restricted access to controlled drugs and lack of coverage in the essential drug supply. A total of 45 patients aged 2 to 15 years received transdermal buprenorphine in the dose range of 3-7mcg/kg. The diagnoses of malignancy were: ALL (31.1%), CNS tumors (20%), bone tumors (15.6%), soft tissue sarcoma (11.1%), histiocytosis (6.7%), lymphomas (6.7%), primitive neuroectodermal tumor (4.4%) and hepatoblastoma (4.4%); of which 25 (55.6%) had progressive disease and 20 (44.4%) metastatic disease.

Conclusions: There are few studies about the efficacy and safety of the use of transdermal buprenorphine for the treatment of chronic moderate-severe pain in children with advanced cancer. The effectiveness of transdermal buprenorphine in the control of moderate-severe pain was confirmed through evaluation with pain scales according to age (<4 years FLACC and >4 years OUCHER and EVA) and in the extended time of action, being a main advantage for patients with transport limitations. Mexico must review its policies to ensure the availability of morphine, so that health professionals can provide adequate pain relief.

V605 SIOP19-1221 | Medical Marijuana Use for Pediatric Oncology Patients: Single Institution Experience

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Background/Objectives: The use of medical marijuana (MM) has become widespread in various fields of medicine, including oncology. Using medical marijuana in pediatric oncology has been rather limited, and research on this topic is scarce, and often showing conflicting results. In Israel, children with cancer can be treated with MM especially at the end of life.

Design/Methods: Between 2010 - 2017, 50 children diagnosed with different types of cancer in our institution were treated with medical marijuana. The main indications for medical marijuana prescription were nausea and vomiting, decreased mood, disturbed sleep, and pain. MM was given as oil drops to 30 (58.4%) patients and, smoking to 11 (21.3%) patients, while other patients received MM via vaporization, capsules, or in a combination of various routes. A questionnaire was submitted to the parents and the children.

Results: Children and parents reported positive effects in 80% of cases. No significant side effects were noted. Short-term side effects occurred in a minority of patients and were observed predominantly in children who received medical marijuana by smoking.

Conclusions: Medical marijuana may serve as complementary therapy to conventional medical treatment in pediatric oncology. In addition, medical marijuana should be considered as an integral part of supportive care directed at the improvement of the quality of life of children mainly at the end of life. Taking into account that we have a profound deficit of knowledge on possible unwanted consequences of the prolonged use of medical marijuana in pediatric populations, further research in this field is needed.

V606 SIOP19-0023 | Phantom Pain in Children and Adolescents with Osteosarcoma Treated at the Civil Hospital of Guadalajara: Prevalence and Clinical Characteristics

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Background/Objectives: Phantom limb pain (PLP) is a frequent problem in pediatric patients undergoing surgery as part of the treatment of osteosarcoma, its prevalence ranges from 48 to 90%. The objective was to determine the prevalence of PLP

Design/Methods: A retrospective study performed on children under 18 years of age by reviewing the clinical history. Variables such as age, post-surgical pain onset, pain classification were analyzed; descriptive and inferential statistics were used, all calculations were made in the SPSS 20 program.

Results: We evaluated 37 pediatric patients from January 1, 2007 to December 31, 2016, 16 patients were amputated (43%), 13 were disarticulated (35%) and 5 with salvage (25%). The prevalence of phantom limb syndrome was 46% (17 patients), the median for age was 13 years; 59% were male (10 patients); the pain developed in the first postoperative month in 94% (16 patients), 88% presented phantom pain (15 patients), 59% phantom limb sensation (10 patients). Severe pain was found in 35% (6 patients). 14/17 (82%) patients with sensation and / or PLP were assessed by pediatric palliative care allowing adequate control of pain before and after surgery. Gabapentin was the main neuromodulator used in patients with PLP.

Conclusions: PLP is a common complication that should receive comprehensive care for timely management with multimodal therapy to avoid chronic pain with temporary or total disability.

V607 SIOP19-1192 | Prevalence of Burnout Among Oncologists and Pediatric Hematologists in México

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Background/Objectives: Although the medical profession is incredibly rewarding, sustained and prolonged stress leads to professional exhaustion, becoming a substantial problem with worrisome consequences for doctors and their patients.

Objective. To determine the prevalence of burnout among oncologists and pediatric hematologists belonging to AMOHP, AMEH in México

Design/Methods: Survey type study, where a questionnaire sent via e-mail was used to collect the data anonymously, the data was analyzed by the SPSS vs 22 program.

Results: Ninety two (92) hematologists and pediatric oncologists were included, a response rate of 39,6% was obtained. 53% of respondents identify symptoms of burnout in themselves, with fatigue (23%) and guilt or feelings of being indispensable (16,3%) the main affections, 66% of respondents identified burnout symptoms in your companions. 57% (52)

of the respondents are between 40-59 years old, being the female gender 65,2% (60), 6,5% (6) smoke, 33% (30) have a chronic disease, 72% (38) assess more than 100 patients with haemato-oncological diseases annually, in 68,5% of cases more than 5 patients die annually, 75% (69) receive calls concerning patients during the weekend, 18,5% of oncologist and hematologist interviewees are not satisfied with their work and 22% with their personal life. 10% would not choose their specialty again.

Conclusions: The values found in our work are consistent with that reported in the literature, where the prevalence of burnout ranges from 20 to 70%. Health institutions need to implement programs and measures that favor the psychological and mental well-being of health personnel.

V608 SIOP19-0963 | Managing the Paediatric Oncology Palliative Care Patient within a Paediatric Share Care Unit: How Are We Doing?

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Background/Objectives: Introduction: In UK, the National Institute for Health and Clinical Excellence clinical guideline on providing palliative care in Children and Young people recommended, 'The child and their family should play an active role in discussions about their care and if possible, the child should receive palliative care, including end of life, in the place they choose. These children should be cared for by multidisciplinary team who meet regularly to discuss the child's care.

Objective: To find out the patient and family's preferences during palliative care (including choice of place of death) and how these impacts on care. This study will provide involvement of MDT team (tertiary and local hospital care, community nursing team and paediatric palliative input from hospices) and how our community oncology share care team provide parents and families support during this time.

Design/Methods: Method: Retrospective study from past 5 years of children that have died from cancer within our local district hospital.

Results: The results shown that the number of patients dying from cancer were around 4-8% of patients treated that year. 70% choice home as preferred place of death, and they were many health professional teams, hospital and hospices involved in providing palliative care to these children. Hospices were involved in 100% of patients, 86% had children's community nurses involved in care. With each death most families were satisfied with the care they received, 20% of

families found the care difficult when including two or three separate healthcare teams caring for their child.

Conclusions: 100% of children under our care received excellent care and died in their place of preference. Families are preferring to stay at home and receive nursing and healthcare treatments in their home environment, with this brings multiple health care teams involved and challenges to ensure good standard of care is provided.

V609 SIOP19-1683 | Integrative Pediatric Palliative Care in Children with Cancer at Songklanagarind Hospital Thailand

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Background/Objectives: Each year approximately 1.2 million children around the world are in need of palliative care services, most of them living in low and middle income countries. Pediatric palliative care provides comprehensive symptom management, psychosocial and spiritual support to children with life-shortening diseases. Since 2010, Songklanagarind Hospital, initiated an integrative palliative care service for children with cancer. Funding for the program initiative came from the Sanofi-Esper Foundation's My Child Matters program. The purpose of this study was to look at the impact of our efforts, and to identify opportunities for improvement and expansion of care.

Design/Methods: We retrospectively analyzed, using comprehensive chart review and palliative care data tracking forms the following information: demographic variables, primary diagnoses, predominant symptoms, the use of palliative sedation, and place of death for children who with cancer who received pediatric palliative care

Results: There were total 151 children who received care through our program. Pain and comfort care guideline were developed and utilized. The most common symptom is pain that required opioids (73.3%). For end of life care, palliative sedation protocol with midazolam and morphine was utilized in 9 patients. All of these children had severe dyspnea (n=6) or uncontrolled pain (n=3). The majority of patients (75%, n=45) died in the hospital, (34 in our hospital and 11 in other hospitals) due to a need for advanced symptom management at end-of-life.

Conclusions: We retrospectively analyzed the major issue during the end of life in children with cancer. In contrast to adult palliative care, most of the children in our setting died in the hospital because of parents' concerns about maintaining effective symptom control. Our results demonstrate the growing acceptance for the use of palliative care for pediatric

cancer patients and also the need for pediatric palliative care education to improve physician's skill on symptoms management.

V610 SIOP19-0685 | Pediatric Palliative Oncology: A Data Analysis of Patients Who Initiate Palliative Care at the Instituto Nacional de Enfermedades Neoplásicas, 2017-2018

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Background/Objectives: Pediatric Palliative Care (PPC) is necessary in the health system, especially in hospitals that have a hemato-oncology service. The aim of this study was to determine the clinical characteristics and survival of patients who initiate PPC in a Peruvian Hospital.

Design/Methods: Retrospective, observational, monocentric study. All infants and children younger than 14 years who initiate palliative care at the Instituto Nacional de Enfermedades Neoplásicas (INEN) between July 2017 and December 2018 were reviewed. Statistical analysis was descriptive and analytic.

Results: A total of 142 children were identified, 82 patients (57.7%) were male and 60 (42.3%) female. The median age was 9 years. The most frequent oncological diagnosis was acute lymphatic leukemia (45%) followed by brain tumors (19%) and osteosarcoma (18%). Twenty one percent had a history of abandonment of treatment. Somatic pain occurred in 40.2% of patients and neuropathic somatic pain in 39.4%. Pain (71.1%) and hyporexia (41.6%) were the most frequent symptoms found. Sixty-nine patients (48.6%) received metronomic treatment. Tramadol (42.7%) followed by morphine (23.9%) were the most used drugs for pain management. One hundred sixteen patients had terminal illness of which 96 (82.8%) died. Fifty-five patients died in the INEN. With a median follow-up of 38 months, the 10-month overall survival (OS) rate for patients who used metronomic and non-metronomic treatment was 24% (standard error, SE 0.06%) and 19% (SE 0.08%) respectively. In the multivariate analysis, the use of metronomic treatment (P=0.616) did not affect significantly OS.

Conclusions: Integrative management of child with cancer should include palliative care since the beginning of his illness. We do not have non-pharmacological integrative measures to prevent and treat pain in our patients. It is necessary to optimize the multidisciplinary management of this patients.

V611 SIOP19-0687 | Pain Prevalence in Hospitalized Children with Cancer: A Prospective Cross-Sectional Survey

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Background/Objectives: Pain in hospitalized children with cancer may be unrecognized and undertreated. The aim of this survey was to determine pain prevalence, the main sources of pain, pharmacologic and integrative treatment of pain in pediatric inpatients in a Peruvian Hospital.

Design/Methods: Prospective, two-day, cross-sectional survey and medical record review of inpatients who received medical care at a Peruvian Hospital. They were asked to report their experience with pain and its management during the previous 24 hours.

Results: Of 50 hospitalized patients, 48 children and parents completed the survey. Fifty-two percent had experienced pain during the previous 24 hours. Twenty-one percent of all children surveyed experienced severe pain and 15% moderate pain in that time period. The worst pain reported by patients who experienced pain was caused by oncological pain (40%) followed by needle pokes (32%). Only one patient had a non-pharmacological integrative measure to treat the pain and 48% of the patients did not receive any treatment. Pain assessments and management were documented in the medical record for 44% of patients in the last 24 hours. The most commonly prescribed analgesic was tramadol. None of the patients with pain had an evaluation by the Department of Pain Medicine. A second survey was carried out the day after the change of intravenous route. Of the 48 patients previously interviewed, 9 did not complete the new survey and 23 patients had central venous catheter. Of the remaining 16 patients who underwent intravenous change, 82% reported pain due to needle pokes.

Conclusions: The prevalence of pain in hospitalized children with cancer is high. Most children with pain do not have a documented assessment of pain and its management. We do not have non-pharmacological integrative measures to prevent and treat pain. It is necessary to implement changes to reduce pain in our patients.

V612 SIOP19-0879 | Analysis of Reasons for Upfront Palliation in Patients of Pediatric Solid Tumors Presenting to a Tertiary Cancer Care Center – A Real-Life Scenario

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Background/Objectives: Outcomes of many Pediatric Solid Tumors (PST) (even metastatic) have improved over last few decades. There are no guidelines suggesting upfront palliation even in advanced PST. In high volume but resource

constraint setting, explanation of poor outcomes and familial socio-economic factors may necessitate this choice by parents.

Design/Methods: We analysed all consecutive patients of PST registered in the single year of 2018 for family demographics, disease characteristics at presentation and intent of initial treatment (Curative Vs. Palliative). Comparison across demographics was done using t-tests for those who were palliated upfront.

Results: In the year 2018, 650 PST patients registered in our center. Of these, 58 (8.9%) did not pursue curative intent treatment upfront.

Median duration of symptoms till first presentation was 31 days (Range - 0 - 1216), average duration was 96 Day.

The diagnoses of this cohort of 58 patients were Neuroblastoma (NB-High-Risk)-12/58 (20%), Rhabdomyosarcoma (IR or HR)-10/58 (17%), PNET-8/58 (13.7%) and Hepatoblastoma, Retinoblastoma and NRSTS each 5/58 (8.6%) and rest were rare tumors.

Of the 46 non-NB patients 39 (84.7%) presented with metastases. Of the 5 non-metastatic tumors, 2 were inoperable liver tumors (cure not feasible without liver transplant which was not possible due to socio-economic reasons).

Family income was less than Rs. 10000/month (~US\$138) in 35/42 (83.3%) and Education was Graduate or above in 7/43 (16%) in whom this information was available.

Reason for upfront palliation was advanced disease and expectation of poor outcomes despite aggressive treatment options in 49/58 (84.5%) and socio-economic constraints in 9/58 (15.5%). Socio-economic constraint and lower education levels correlated with more chances of families to opt for palliation ($p < 0.05$).

Conclusions: In real-life scenario, upfront palliation is opted by significant (8.9%) families of PST patients presenting to a tertiary cancer care center in a resource limited setting.

Treatment and Care - Psychosocial (PPO)

V613 SIOP19-1208 | Innovation in Global Health Communication: A Qualitative Research Approach in Exploring Themes in the How I Live Documentary

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Background/Objectives: Although storytelling and films have been used as effective health communication tools to improve population outcomes, limited studies have analyzed

qualitative data collected in documentaries. *How I Live* is a documentary about closing the global survival gap in pediatric oncology and applied a systematic methodology to capture stories of diverse stakeholders in global childhood cancer. The objective was to explore key elements and recurring themes identified in the interviews by applying a qualitative research approach.

Design/Methods: Using the Social Ecological Model as the theoretical framework, two sets of qualitative data were analyzed: First, document review (production schedules, call sheets, notes from meetings and site visits, reports on health systems), Second, in-depth interview data from 3 key informant groups, 37 key informants, 59 interviews, 49 transcripts, 7 countries (Egypt, Ghana, Guatemala, El Salvador, Myanmar, Switzerland, United States). NVivo was used to code and analyze transcripts.

Results: Fourteen overlapping themes were identified among all respondents such as religion, need for support, malnutrition, and challenges in care delivery and access. Most referenced themes among the three key informant groups (patients and families, healthcare professionals, and experts) were: support, solutions, LMIC conditions, and religion. Themes were categorized in 4 levels of the Social Ecological Model: 1. Individual (faith, education, optimism), 2. Interpersonal (stigma, abandonment, transportation) 3. Institutional (insurance, supportive care, cultural beliefs), and 4. Societal (access, equity, political climate).

Conclusions: Films can serve as powerful catalysts for social impact and innovation, and inspire action for change. Data from narrative storytelling can not only assist in raising awareness but also create relevant and persuasive messages about pressing global health issues. Next steps include impact measurement of the film and implementation of a stakeholders analysis to develop a successful film distribution and advocacy plan.

V614 SIOP19-0393 | “Bears Get Sick, Too”, and “The Giving Bear”: Preparing Children for Stem Cell Transplant and Stem Cell Donation

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Background/Objectives: Stem cell transplant (SCT) is a complex and intimidating process for adults, and all the more so for children and their worried parents. With the financial backing of Amutat Chaim, a local philanthropic organization, we have developed a pair of user-friendly books designed to prepare children aged 4-11 for stem cell transplant and donation. We feel that the shared reading experience pro-

motes interactive parent-child dialogue and encourages effective communication within the family.

Design/Methods: In the first book, which has been translated into 4 languages, SCT is experienced by a teddy-bear. The second book in this series, *Little Bear's* sibling experiences marrow donation. The discomfort of the procedure and the ambivalence that it may engender in young donors are discussed in age-appropriate and gentle terms. The psychological burden of sibling loneliness and detachment from parents and the ill sibling are addressed. The possibility of graft failure and transplant-related mortality are discussed matter-of-factly, but with emphasis on the altruism of the donor and hope for *Little Bear's* eventual recovery. Although age appropriate colloquialisms are used, the text is simple and easy to translate. Accompanying illustrations facilitate discussion between parents and their children about life in the SCT Unit and the process of marrow donation.

Results: Parents relate that children who are the target audience for this pair of books benefit from the discussions engendered by the first book, and enjoy retelling it to their family and friends.

Conclusions: Printed, age-appropriate books are an ideal medium for patient and family education. We plan to collect data proving the utility of these books and invite centers to translate them into their local languages.

V615 SIOP19-0203 | Post-Traumatic Growth in Parents of Long-Term Childhood Cancer Survivors Compared to Parents of the General Population

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Background/Objectives: Post-traumatic growth (PTG) describes perceived positive changes following a traumatic event. We describe i. PTG in parents of long-term childhood cancer survivors (CCS) compared to parents of similar-aged children from the general-population (comparison-parents), and ii. its associations with socio-demographic and cancer-related characteristics.

Design/Methods: We conducted a questionnaire survey among parents of long-term CCS (aged ≤ 16 years at diagnosis, ≥ 20 years at study, registered in the Swiss Childhood Cancer Registry), and in the Swiss general population. We used the *PTG Inventory (PTGI)* to assess five domains of PTG (relating to others, spiritual change, appreciation of life, new possibilities, personal strength) and overall PTG. We analysed

data using i. descriptive statistics to assess mean PTG-scores and ii. multilevel regression models accounting for family clustering to evaluate associations between overall PTG and socio-demographic and cancer-related characteristics.

Results: In total, 746 parents (41.7% fathers) of 513 survivors and 411 comparison-parents (42.8% fathers) completed the PTGI. Average overall PTG was higher for CCS-parents (52.3; 95%-CI: 50.8-53.8) than for comparison-parents (50.4; 95%-CI: 48.1-52.7). CCS-parents showed higher PTG than comparison-parents in the domains 'relating to others' (18.4 vs 17.3, $p=0.010$), 'spiritual change' (3.3 vs 3.0, $p=0.038$) and 'appreciation of life' (9.3 vs 8.4, $p=0.027$). We found no difference in 'new possibilities' and 'personal strength' ($p>0.05$). Those with migration-background (coef=7.0, 95%-CI: 0.8-13.2) and mothers (coef=9.4, 95%-CI: 6.4-12.4) reported higher overall PTG. CCS-parents of children who were treated with stem cell transplantation (coef=11.7, 95%-CI: 1.3-22.1) and who experienced cancer-related late effects (coef=4.6, 95%-CI: 0.4-8.8) reported higher overall PTG.

Conclusions: Our study highlights that families can grow from the challenging experiences following serious illness. Our findings help inform clinical practice and interventions, which may support parents in reframing their experiences.

Acknowledgments: This study was supported by the Swiss National Science Foundation Grant-Nr 100019_153268.

V616 SIOP19-0206 | Development and Evaluation of an Outpatient Support Group Intervention for Caregivers of Children with Cancer: A Cancer Center Psychosocial Services – Community-based Partner Organization Collaboration

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Background/Objectives: Caregivers of children with cancer experience increased distress and reduced quality of life from diagnosis through survivorship. Support for caregivers is inconsistent across cancer centers, settings, and treatment phases, and online support is not integrated with in-person support for geographically distant caregivers. We describe the partnership of psychosocial services programs with caregiver stakeholders (Momcology) to develop and evaluate a series of workshops addressing caregiver-specific Psychosocial Standards of Care in Pediatric Oncology: Standard 6 Psychosocial Care for Parents and Standard 7 Anticipatory Guidance and Psychoeducation.

Design/Methods: Feedback from Momcology caregivers and psychosocial staff at two children's cancer centers identified

topics related to family management and self-care. Twelve semi-structured modules were developed to guide each session. Bimonthly workshops were co-facilitated by Momcology leaders and psychosocial staff and Momcology distributed a survey at the end of each year.

Results: Attendance at workshops ranged from 8-16 caregivers and was consistently higher than prior to implementation of this intervention model. Across sites, 22 participants completed the survey. They endorsed peer support (91%), connection to other families (82%), and education (64%) as reasons for participation. They reported improvements in emotional well-being (77%), self-care (82%), physical health (65%), and family functioning (60%). Additionally, 100% indicated they would refer others, and endorsed feeling that their hospital was addressing the need for caregiver support. Momcology leaders noted that online conversations were positively impacted by these workshops through an improved problem-solving framework when discussing challenges, reminders regarding self-care, and enhanced sense of community.

Conclusions: Workshop participation was high, and caregivers indicated the sessions were worthwhile, feasible, and effective in improving coping and well-being. Now implemented in four cancer centers, these results reinforce a call for deeper collaboration between caregiver stakeholders and professional staff to share knowledge and expertise to build an accessible, engaging curriculum that is responsive to the range of caregiver needs.

V617 SIOP19-0243 | Childhood Craniopharyngioma and Impaired Quality of Life: An Evaluation of a Family Centred Multi-Disciplinary (MDT) Approach to Improve Wellbeing – A Pilot Project

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Background/Objectives: Children with Craniopharyngioma are at risk of physical and psychosocial impairments (Hermann & Muller, 2018). Treatment associated comorbidities including hypothalamic dysfunction, obesity and behavioural changes reduce quality of life (QoL) (Wijen et al. 2017). Craniopharyngioma should be managed as a chronic condition, with preventative strategies (Muller 2017). Studies report unhealthy routines in this cohort (Caminiti et al. 2017) for which family-centred intervention have shown improvements in wellbeing (PHE, 2017). This project aimed to evaluate if a wellbeing clinic, in addition to routine clinical follow-up would 1) be acceptable to children and their parent/carers and 2) be beneficial to health and wellbeing.

Design/Methods: Families from the SW of England (n=7), with a child with Craniopharyngioma (<18yrs), were offered a wellbeing appointment in Bristol three monthly. Attendees (n=5) saw a Dietician, Physiotherapist, Neuro-Oncology Nurse Specialist and Health-Promotion Practitioner, to focus on holistic needs assessment and family-centred lifestyle changes. Self-reported QoL data (Using PedsQL), height, weight and BMI were collected. Families received health education packs and signposting. Changes in BMI, QoL, nutritional intake and activity were evaluated after eight attendances, over a two-year period.

Results: 1.) Acceptability - All rated the clinic useful and would recommend to others. 2.) Benefit - All (n=5) improved QoL (health activities, psychological wellbeing, social interaction, educational engagement) and increased activity, consumption of fibrous foods, fruit and vegetables. At baseline three children had an unhealthy BMI on the 99th percentile, which at 2 years had decreased (n=1), stabilised (n=1) or increased (n=1).

Conclusions: Results suggest improving modifiable factors e.g. diet, exercise, engagement in social interaction and education, benefits QoL for children with Craniopharyngioma. This novel family-centred MDT approach, offers focus and continuity on lifestyle changes and findings are encouraging in management of this chronic condition. Further study is required to determine transferability between centres and illness e.g. hypothalamic glioma.

V618 SIOP19-1607 | Photographs of Meaning: A Novel Psychosocial Intervention for Patients, Survivors and Caregivers

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Background/Objectives: Adolescents and young adults (AYAs) and pediatric palliative caregivers (PPCGs) are often overlooked healthcare populations. AYAs' unique psychosocial needs are often unaddressed during and after cancer treatment. Similarly, PPCGs report high levels of burden and isolation due to society's lack of understanding of their role. We introduce Photographs of Meaning (POM), a novel intervention based on meaning-centered psychotherapy and photovoice through a social media application, as a way to reach these populations. POM has been tested among AYA cancer survivors (POM-AYA) and pediatric palliative caregivers (POM-PPCG).

Design/Methods: For POM-AYA, a 10 week curriculum was introduced. Enrollment, retention, and satisfaction data deter-

mined feasibility while BDI-II, PedsQL-YA, and FACIT-Sp assessed for changes in depressive symptoms, quality of life, and spiritual well-being over time. For POM-PPCG, 8 or 9 week curriculums were implemented, assessments were completed measuring meaning in life, subjective well-being, and perceived social support, and weekly photo narratives underwent thematic analysis. At the conclusion of POM-PPCG, participants selected a photograph and narrative they felt to represent their experiences for a photo exhibit, further increasing awareness about the role of PPCGs.

Results: Thirty participants enrolled in POM-AYA. There were significant changes in depressive symptoms and improvement in quality of life, and no effect spiritual well-being. Participant feedback (n=17) showed 94% describing the experience as positive or very positive. Twenty-seven caregivers participated in POM-PPCG, resulting in 230 photo narratives. Qualitative analysis of the first iteration found themes of *Love, Challenges, Loss, Coping, and The New Normal*. Significant changes in meaning in life, subjective well-being, and perceived social support were also established. Feedback showed 100% of participants felt they benefitted from POM-PPCG and were able to participate due to the social media format.

Conclusions: POM is an effective method in engaging challenging hard-to-reach healthcare populations. Utilizing social media encourages engagement while offering effective methods for psychosocial intervention.

V619 SIOP19-1702 | Parental Attitudes, Optimism, and Experiences by Childhood Cancer Subtypes

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Background/Objectives: Upon receiving a childhood cancer diagnosis, parental concerns include a lack of disease knowledge, time management difficulties, financial strain, and worries about the family's emotional well-being. These factors can influence parental optimism, quality of life, or their personal emotional state. The objective of this study is to descriptively characterize these domains by childhood cancer subtypes and to consider the role of family support, self-care, and confidence in clinicians.

Design/Methods: Data was provided by the My Childhood Cancer (MCC) Survey Series collected by the Alex Lemonade Stand Foundation from 2011-2018 consisting of 5,998 parents with children who had diagnoses of Leukemia-Lymphoma (41%), Central Nervous System (CNS) Tumors (17%), Neuroblastoma (14%), Sarcomas (12%), Wilms Tumor (6%),

Other Solid Tumors (6%), and Other Cancers (4%). Analysis of Variance was calculated for differences in means by cancer subtype for items scored on a Likert scale ranging from 1-7 for Disease Knowledge (unanswered questions, cancer out of control, hard choices); Time Management (changed schedule, less time with family, living day-to-day, difficult to maintain routine); Financial Strain (financial difficulties, diagnosis impacted finances, hard time making ends meet); Worries about Family (relationships, emotional well-being); Optimism/Pessimism (child would survive, satisfied with quality of life, depressed all the time); Family Support (emotional support, help not available, relied on others); Confidence in Doctors; and Self-care (sleeps well, coping, and time for self).

Results: Cancer subtypes differed for each of the domains related to concerns, optimism, and experiences. In particular, parents with children of CNS tumors had statistically higher means ($p < .05$) for items related to Lack of Disease Knowledge, Feeling depressed all of the time, and Lack of Family Support.

Conclusions: Parents with children with CNS seem to fair worse than other childhood cancer subtypes.

V620 SIOP19-1491 | Emotional Distress Among Parents of Children with Cancer in the Indian Scenario

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Background/Objectives: The diagnosis of cancer in a child is very often a sudden and rude shock for parents. The level of distress experienced by parents and the coping mechanisms that they adopt vary between mothers and fathers.

Design/Methods: We aimed to study the levels of emotional distress and coping mechanisms among parents of children diagnosed with cancer in the Indian cultural context.

Results: Twenty parents including fathers and mothers referred to the Psycho-oncology Department were interviewed to screen for emotional distress and understand coping mechanisms. The subsequent psychological evaluation and intervention was planned accordingly. The patients were at various stages of treatment at the time of referral. Over 90 percent of the parents were severely distressed at the time of referral. There were differences in the reasons of distress and the coping mechanisms of mothers and fathers. Mothers were distressed due to the physical pain and suffering of the child and the fear of death. Financial worries, fear of recurrence and academic as well as career prospects after treatment were the main cause of distress in fathers. These could be attributed to the culturally relevant roles and characteristics assigned to men and women in the Indian culture. Mothers used emotion

focused coping mechanisms by actively engaging in child care during hospitalization, talking about and sharing their feelings with family, friends and professionals and by forming a social support network with fellow caregivers of children. Fathers were more prone to using problem focused coping and were less likely to talk about or share their feelings or concerns, while they continued to engage in their professional commitments to manage the financial burden of cancer treatment.

Conclusions: The study provides a framework to create a model of Psycho oncology care for parents of children registering for pediatric oncology care in the Indian healthcare set up

V621 SIOP19-0457 | The Role of the Allied Health Professional in Addressing the Unique Needs of Children with Brain Tumours During Radiotherapy: Individualising Care and Innovative Thinking

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Background/Objectives: Forty children each year are diagnosed in the UK with Diffuse Intrinsic Pontine Glioma (DIPG). Although curative treatment is not possible, radiotherapy and rehabilitation aim to prolong and optimise quality of life.

There is a lack of evidence around the efficacy of allied health professional (AHP) intervention (Physiotherapy, Occupational Therapy and Speech & Language Therapy) during radiotherapy in children with DIPG.

Quantitative evaluation of the efficacy of AHP intervention can be challenging due to the unpredictable trajectory of this patient group. As the UK's largest paediatric radiotherapy service, we aimed to understand the family's importance of the role of the AHP in neuro-oncology rehabilitation during radiotherapy.

Design/Methods: We selected a (qualitative) questionnaire based methodology with a mix of open and closed questions in order to understand the uniqueness of each individual family's experience. Questionnaires were given to families on completion of radiotherapy. Returned questionnaires data was analysed using a variety of methods including thematic analysis.

Results: 10 families responded over a 16-month period. This small sample was expected due to the rare nature of DIPG.

Overall, AHPs were rated highly at average 4 on a 5-point scale. Families valued the improvements gained through

rehabilitation and emotional support given by AHPs during radiotherapy.

Conclusions: The role of the AHP during radiotherapy in children with DIPG is vital to provide both rehabilitation and support to families.

Rehabilitation is essential to optimise physical and cognitive recovery and ensure quality of life despite the non-curative nature of DIPG.

Through their therapeutic relationship, AHPs play a vital role in emotionally supporting and containing children and families through radiotherapy. The pathway is often uncertain and can be an unsettling time for families. Through goal setting and focussing on achievements, AHPs can support families through treatment as well as focussing them on finishing treatment and returning to life outside the hospital setting.

V622 SIOP19-1577 | Psychosocial Assessment of Families Caring for a Child with Acute Lymphoblastic Leukemia: Psychosocial Risk as Network of Interacting Symptoms Using the PAT

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Background/Objectives: To assess psychosocial risk across various domains of function and test the hypothesis that psychosocial risk is driven by risk specific connectivity and interdependencies among various domains of function using the Psychosocial Assessment Tool (PAT) and that domains of psychosocial functioning are affected diversely over time.

Design/Methods: A multicenter prospective cohort study of 254 patients, aged 1-18, diagnosed with acute lymphoblastic leukemia. Parents completed the PAT2.0 at the onset of disease and a subgroup of 90 patients was followed at three subsequent time points, at one years into treatment, at stop therapy and at two years into follow-up. Adjacency matrixes were calculated and Graph theory and Network analysis was used to calculate the strength of the connectivity and interdependencies among the 48 items that make up the seven subscales of the PAT as well as the percentage of change over time.

Results: Network analysis established unique patterns of interconnected domains of psychosocial risk factors and found that different interdependencies exist between the most central and most connected domains. The domains that drive overall risk, that is, with a high degree of centrality and high betweenness and closeness centrality are the stress reactivity of the caregivers and the lack of faith in the future health of their child as well as emotional and behavioral problems of the patient.

Conclusions: In order to implement adequate follow-up it has become critically important to quickly and effectively identify the subset of children and families at greatest risk for ongoing and/or escalating psychosocial difficulties Implementing a network approach improves our comprehension concerning the character of the problems central to the development of psychosocial difficulties. Therapy directed at the most central and connected domain (s) constitutes the more efficient approach because it unquestionably carries over to other domains that depend on this more central function.

V623 SIOP19-1409 | First Kan'athon in Oncology/Hematology: Share Learnings and Preliminary Results for Pediatric and Adolescent Patients

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Background/Objectives: Cancer patients are facing numerous issues in their daily life, including new emerging questions related to novel therapeutic options. With the support of four associations and a steering committee, we organized the first Kan'athon to identify the daily needs of cancer patients and relatives, based on a hackathon-type event* to build innovative and relevant solutions to meet these needs.

*Hackathon: event in which computer programmers and others collaborate intensively on projects to create a functioning software by the end of the event.

Design/Methods: This first Kan'athon was held at "42" (a place dedicated to computer science in Paris, France). Four themes were defined, in order to: improve adherence in the pediatric and adolescent population, support families and friends, help patients to get away from the disease, and facilitate the after-disease. Approximately 110 attendees (assigned in 14 teams), including people coming from the disease environment and people naïve from this domain, were mobilized during 2 days. They were supervised by certified coaches to provide method, and by experts and people from associations to share their experience and expertise.

Results: Thirteen very innovative solutions were presented (some under development). Three solutions have been proposed in the pediatric and adolescent area: Onc'ose (an app to create a teenagers community, proposing testimonials, activities, games, etc. to avoid isolation), BilliPill and "le Loup" (2 playful apps to get children involved in taking their medication while cooperating with their family).

Conclusions: This innovative event has allowed to remove barriers between patients, caregivers, associations and healthy people and to freely speak about disease. Kan'athon 2019 brought simple, but important answers to improve especially the lives of pediatric and adolescent

V624 SIOP19-0892 | The Emotional Impact of Working Within Paediatric Oncology in Developing Countries and the Support Available to Nurses

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Background/Objectives: Nurses working within paediatric oncology in developing countries have heightened exposure to death and dying due to lower survival rates; pain and suffering due to reduced access to pain relief and treatment abandonment issues, along with staff shortage and high workloads. This study explores the impact working within paediatric oncology has on nurses and the support available to them.

Design/Methods: World Child Cancer's Psychosocial Support Advisor spent one-year volunteering in Ghana, Malawi and Myanmar, delivering training to nurses on how to support families and how nurses can support themselves and each other. This training involved 1-hour focus group discussions where nurses explored 5 questions about the emotional impact of working within paediatric oncology and what support is available to them. Across the 3 countries, 35 nurses participated.

Results: 100% of nurses expressed sincere concerns about the emotional impact the work has on them and the lack of support available. The impact of death was central to discussions along with the impact of witnessing children in pain and suffering, misdirected anger from parents, heightened concerns about their own children getting cancer, impact on personal relationships and the effect of not having enough time or resources to provide best possible care. 83% of nurses expressed sadness, 49% anger, 43% stress, 26% guilt, 80% felt tired and 46% felt withdrawn. All nurses stated that no structured or professional psychological support was available to them.

Conclusions: The evidence shows that working in this highly pressured and emotive working environment has a significant emotional impact on nurses and lack of time and

resources means that little, or no support is available. Exposure to these working conditions can lead to burnout, compassion fatigue and secondary traumatic stress. Therefore, structured and professional psychological support for nurses working within developing countries needs to be explored and developed.

V625 SIOP19-1483 | Feasibility of a Novel Approach to Understanding Social Behaviors in Pediatric Brain Tumor Survivors

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Background/Objectives: Pediatric brain tumor survivors (PBTs) may experience significant impairments in social competence (e.g., Hocking et al., 2015). However, limited information is available regarding what specific social behaviors (or absence of) might be contributing to these social impairments. This is the first study to assess the feasibility of using the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2) to objectively assess discrete social interaction behaviours in PBTs.

Design/Methods: PBTs, aged 8-16 years, at least one year post treatment, English speaking, and not in palliative care were eligible to participate in the one-time assessment. The ADOS-2 is a semi-structured interactive interview which allows the clinician to code thirty-two behavior items during social interaction; items are typically coded as reflecting no impairment, mild impairment, or significant impairment. Recruitment will end in May 2019.

Results: Currently, 20 PBTs consented and completed the study, and all assessments were deemed valid by the ADOS-2 trained clinicians. PBTs are on average 7.6 years from diagnosis, 50% male, and diagnoses included low grade glioma (30%), ependymoma (20%), medulloblastoma (10%), high grade glioma (10%), other (30%). Rate of PBTs experiencing impairment on ADOS-2 items ranged from 0-50%. Items with the highest rates of impairment are: asking for information (50%), quality of social response (50%), and reporting events (40%). Thus far, the primary challenge to feasibility is the limited availability of clinicians trained to administer the ADOS-2.

Conclusions: The ADOS-2 is a feasible tool able to capture specific social interaction behaviours in which PBTs demonstrate impairment. The findings from this study bear important implications for the development of targeted social skills interventions for PBTs. A potential impediment to broader use of the ADOS-2 in assessing PBTs social behaviors may be the limited availability of ADOS-2 trained clinicians.

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V626 SIOP19-0066 | The Experiences of Young Adults Living with Metastatic/Advanced Cancer: A Scoping Review

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Background/Objectives: While survival rates have improved in nearly all cancers over the past thirty years, the young adult (YA; 18-39 years of age) cancer population has not seen progress comparable to that of pediatric and older adult oncology populations. Major gaps exist in YA oncology research and there is even less concerning those living with metastatic/advanced cancer. This systematic scoping review maps what is known about the experiences of YAs living with metastatic/advanced cancer.

Design/Methods: A systematic scoping review, guided by Arksey and O'Malley's methods, was conducted to examine the experiences of YAs living with metastatic/advanced cancer. The search strategy included relevant databases (MEDLINE, CINAHL, PsycINFO), ProQuest dissertations, grey literature and hand-searches of three relevant journals and reference lists from reviews identified via the literature search. Applied key words included but were not limited to: palliative care; experienc*; end of life. These were used with Boolean operators AND and OR. Articles written in languages other than English were excluded. The population included YA living with a metastatic/advanced cancer and the concept included their psychosocial experiences. The context was within both the hospital and community environments. Search terms were developed in collaboration with a medical research librarian.

Results: From the search strategy, 2846 references were obtained and 564 duplicates were removed. There were 10 included studies that were published from 2011-2018. Their findings covered four major themes: 1. Search to make meaning of their illness; 2. Relationships with others; 3. Mental health and psychosocial well-being; 4. Physical health.

Conclusions: The body of empirical knowledge around the psychosocial experiences of YAs living with metastatic/advanced cancer is scarce. Three knowledge gaps were identified: 1. How YAs experience cancer care delivery; 2. Relationships with their children and partners; and 3. How socio-demographics (i.e. sex, gender, race, socio-economic status, sexuality) influence the experiences of YAs.

V627 SIOP19-1379 | Parenting A Child with Malignancies: What Do We Know About the Impact on Professional and Financial Situation?

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Background/Objectives: Emotional support, upbringing and development are every child's needs that are conditioned by parents' availability. Designing regulations enabling such availability is therefore a matter of patients' rights (UNICEF, CRC, art. 18.2). Evidence synthesis is needed on inequalities, risks of disruptions and interventions to mitigate them, especially at a time when treatment regimens are evolving, and some care pathways might require novel forms of parental support.

Design/Methods: A systematic literature review gathers both quantitative and qualitative evidence on changes in parents' professional status or financial burden during and after childhood cancer treatments. The literature review is carried out using main bibliographic databases (MEDLINE, SCOPUS, PSYCHINFO) following PRISMA guidelines. Methodological quality of eligible articles is assessed following suitable guidance for quantitative and qualitative research.

Results: Negative impact has been shown on both professional status and financial situation but results are stronger for lower socio-economic classes and levels of education. Results are gender-, system- and time-dependant. Major causality biases exist, which need to be accounted for, and which question concepts of parenting, work and (informal or formal) care. These challenges must be addressed in order to design interventions susceptible to prevent adverse consequences on parents professional and financial situation. This is a domain where social sciences can help improving the outcomes for patients, siblings and parents.

Conclusions: Given the diverse (qualitative and quantitative) and mixed nature of the evidence published, the interpretation of the results puts emphasis on two main methodological research avenues for social scientists. First, we lack a unified theoretical framework allowing to define and test a priori hypotheses about the causal mechanisms at work when defining interventions to mitigate inequalities. Second, we need to contribute towards designing intervention strategies tailored to families' needs, based on multidisciplinary contributions.

V628 SIOP19-0275 | Does Development of Paediatric Oncology Services In Low-Middle Income Countries (LMICS) Bring Benefits to Other Children in Hospitals ?

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Background/Objectives: There is a perception by those involved in International twinning programmes that there are benefits for other children's services. We wished to investigate any evidence of this effect.

Design/Methods: We first asked 5 doctors and 2 nurses from high income countries involved in twinning if they were aware of any published evidence of benefits and whether they had identified any in their work. Secondly we invited 8 lead paediatricians in 7LMICs (4 in Africa, 3 in Asia) developing their oncology service if they could cite any benefits for other hospital specialities

Results: No published data of benefits for other children was identified. The initial 7 respondents cited, the benefits of training programmes in LMICS extended to non-oncology staff, improvement in laboratory and radiological services/facilities and increased access to blood products. Paediatricians from all the 7LMICs reported that education/training included non-cancer doctors, nurses and other health workers in hospitals and community. Five reported greater access to better laboratory and pathology services for all children. Multi-disciplinary team-working increased across 4 hospitals. Four cited improved radiology especially ultrasonography for all who needed it. In one centre CT and MRI scanning was made available for all children. Improved infrastructure was shared with other specialities in 4 centres, Accommodation created for oncology families is shared with all families in 2 hospitals. In one centre a hospital-wide nutrition programme and palliative care service benefitted the oncology service especially.

Conclusions: This pilot study has identified previously undocumented benefits for all children when cancer units are created. This should be documented and reported regularly and can build into the World Health Organisation Global Initiative and provide advice to governments regarding the wider benefits for child health services of developing paediatric cancer units. A more structured investigation with outcome measures is now required.

V629 SIOP19-1656 | Sharing Psychosocial Risk Assessment with Health Care Providers After Diagnosis of Childhood Cancer: Service Utilization and Related Factors

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Background/Objectives: Psychosocial screening has been proposed as an important standard of care in pediatric oncology (Kazak et al., 2015). However, standardized screening remains limited in this population (Scialla et al., 2018). The

primary aim of the present study was to examine whether providing psychosocial risk screening information to health care providers (HCPs) influences rates of psychosocial service utilization. Psychosocial provider discipline as well as demographic and medical factors were examined as context.

Design/Methods: Ninety-five patients newly diagnosed with cancer (birth-17) and their families were randomized to either intervention (IG) or control (CG) groups. HCPs treating families in the IG received a psychosocial risk profile derived from the Psychosocial Assessment Tool. Those treating families in the CG received no risk profile. Frequency of documented psychosocial services (social work, psychology, psychiatry, and palliative care) were extracted from the medical charts. Demographic and medical variables such as age, gender, diagnosis, treatment intensity were recorded. T-tests, univariate ANOVAs and correlational analyses were computed.

Results: The IG and CG did not differ in terms of the total number of psychosocial services received by patients and their families ($p > 0.05$). HCP discipline was a significant covariate of the rate of services provided ($F(3, 364) = 16.742, p < 0.01$). Post hoc analysis revealed that social workers documented more services than any other provider ($p < 0.01$). Additionally, there was a positive correlation between total psychosocial services and the intensity of the child's treatment ($\rho = 0.344, p = 0.001$).

Conclusions: Knowledge of psychosocial risk through screening alone is not sufficient to increase psychosocial services in pediatric oncology. Consistent with findings from adult oncology (Meijer et al., 2013), these findings suggest that multiple factors contribute to the provision of psychosocial intervention in pediatric oncology. An integrated approach to the child's medical and psychosocial care is necessary.

V630 SIOP19-0115 | Experiences of Parents Caring for a Child with Medulloblastoma, in the Indian Context: An Interpretative Phenomenological Analysis

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Background/Objectives: Medulloblastoma is one of the common embryonal childhood brain tumours, accounting for 12-25% of childhood malignancies. Caring for a child with brain tumours can be challenging. The lived experience of parents caring for a child with medulloblastoma, in the Indian context, has never been explored. This study aims to explore the lived experiences of the parents, in the Indian context, and interpretatively elucidate the meaning of those experiences.

Design/Methods: Fifteen consenting parents of children with Medulloblastoma were purposively chosen for the study.

All of them were interviewed once, in-depth, in a private setting, for about an hour. The interview transcripts were then coded. Thereafter, themes were generated using interpretative phenomenological analysis (IPA) method. Subsequently, the themes were interpreted through the theoretical lens of Bronfenbrenner's ecological systems theory.

Results: IPA analysis of the transcripts produced three master themes

Theme 1: Burden of situational demand The parents experienced overwhelming burden due to their inability to meet the situational demands, at home and hospital.

Theme 2: Emotional Distress The parents experienced emotional distress due to limited resources, maladjustment to new environment, challenges in hospital navigation, lost opportunity of being with the child, guilt, self-doubt about care-giving ability, fear of uncertain illness trajectory.

Theme 3: Finding hope The parents tried to cope by drawing strengths from their peers and resilient self. Supportive health care providers, family support and belief in god were the other factors that enabled coping in these parents.

Conclusions: Parents of children with Medulloblastoma experience overwhelming burden and emotional distress.

Resilience, support from family and peers, positive health care environment facilitates coping in the midst of distress.

V631 SIOP19-0807 | Grandparental Care in Chronically Ill Children: A Systematic Review

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Background/Objectives: If a child is chronically ill, the entire family system is affected and grandparents are often an important part of the family dynamic. They are frequently the main resource for families when parents need to work, for personal relief, and in difficult situations. However, little is known on type and role of care and support if a grandchild is suffering from a chronic disease. We aimed to gain insight into the i) role of grandparents' care, ii) extent of their responsibilities, and iii) differences between grandparents and parents in caring for chronically ill grandchildren.

Design/Methods: We systematically searched the databases Pubmed, PsycInfo, and SCOPUS for peer-reviewed original research articles. We included publications on grandchildren aged younger than 13 years suffering from a chronic disease and presenting results on type and role of grandparents' care or Support.

Results: We included 11 publications on 10 studies. These consisted of one cross-sectional questionnaire survey and nine qualitative interview studies. We found that the role of grandparents consists of both, physical and emotional support. Their role was on the sideline, but a reliable support for the entire family. The experience of a chronically ill child was often reported to have strengthened family bonds. However, grandparents reported lack of knowledge regarding the grandchild's condition.

Conclusions: Grandparents provide their support from the sidelines, but they often take care of the entire family. Making adequate information about the disease available to grandparents might help to increase knowledge and facilitate appropriate support and care provided by grandparents.

V632 SIOP19-0887 | Sports Therapy in Pediatric Oncology at the Children's Hospital Munich Schwabing – Results After 3 Years of Interdisciplinary Collaboration

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Background/Objectives: Treatment of childhood cancer is associated with physical inactivity, a reduced quality of life and motor performance. Therefore, sports interventions over all phases of treatment might be a supportive therapy option to improve the patients' physical and mental well-being.

Design/Methods: The approach of accompanying sports therapy was investigated and implemented by a feasibility study at our department. Aiming at a long-term and holistic model we promote physical activity in pediatric oncology from diagnosis to aftercare during in- and outpatient treatment among children from 2 years. Accomplishing the objectives experienced sport scientists work closely together with physiotherapists, psychosocial care-givers and physicians. Furthermore, continuity is ensured supporting the process of reintegration into sports structures after medical treatment among childhood cancer survivors.

Results: Since sports therapy was established in June 2016, 120 patients (aged 8.5±4.8 years) with different cancer entities (leukemia: n=42, lymphoma: n=20, bone tumors: n=17, brain and other CNS-tumors: n=11, further solid tumors: n=22, hematological diseases: n=6, no malignant diseases: n=2) participated in a daily sports program. Two part-time sports scientists provided 1284 exercise sessions (61.3% inpatient) with mean duration of 29.0±17.2min [range: 5-180min]. Training content and intensity were specifically adjusted regarding age, interests and individual exercise capacity. Var-

ious sports groups (instructed strength training, therapeutic climbing, rowing) and outdoor camps are completing our offers in the aftercare.

Conclusions: Continuous sports promotion over all phases of treatment increases physical activity as well as fitness level and supports the maintenance of mobility and autonomy in the aftercare. In order to develop a long-term active lifestyle and reduce possible disease- and therapy-related late effects the patients have to be sustainably encouraged after diagnosis. Further multi-center research projects will be essential to investigate the effects of physical exercise during pediatric cancer treatment with the intension of establishing sports therapy as part of standard care.

V633 SIOP19-0640 | Through the Eyes of Caregivers: A Prospective Survey of the CHOC Volunteer Programme

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Background/Objectives: The CHOC Childhood Cancer Foundation has run a volunteer training programme in South Africa for 23 years. Volunteer services provide psychosocial support for patients and caregivers. This study aimed to determine if the programme trained volunteers appropriately and met the non-medical needs of the families and caregivers.

Design/Methods: The 13 part anonymous English language questionnaire was completed with the aid of translators as necessary. Questions were both closed and open-ended, and were based on the formal two day volunteer training programme. Data included demographics and perceptions of services provided by CHOC volunteers.

Results: Between June and November 2018, 96 Participants (88% female) completed the survey and two declined. The surveys were completed while caregivers waited for their appointments to prevent disruption to the administration of care. One quarter spoke English as a first language, while 13 languages were spoken by the remainder. The majority of participants (94%) reported that they were able to communicate with the volunteers; 84% felt that they were emotionally supported and 83% of adult caregivers themselves participated in activities targeted at the paediatric patients. The offering of religious, spiritual, and holistic advice was reported by 43% of participants and 13% reported contact with volunteers outside the hospital. The majority felt that volunteer's activities relieved emotional stress for the child (81%), and the caregivers (80%). Despite language barriers, the majority of participants felt understood and supported.

Conclusions: The study found that the presence and support from volunteers made a positive difference in the lives of both patients and caregivers. Of concern, although there was explicit training on boundaries, a small number of volunteers feel the very human need to give spiritual, religious and medical advice to caregivers. The strong compassion that led people to volunteer also led them to cross boundaries, which will be addressed in future training.

V634 SIOP19-1269 | Locus of Control- A Way for Psychological Well-Being in Caregivers of Children with Cancer

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Background/Objectives: Locus of Control (LOC) refers to the extent to which people feel that they have control over the events that influence their lives. It is a distressing event for the caregivers of a child suffering from cancer and it requires lot of adjustment and coping adaptability. Hence this tool can help us to understand psychological dilemmas and help them for mental and emotional readiness.

Design/Methods: We have used the LOC tool on the immediate caregivers (mothers) of children who are undergoing chemotherapy in our center. It is a questionnaire based tool which contains total 40 items. It was administered on mothers of 20 children. The period of assessment was for 2 months and then intervention was done based on LOC findings till the end of treatment. The age group of children ranges from 1 year to 16 year with various types of cancer.

Results: Out of 20 LOC administration, 7 were of External locus of control, 1 internal locus and 12 were intermediate scores. This result showed that majority of mothers have accepted the situation and were willing to cope up with it. Out of 20 mothers 11 were home makers and 9 were professionals. It has been observed that there was no significant difference in terms of type of locus between professional and homemaker mothers. On the basis of these findings we started Cognitive Behavior Therapy (CBT), marital therapy (MT) and support group meetings which helped the coping adaptability during treatment of the child.

Conclusions: This tool is a reliable indicator for overall psychological being and therapeutic assistance indicator.

V635 SIOP19-1012 | Telepresence Robots in Protected ONCO-Hematology Unit: A Survey of the Experience of Patients, Families and Caregivers

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Background/Objectives: Treatment of pediatric cancers and hematological malignancies requires long periods of isolation in a sterile room. In order to promote the retention of family connections, telepresence robots have been made available in the homes of hospitalized patients. The aim of this study was to evaluate the perceived benefits and the difficulties encountered by the users and their families, the impact of the presence of these robots at home on family dynamics, the impact of the presence of the robot on how the caregivers experience the therapeutic relationship, and on organization of the daily care, and the formulation of guidelines for the purpose of a possible expansion.

Design/Methods: observational study with semi-directed interviews and questionnaires for the patients (7 to 25 years of age) and their parents conducted by a psychologist on D+15 and then after the patients have gone home. Interviews of the caregivers by an SHS researcher prior to the robots being made available and at D+21.

Results: Seventeen youths and their families were included in the study and 15 caregivers were questioned. A benefit for the patients was noted with particularly maintenance of a link with siblings and retention of the role in the family. For the parents, the device provided reassurance of being able to stay in touch with the child. The caregivers reported the relevance of developing more than a professional relationship with the child and the possibilities of interaction with the extended family. The limitations of the virtual nature of the caregiver/family relationship were noted, a possible feeling of frustration for the patients of being witness to what they cannot access, and a degree of concern for the parents during periods of disconnection.

Conclusions: This study shows an overall benefit for patients, families, and caregivers. It also highlights relevant issues that need to be considered in case of deployment of this device

V636 SIOP19-0951 | Impact of Universal Health Coverage on Childhood Cancer in Indonesia

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Background/Objectives: Starting from 2014 the Indonesian government has implemented Universal Health Coverage

(UHC) with the aim to make health-care services accessible and affordable to all Indonesian citizens. The main reason for childhood cancer treatment failure in low and middle-income countries, particularly among the poor, is abandonment of expensive cancer treatment. Our study compared childhood cancer treatment outcomes and event-free survival of the overall, poor and prosperous population before and after introduction of UHC at an Indonesian academic hospital.

Design/Methods: Medical records of 1044 patients diagnosed with childhood cancer before (2011-2013, n=512) and after (2014-2016, n=532) the introduction of UHC were abstracted retrospectively. Data on treatment outcomes, parental socio-economic status and health-insurance status at diagnosis were obtained.

Results: After introduction of UHC the number of insured patients increased from 38% to 82% ($P < 0.001$). Most of cancer patients were hematologic malignancy group (68.1%) that 47.3% of those patients were Acute Lymphoblastic Leukemia. In the overall population treatment abandonment decreased ($P = 0.001$) and event-free survival increased ($P = 0.002$). Poor population group showed that treatment abandonment decreased ($P < 0.001$) and event-free survival increased ($P = 0.046$) significantly. The prosperous population had no significant differences in any treatment outcomes comparing before and after its introduction.

Conclusions: Introduction of UHC in Indonesia contributed significantly to better treatment outcomes and survival of childhood cancer.

V637 SIOP19-1669 | Conditions for Relationship Satisfaction Among Parents of Children with Cancer – Pilot Studies

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Background/Objectives: Cancer in children and adolescents accounts for 1 to 2% of the total number of cancers in Poland. Every year 1200 new cases are diagnosed in Poland.

It is proposed that paediatrics should be about the so-called "collective patient", i.e. the whole family should be taken into account, and not only the chronically ill child.

The objective of this study is to analyse the relationships between relationship satisfaction and several psychological variables, including: stress severity, preferred values, resilience, and attachment style.

Design/Methods: Twenty parental couples with children treated in the Department of Paediatrics, Haematology and Oncology of the Antoni Jurasz University Hospital No 1 in Bydgoszcz took part. The parents completed a set of

questionnaires consisting of: The Quality of Relationships Inventory, Schwartz's PVQ-R2 Questionnaire surveying values, Experiences in Close Relationships-Revised questionnaire, Connor-Davidson Resilience Scale, and PSS-10 Perceived Stress Scale, which allows you to assess the intensity of stress

Results: Based on the analyses carried out, it has been found that the parents rate the quality of their relationship in terms of perceived support ($M=3.37$; $SD=0.50$) and depth of relationship ($M=3.37$; $SD=0.59$) quite high. Moreover, they indicate that they experience few situations of interpersonal conflict with their partners ($M=2.04$; $SD=0.42$). However, as shown by the research data, they are severely stressed ($M=22.87$; $SD=4.65$). Within the study group, perceived support correlates significantly with relationship depth ($rs=0.57$) and interpersonal conflict ($rs=-0.42$). Perceived support ($rs=0.57$) and resilience ($rs=0.42$) positively correlate with relationship depth, and avoidance correlates negatively with it ($rs=-0.35$).

Conclusions: The parents included in the sample being studied exhibit a fairly high partner relationship quality. They feel adequately supported by their partners. Moreover, they quite highly rate the depth of their relationships. However, they are severely stressed. It is important to conduct further research to identify personal resources that can be used to deal with stress.

V638 SIOP19-0861 | Building A Program for Siblings in a Pediatric Cancer Centre: Siblings' Voices

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Background/Objectives: The Princess Maxima Center treats every child with cancer in the Netherlands. The mission is to offer family centered, developmental oriented care. In this center, around 550 new patients are diagnosed every year. On average they have one sibling. Siblings of children with cancer are at risk for developing psychosocial problems. In order to offer a suitable program for siblings, it is important to know what their needs are.

Design/Methods: To explore siblings' needs in the hospital, a survey was conducted. The survey asked for siblings' opinion regarding ingredients for a siblings program. The survey was published online with open access. Siblings were invited to participate through the hospital's and the patient association's website and social media.

Results: A total of 91 siblings (63% girls, mean age 13.9 years) completed the questionnaire. Of those, 70% were interested in making use of information on the website, 52% would join an online group course, 64% would join a face-to-face group course, 68% would use a forum and 79% would like

to join sibling activities in the hospital. Younger children (0-11 years old) especially liked activities, whereas older children (12+) especially liked information on the website. As a response to an open question about desired program ingredients, the top three was: activities, getting attention and getting information.

Conclusions: Based on these findings and our professionals' input, a program was designed with the following ingredients: A) provide information for siblings through the website, B) educate health care professionals about the impact on siblings, C) educate school teachers about the impact on siblings, D) screen and monitor siblings, E) provide online and face-to-face educational courses for siblings so they can meet each other and share experiences. In cooperation with psychosocial and medical health care professionals, we hope to implement this program in the Princess Maxima Center.

V639 SIOP19-0988 | The Isolation of Being in Isolation: The Parental Experience of Isolation for Infection Control and Bone Marrow Transplant (BMT)

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Background/Objectives: The impetus for this study arose from parents in the Irish paediatric cancer service who identified the need for increased parental support. The ensuing study investigated the social-support needs of parents in order to guide the development of support-services. This abstract encapsulates one key finding: the impact of isolation for parents.

Design/Methods: Action research informed every methodological detail of this study and guided the creation of two working groups: a project team (consisting of parents, staff, and researchers) and a steering group (consisting of stakeholders, managers, and researchers).

With direction from these two groups, the field research was undertaken in two stages:

- 1) Semi-structured interviews/focus groups with 17 parents (from diverse stages of treatment) and 18 staff members. These interviews were analysed with a directed content analysis which guided the creation of a survey.
- 2) Surveys were distributed to 580 families - two surveys were sent to each family. 232 surveys were returned from parents of children in treatment and remission, and 9 from bereaved parents.

Results: The emotional vulnerability incurred by isolation was evident, as one parent expressed "I found this stressful

and soul destroying". Parents whose children were isolated on account of infection, rated *loneliness, exhaustion, boredom, being unable to leave the room, and being excluded from social activities* as more problematic than parents who experienced isolation on account of a BMT. In Ireland, isolation on account of a BMT is fore-planned, the family are prepared, and a programme is generally put in place for the child. In contrast, isolation for infection is initiated unexpectedly and without preparation or a programme. Parents requested four supports to ease the strain of isolation: 1) meals for the parent, 2) play therapy, 3) volunteers to entertain the child, and 4) technology for the child.

Conclusions: These findings provide guidance for supporting parents during isolation.

V640 SIOP19-1039 | Breaking News to Children in the Context of Childhood Cancer

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Background/Objectives: The impetus for this study arose from parents in the Irish paediatric cancer service who highlighted the need for additional parental support. The ensuing study concentrated on the social support needs of parents with a view to developing the services offered to them. This abstract reports on one key finding: the parents' experience of breaking news of a cancer diagnosis to the child with cancer and their siblings.

Design/Methods: Action research informed every methodological detail of this study. The field research was undertaken in two stages:

- 1) Semi-structured interviews/focus groups with 17 parents (from diverse stages of treatment) and 18 staff members (from 8 different disciplines). This data was analyzed with a directed content analysis which guided the creation of a survey.
- 2) Surveys were distributed to 580 families in total. 232 surveys were returned from parents of children in treatment and remission, and 9 from bereaved parents.

Results: Parents experienced deep distress in the task of breaking news to the child with newly diagnosed cancer and their siblings. Parents identified four supports that made a difference in these painful conversations: 1) receiving coaching, 2) receiving resources, 3) a family meeting with the multi-disciplinary team, 4) the power of play therapy. When asked what supports could be developed parents identified: 1) more resources (e.g. digital media), 2) therapeutic support, 3) more coaching, 4) formalise and standardise a family-meeting

with the multi-disciplinary team which includes siblings. Parents expressed deep concern for siblings. The long periods of time parents spent in hospital with their sick child caused immense guilt as they worried about the impact of their absence.

Conclusions: This data resonates with the Standards for the Psychosocial Care of Children with Cancer and Their Families (Wiener et al. 2015) which identifies the psychosocial risks siblings are vulnerable to, and the supports they require.

V641 SIOP19-1051 | Staff Stresses and Rewards in Pediatric Cancer

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Background/Objectives: The purpose of this study was to explore the social support needs of parents of children with cancer in Ireland. While the voice of the parent was central to this study, there was also an important staff component to understand their experience of caring for families, and to identify the stresses and rewards of their role. This abstract specifically reports on these staff findings.

Design/Methods: Action research guided every detail of this study. Staff were engaged through two working groups: a project team (consisting of staff and parents) in addition to a steering group (consisting of staff at a managerial level as well as stakeholders). Within the field research, 18 staff opted to participate in interviews/focus groups. This data was analysed with a directed content analysis. In addition *The Work Stressor Scale-Pediatric Oncology* (2012) and *The Work Rewards Scale-Pediatric Oncology* (2012) were distributed to the entire multi-disciplinary team (143 staff) in the children's cancer ward, with a response rate of 33%.

Results: Staff expressed their guilt and frustration when encountering the emotional needs of parents but not being able to engage to the capacity they would like due to their workload. The issue of compassion fatigue and staff burnout was also highlighted as staff described the lack of support structures in place for them. Within *The Work Stressor Scale*, the three greatest stresses staff identified were:

1. Families being aggressive towards other members of the multidisciplinary team
2. Not being able to do your job to the standard you would like
3. When a child deteriorates very quickly

In terms of the greatest rewards staff experience, the following two scenarios emerged in joint first place:

1. Feeling that you've made a difference to a child
2. Doing something that makes a child feel better

Conclusions: These findings should guide the support offered to staff.

V642 SIOP19-0760 | Basic Assumptions, Emotional Distress, Coping Strategies and Family Functioning Among Mothers of Adolescents Undergoing HSCT in Russia

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Background/Objectives: According to the Yanoff-Bulman theory of psychological trauma, the subjective appraisal of the stressful situation and coping are largely based on the individual assumptive world which in turn can be challenged by following traumatic events. The aim of the study was to evaluate the potential associations between maternal basic assumptions and their distress, coping strategies, as well as family functioning in the course of HSCT.

Design/Methods: Measures of the emotional distress and coping strategies were obtained from 28 mothers (aged 31-53; $M = 41.1 \pm 5.65$) of adolescents with oncohematological diseases prior to HSCT (T0: -1 week) and during the transplantation (T1: +3 week). Basic assumptions and family functioning were carried out prior to HSCT (T0).

Results: No significant correlations between basic assumptions and levels of emotional distress were found. A lower level of assumption "benevolence of the world", lower belief that the world is a good place and people are basically good and caring, were associated with the intensive use of coping strategies Behavioral disengagement (T0: $r = -0.427$, $p = 0.026$, T1: $r = -0.492$, $p = 0.017$) and Substance use (T0: $r = -0.411$, $p = 0.033$). Basic belief in "luck" was correlated with more active use of Instrumental social support (T1: $r = 0.454$, $p = 0.029$), belief in "justice" with coping Acceptance (T0: $r = 0.431$, $p = 0.025$). The higher "self-worth" was associated with: more active use of Acceptance (T1: $r = 0.565$, $p = 0.005$), higher Family cohesion ($r = 0.476$, $p = 0.012$) and less Prohibition of the adolescents' emotional expression ($r = -0.433$, $p = 0.024$).

Conclusions: Maternal basic assumptions about themselves and the world can play the important role in their coping with the stress and family functioning during the treatment. The results of the study confirm the importance of incorporat-

ing the meaning-centered psychotherapy components into the supportive programs for the families with adolescents undergoing HSCT in Russia.

V643 SIOP19-1539 | Speech and Language Disorders in Pediatric Oncology Due to Brain Tumors, Ototoxicity of Cytostatics and Genetic Syndromes. Recommendations for Psychological Interventions

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Background/Objectives: Speech and language disorders in context of pediatric oncology are separate problems or connected with ototoxic cytostatics induced hearing loss. In which cases speech disorders and hearing loss could be partial or total, occurs immediately or as a progressive disease, touch children in various ages and level of development. Symptoms of hearing loss and speech disorders are variable and determine different ways of early intervention, assessment and psychological support.

Design/Methods: Whole oncological population in our center (since 2000 year) we search for speech and language deficits and hearing loss and assessed their special needs, determined by specific mechanism of sensory loss. We prepared recommendation for psychological procedures, including: challenges in the assessment of this population, the most effective speech and language functional assessment, psychological early rehabilitation and stimulation, psychological support for parents in decisions making about their child's treatment, rehabilitation and education.

Results: In the searched population common speech problems due to brain tumors are akinetic mutism and dysarthria. Some cases are connected with facial nerve palsy. Late effect of posterior fossa tumors is cerebellar cognitive affective syndrome (CCAS) with impaired of verbal fluency, limited verbal learning, deficits in linguistic processing and abnormal prosody. Hearing damage as a result of ototoxicity is observed in young children treated with cisplatin. Patients with same genetic syndromes (neurofibromatosis type 1 - NF1, Nijmegen Breakage Syndrome - NBS) present very specific language development and speech disorders due to phenotype of these genetic condition.

Conclusions: Speech and language disorders, and ototoxic-induced hearing impairment in oncological population are specific and requires special psychological procedures and early intervention, started at the time of treatment. Primary recommendations for this care will be presented and discussed.

V644 SIOP19-0752 | Virtually Swimming with Dolphins as a Distraction Intervention During Medical Needle-Related Procedures in Pediatric Cancer

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Background/Objectives: Needle-related procedures during treatment for pediatric cancer are known to cause significant pain and distress. It is essential to minimize this and prevent medical traumatic stress. Child health specialists use different techniques and Virtual Reality (VR) has potential to provide distraction during the procedure. We were interested whether VR could be an additional option in our repertoire of distraction techniques. We aimed to explore which children could potentially benefit from the use of VR and to evaluate the experiences of children who wear VR-glasses during a medical needle-related procedure.

Design/Methods: One day before daycare children were selected which could be offered the VR-glasses. Observational pain and stress scores were collected during the procedures by using the Procedure Behavioral Rating Scale (PBRs, Katz et. al 1980) which measured fourteen behavioral constructs during the procedure. After the procedure, the child, the parent (s), the play therapist and the nurse were questioned about their experience during the procedure, including a score from 0-10. During the procedure VR-glasses with a movie with dolphins were used.

Results: Offering the VR-glasses appeared to be related to age (<5 too complicated), diagnoses type (too sensitive for patients with a brain tumor) and type of coping (not interrupting ritual). Preliminary results show that children wearing VR-glasses scored low on the behavioral constructs 'crying' and 'verbally expressing pain/fear' and high on 'laughing' and 'getting caught up in the distraction tool' during the VR experience. Most children used the sound during the procedure. High scores were given (mean 8) about the use of VR.

Conclusions: Despite the fact that multiple studies show VR technology could minimize pain and distress, very few hospitals actually use VR glasses. While more research is necessary to determine the complex aspects of VR in pediatric care, and the long-term use, our first experiences are positive.

V645 SIOP19-0878 | Ego Defense Mechanisms of Parents Whose Children are Diagnosed with Cancer

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Background/Objectives: The diagnose of childhood cancer has an undeniable effect on the emotional state of the whole family, especially on the parents of the child who has been diagnosed with cancer. Being the caregivers of the family, parents face an enormous stressor which inevitably effects their own mental health and activates their psychological coping mechanisms. Speaking in psychodynamic terms, the ego defenses of the people whose family member is faced with cancer can, depending on their personality traits and the „maturity level“ of previously used coping mechanisms, use primary or secondary ego defenses, or in other words more mature or immature ego defenses. A certain degree of distress and regression accompanied with child's cancer treatment is to be expected, but the results can vary depending on how often the ego defense is used, what are the triggers for the defense and what is the behavioral manifestation of a particular defense.

Design/Methods: Qualitative research; Interviews

Results: Results after conducting the research show that all the interviewed parents use some „immature“ ego defenses, for example denial and regression in the beginning of the treatment, usually when they are presented with the child's diagnose or informed about some unforeseen events during the treatment. Their reactions also depend on the way their doctor and other professionals communicate about the disease, therefore being a potential for confirming the existing healthy resources or being a trigger for a more immature coping mechanism.

Conclusions: Some degree of immature ego defenses is inevitable in coping with the cancer diagnose of one's child, but it is equally important to recognize the impact of communication skills of medical health professionals on how parents cope with the diagnose and other stress triggers during the child's treatment.

V646 SIOP19-0025 | Addressing the Needs of Childhood Cancer Survivors - Evolving Our Non-Profit Organization

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Background/Objectives: As a non-profit, the success of Candlelighters relies on addressing the needs of our membership. Over the past twenty years, Candlelighters has grown in size to over 300 members families; 36% on treatment, 58% off treatment and 6% bereaved

Design/Methods: Survivorship is most often the longest portion of the childhood cancer journey. The adolescent survivor population within our membership share many of the non-medical results of treatment including poor social skills, anxiety and low self-esteem. In response to these, Candlelighters

YSI program was created. In evaluating and gathering feedback from our Youth Survivor Initiative (aged 13 – 18) the challenges survivors face in late adolescence and the transition to adult care, the pursuit of post-secondary education and employment emerged.

Results: In 2019, Candlelighters added a new pillar to the existing 3 program delivery areas; Education Support, Family Support, Financial Support and now Survivor Support. Programs and services were developed to address the need for ongoing support through the transition to adult services, the pursuit of, and success in post-secondary academic pursuits, and to assist survivors in accessing psychosocial care. The addition of a childhood cancer survivor in the staffing compliment provides the organization perspective and credibility, and our members hope and inspiration.

Conclusions: Childhood cancer is a journey that doesn't end with the completion of treatment. It changes the lives of those impacted forever. In responding to the needs of survivors, Candlelighters hopes to positively impact their ongoing quality of life.

V647 SIOP19-0026 | Supporting Parents of Childhood Cancer Patients Along the Childhood Cancer Journey – There is Need for Ongoing Psychosocial Care

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Background/Objectives: When a child is diagnosed with cancer it is a life changing event for families. Parents are thrust into an unknown world. Managing their child's care becomes paramount while much needed emotional self-care may be forgone.

Design/Methods: A study was conducted using Candlelighters' family membership data from 2016, 2017 and 2018. A survey was emailed to 442 families including question for parents of children on treatment, off treatment & survivors (5+ years off treatment) or bereaved. Either or both parents could respond.

Results: The open rate of the survey was 66% with a response rate of 23%. Of the respondents, 33% had children in active treatment, 50% were off treatment, 13% survivors and 4% were bereaved parents. Overall, 64% of the respondent parents reported feeling they have adequate support. However, of the parents of children on treatment, 49% feel they do not have adequate support. Of parents whose children are off treatment or survivors, 38% feel they do not have adequate support. 49% of total respondents feel having either professionally facilitated groups or one-on-one counselling with a professional would be most helpful to them with 62.5% of respondents indicating they would plan on attending a

professionally facilitated support group if it was offered. 19% report wanting to access professional counselling but lack financial capacity and another 26% report a desire to seek professional counselling but do not know where to go or who to ask how to access this type of service.

Conclusions: It would be highly beneficial to provide Candlelighters' members professionally facilitated support groups for parents of both on and off treatment patients and parents of childhood cancer survivors. Providing guidance and education on how to access community based psychosocial care and financial assistance to do so would help parents get the support they need.

V648 SIOP19-0677 | Current Status of Hospital School System for Children with Cancer in Korea: Parallel Class of Off-Line and On-Line System

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Background/Objectives: The continuity of education is needed for quality of life in childhood cancer survivors. Korean government has established an administrative and financial support for hospital schools since 2005. We will review the current status of hospital school system for children with cancer and look for future directions.

Design/Methods: This study was reviewed with the official data from the Ministry of Education as well as the internet homepages of hospital schools in Korea.

Results: As of 2018, there are 33 hospital schools nationwide, and the number of students currently enrolled in off-line class is 456, and in online class 1,167. The off-line class has been operated with 1-2 full-time teachers as well as volunteers in one or two classroom. The off-line class schedules have been individualized in each hospital school and tailored to medical conditions of students. For the students who have difficulties for off-line classes, internet real-time interactive two-way classes or video on demand (VOD)-type classes have been performed during hospitalization or at home. There are 4 regional agencies operating on-line classes. For the approval of attendance to their original school, elementary students must attend more than 1 hour of off-line lessons a day or more than 1 lesson with 20 minutes a day of on-line system in hospital school. In the case of junior and high school students, 2 hours of off-line lessons or more than 2 lessons of each 20 minutes a day of on-line system have been required. The students in hospital schools have to take the assessment tests in their original schools to promote their grades.

Conclusions: It seems desirable to combine the off-line classes with on-line classes for the children with cancer. Advances in class contents of hospital schools and alterations

in management of academic performance would be considered.

V649 SIOP19-1651 | Update of The PSAPOH Guideline “Psychosocial Care in Pediatric Oncology and Hematology”

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Background/Objectives: The consensus- and evidence-based guideline of the Psychosocial Working Group (PSAPOH) within the German-speaking Society for Pediatric Oncology and Hematology (GPOH) was first published in 2008. After revision in 2013 the second update was provided in 2018/19. It contained a survey of psychosocial staff as well as a systematic review of scientific literature and other relevant guidelines or standards.

Design/Methods: Electronic databases such as PubMed, PsychINFO, SCOPUS and Google Scholar were searched by setting filters for year of publication (2013 -2018). Studies on 7 previously defined research questions regarding psychosocial aspects of childhood cancer were included: structures /frameworks, stressfulness and resources, psychosocial assessment, indication, symptoms of distress/disorders, interventions, rehabilitation and follow-up care. Through screening of 112 guidelines on title/abstract level, 9 of those were identified for full text analysis, including the 15 psychosocial standards published by Wiener et al. (2015). Considering the strong thematic similarity, additional literature search was restricted to date of publication between 2015 and 2018. The online questionnaire for psychosocial staff reflected on benefits and barriers regarding guideline implementation and was distributed to psychosocial providers in German-speaking countries.

Results: Analysis at full text level covered 1068 articles. Quality of evidence and strength of recommendation were rated using the GRADE system. Rating results with moderate to high level of evidence were discussed within the expert group and integrated into the guideline along with findings

from the online survey (N=71). Finally, a multidisciplinary consensus group including survivors and parent organizations agreed on the updated version.

Conclusions: The updated guideline (available online from 7/19) incorporates new psychosocial assessment and intervention methods as well as methodological and ethical considerations. Furthermore, it now has a stronger, evidence-based focus on issues like late effects.

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V650 SIOP19-0560 | Impact of the Participatory Approach on the Quality of Work Life of Healthcare Providers and on the Quality of Care

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Background/Objectives: Psychological health at work for care providers is an important issue since they are directly involved in quality of patients care. So far, few studies have studied psychological health at work of care providers in paediatric oncology. The participatory approach (PA) is a unique organisational model specific to France previously associated with quality of work life (QWL) or job performance. The aim of the present study was to explore the relationships between the participatory approach, QWL of care providers and quality of care of children in paediatric oncology in France.

Design/Methods: A multicenter study was conducted in pediatric oncology centers in France. Through regression analyzes we investigated the relationship between the PA, QWL, consequences of QWL and quality of care (assessed by caregivers and patients).

Results: 510 healthcare professionals working in french pediatric oncology centers and 440 patients responded to the survey. The PA was associated with the care providers' QWL ($\beta = .274$; $p < 10^{-9}$), work engagement ($\beta = .167$; $p < .001$), job satisfaction ($\beta = .166$; $p < .001$) and with quality of care assessed by care providers ($\beta = 0.236$; $p < 10^{-6}$). The PA were also related to quality of care perceived by patients notably with quality of communication ($\beta = .161$; $p < 0.005$) and information ($\beta = .226$; $p < 10^{-6}$).

Conclusions: PA is an innovative organisational model appear to play a role in all aspects of psychological health at work for care providers, and with quality of care perceived by care providers or by patients.

V651 SIOP19-0978 | How to Improve the Quality of Care in Pediatric Oncology: The Role of Healthcare Providers' Psychological Health at Work

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Background/Objectives: Psychological health at work for care providers is an important issue since they are directly involved in quality of patients care. Organizational and managerial determinants have been found to be indicators of psychological health at work. The main objective of this study was to explore the relationships between the psychological health at work of pediatric oncology care workers with managerial and organizational determinants and with quality of care.

Design/Methods: We performed regression analysis between psychological health at work (quality of work life (QWL), job satisfaction, work engagement), managerial determinants (transformational leadership, perceived autonomy support), organizational determinants (organizational support, organizational justice and participatory approach) and perceived quality of care.

Results: Participants were 510 healthcare professionals working in french pediatric oncology centers. No significant differences in the psychological health at work of the participants were found based on age, gender, length of employment, or professional discipline. In simple regression, significant associations were found between psychological health at work with all managerial and organizational determinants. In multiple regression, a significant link was found between QWL and perceived organizational support ($p < .001$), organizational justice ($p < .01$), and overall PA ($p < .05$). Job satisfaction was also related to perceived organizational support ($p < .01$). Finally, perceived quality of care was linked to QWL ($p < .01$) and job satisfaction ($p < .001$).

Conclusions: These results emphasize the importance of the role of managers and the organization in psychological health at work of healthcare providers, and also in the quality of patient care.

V652 SIOP19-1028 | Our Information's Briefcase: A Study About Information in Pediatric Hematology and Oncology

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Background/Objectives: Information about disease and treatments is an ethical issue. There are different medias of information. This study was performed to evaluate if selected documents presented in a briefcase, meet the expectations of patients and their family and to describe how the French pediatric oncology caregivers share the information with them. It also aimed to assess the difficulties for families to assimilate information.

Design/Methods: A prospective and evaluative multicentric trial conducted between march 2017 and December 2018.

Two types of briefcases (oncology and hematology) were created. Fourteen documents were selected among the french database about pediatric cancers, emotions, medical acts to be in each briefcase. Twenty seven briefcases were given to the family of 27 new patients during 2 months in 3 SFCE (French Pediatric Oncology Society) centers.

A sociologist interviewed 14 of the 27 families who received a briefcase.

Patients' age ranged from 0 to 14 years.

Meanwhile, all the 31 SCFE centers were consulted about their practices.

Results: All the interviewed caregivers are usually afraid to give too much information. Information is preferentially given to the parents. Most of the time information is given orally. Despite internet, all families valued paper information. Parents used the documents of the briefcase to inform their young child. All caregivers showed a keen interest in the briefcase. The briefcase was well received by the families, it was considered as a personal gift. The documents within the briefcase were consistent with the information given orally. Teenagers didn't show much interest in the briefcase.

Conclusions: Face to this success, the use of an updated briefcase will be generalized in all SFCE centers for 2 years. This will allow information to be normalized, all patients and families will be informed the same way even if the content of the briefcase is personalized. Other medias should be considered for teenagers.

V653 SIOP19-1284 | Impact of Sarcoma on Adolescents and Young Adults' Wellbeing: Qualitative Study of Challenges and Protective Factors

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Background/Objectives: A cancer diagnosis during adolescence or young adulthood generates unique medical and psychosocial needs as developmental milestones are simultaneously impacted. Treatment of sarcoma often involves long-term hospitalisation, extensive surgery, loss of mobility, complex rehabilitation programmes, and is in many cases accompanied by low expectations of survival. Therefore, adaptation to sarcoma and physical constraints requires significant multidisciplinary support. We aimed to explore the experiences of adolescents and young adults (AYA) with sarcoma.

Design/Methods: Thirteen AYA diagnosed with soft-tissue and bone sarcoma (7 male) participated in semi-structured telephone/face-to-face interviews. They were 8-24yrs (M=18.2; SD=5.3) at diagnosis and 13-29yrs (M=22.3; SD=5.5) at the time of study. Six AYA had sarcoma in their lower/upper limb; 2 in the pelvis, 2 in the spine, and 2 in the head and neck. Interviews were recorded, transcribed verbatim and analysed using Framework analysis.

Results: AYA with sarcoma experienced mobility difficulties and a number of body image issues. Establishing/managing romantic relationships, fertility and fear of recurrence were key concerns. The impact of mobility restrictions and fatigue on career/academic development was also discussed. Adaptation after treatment and/or surgery was influenced by the way they dealt with stress and adversity, with some struggling with finding their 'new normal'. Family, friends and peers with cancer were core elements of support. AYA also described experiences of being reassured and receiving information at the right level from professionals. Rehabilitation and therapy/counselling services had a considerable role in AYA's physical and emotional wellbeing; however access to these services was not equitable.

Conclusions: AYA with sarcoma experiences are multi-layered, with interacting variables contributing to post-treatment outcomes. Functional impairment impact on daily practical activities, exclusion from important aspects of life and loss of previous identity needs to be assessed so age-appropriate information and support regarding practical options, and social support can be provided.

V654 SIOP19-0711 | Societal Participation from the Perspective of Children with a Long-Term Disease: A Qualitative Analysis

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Background/Objectives: Although life expectancy and opportunities to participate in society improved considerably for many children with a long-term disease, such as children who underwent cancer treatment, these children still face challenges that can affect every aspect of their lives. To help these children, using a patient-centered approach, we must first understand children's own perspective on societal participation and the main factors that affect participation in a stable phase of disease.

Design/Methods: Qualitative design. Semi-structured in-depth interviews were conducted. Thematic coding and constant comparison were used for data-analysis. Children with a long-term disease were recruited from a pediatric cohort study involving post-treatment pediatric cancer in the first year after end of treatment, cystic fibrosis, and autoimmune diseases; we purposefully chose patients with maximum variation in age, sex, school absences, and levels of fatigue and pain.

Results: From the perspective of children with a long-term disease, participation is considered more than merely engaging in activities; rather, they view having a sense of belonging, the ability to affect social interactions, and the capacity to keep up with peers as key elements of full participation. For most children, the pursuit of full participation is an ongoing search for a balance between the limitations imposed by their (prior) disease and the desire to participate. This search involves elements such as being forthcoming about their limitations and the extent to which they give in to the intrinsic and extrinsic barriers they encounter.

Conclusions: Focusing on full participation from the child's own perspective will improve patient-centered care, helping children self-manage participation. Caregivers can stimulate the child's participation, by working towards whether the child experiences a sense of belonging, seeks active involvement, and/or feels able to influence his or her role within a peer group. Such an approach requires active collaboration between children, their healthcare providers and caregivers.

V655 SIOP19-1040 | COMETE: An Innovative Multi-Modal Program for Pediatric Brain Tumor Survivors and Their Family

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Background/Objectives: Pediatric brain tumors (BT), the second most common type of childhood cancer, account for approximately 20% of the pediatric oncology population. Pediatric BT survivors face treatment-induced sequelae of all sorts. These directly impact their schooling, social relations, and quality of life. The literature highlights the role of family functioning, parental experience, and early stage integrated care in child disorders' reduction. Thus in 2019, a multi-modal program for children survivors and their family has been set up in Gustave Roussy Cancer Campus.

Design/Methods: Based on cognitive-behavioural theory, this program named COMETE provides a progressive training through 6 modules proposed to children of RISK-N cohort (N=250) and their family. Two modules are mandatory for children joining the program: social-skills and neurocognitive skills modules. Four other modules are optional, depending on each family's specific needs: difficult emotions management module for children; parental support and guidance module for parents only; family functioning and relaxation techniques modules designed for the whole family. A multi-disciplinary team leads these modules: a child psychiatrist, a neuro-psychologist, several psychologists and a psychomotor therapist.

Results: Group management with a focus on cognitive remediation makes it possible to work more effectively on the common difficulties presented most widely by these children. For this first year, 2 sessions for children from 6 to 9 years old and 2 for children from 10 to 14 are scheduled. Nearly 25 families should integrate the program before the end of 2019. A feasibility study is currently conducted.

Conclusions: This innovative program aims to improve the global caring of pediatric BT survivors and their family; to reduce inequality in care access and brain tumor's long term impact. A pilot study will be conducted to evaluate the effect of this multi-modal program on children survivors' emotional, cognitive and behavioral skills, as well as family functioning, and parental distress.

V656 SIOP19-0403 | Psychosocial Experiences in Grandparents Whose Grandchildren Suffer from Severe Health Impairments: A Systematic Review

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Background/Objectives: Grandparents often are the most important source of emotional and practical support for families of children with severe health impairments. However, little is known about the psychosocial experiences of grandparents when their grandchild suffers from a severe health impairment. The aim of this systematic review was to investigate the current state of research on how a severe health condition in a grandchild psychologically affects grandparents.

Design/Methods: We systematically searched the databases PubMed and PsycINFO for relevant publications and narratively synthesized the included studies.

Results: The search resulted in 633 eligible publications. After screening, eight studies were included in the review. Psychological impacts on grandparents of ill grandchildren consisted in rapid adaptation and acceptance of the situation, adjustment of the identity as grandparents and putting one's own needs in the background. Studies indicated that grandparents experienced helplessness, uncertainty, lack of control over the situation, and higher levels of stress, anxiety, depression, and anger as compared to control groups. Positive psychological effects have also been reported, i.e. personal growth, tighter family bounds and pride in how family members were coping with the situation.

Conclusions: Our systematic review highlights the impact of a severe disease in a child on the larger family, including the grandparents. Despite positive experiences, many grandparents reported psychological problems. Information and support for this group could help families cope better with the difficult situation.

V657 SIOP19-1204 | Fear of Cancer Progression in Adolescent and Young Adult Cancer Patients

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Background/Objectives: Fear of progression (FoP) is a very common psychological burden among the majority of cancer patients. Especially in the patient group of adolescent and young adult cancer patients (AYA) that will live a long time as survivors and are therefore exposed to FoP for a long time, FoP should be examined. So we investigated prevalence and predictors of FoP in this population.

Design/Methods: Participants between 15 and 39 years with different tumor entities completed a web-based cross-sectional survey from November 2017 to February 2018 assessing medical and sociodemographic variables. FoP was measured with the short form of the Fear of Progression Ques-

tionnaire (FoP-Q-SF) with a range of 12 to 60 and a cut-off ≥ 34 indicating high FoP. Statistical analyses included correlations, descriptive and hierarchical regression analyses.

Results: A total of 247 AYA patients (81.8% female; on average 45 months since diagnosis) participated. The total mean score of FoP in our sample was 35.9 (SD=9.9). The majority reported having high FoP (59.5%) according to the cut-off. Female gender ($\beta=6.31$, $p<0.001$), having children ($\beta=6.31$, $p<0.001$), being on sick leave ($\beta=3.75$, $p<0.05$), longer time since diagnosis ($\beta=-0.05$, $p<0.01$), and comorbid diseases ($\beta=2.69$, $p<0.05$) emerged as significant predictors of high FoP. These variables explained 30% of the variance of FoP morbidity. There were no effects for age, partnership, education, tumor entity employment or treatment status.

Conclusions: The majority of AYA patients have high FoP and this issue is linked to sociodemographic and clinical variables. It would be necessary to investigate to what extent patients are burdened by FoP and the underlying mechanisms of sociodemographic variables such as gender. Further predictors should be investigated in longitudinal studies in order to capture the model FoP as a whole.

V658 SIOP19-1162 | A Narrative Approach to Distress Screening for Families Experiencing Paediatric Cancer

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Background/Objectives: Distress is an expected and understandable part of the paediatric cancer journey, through diagnosis, treatment and survivorship. The Competency-Based Model of Coping (Kazak et al, 2007) suggests that despite initially experiencing high levels of distress, most families are competent and will adjust and cope long-term. However, emotional distress encompassing low mood, anxiety, trauma and social isolation may lead to worse psychosocial outcomes for young people and family members, and thus needs to be screened for regularly. The need to consider the effects of cancer at a developmental and systemic level means that all members of the family should be screened, and that this should be an ongoing process in the cancer trajectory.

Design/Methods: Our goal was to devise an easy to use and effective measure to capture both level of distress, as well as the stressors people are currently managing. This provides a way to start a conversation that normalises distress, whilst identifying those in need of additional services (and what support would be most appropriate), in line with the Paediatric Preventative Psychosocial Health Model (Kazak, 2007).

Results: The therapeutic relationships young people and their families build with family support workers facilitates screening, knowledge and information sharing, and access to the appropriate services and people that young people and their families may need to support them through their cancer journey. We had a number of key beliefs underpinning our project; firstly, we took a systemic, social-ecological approach, recognising the reciprocal impact of paediatric cancer on the wider family. Secondly, we emphasised strengths to focus on competency, and enhancing and respecting resilience. Finally, we devised a narrative approach to ensure that the whole person was considered when screening for distress.

Conclusions: Narrative distress screening, using family support co-ordinators in the community, is an innovative and novel evolution in distress screening internationally.

V659 SIOP19-1087 | Media Use and Sleep in Survivors of Pediatric Cancer, Siblings, and Healthy Controls

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Background/Objectives: Insufficient sleep negatively impacts the mental and physical health of children. For survivors of childhood cancer, healthy sleep is critical for promotion of resilience and recovery from chronic illness. Media use has been found to consistently predict less subjective total sleep time (TST), though little research has investigated associations with objectively assessed sleep outcomes. Subjective and objective sleep data are poorly correlated and evaluate different aspects of sleep. Relationships between media use and sleep have not been established in families impacted by childhood cancer. This study examined the association between parent-reported media use and objectively assessed child sleep outcomes in a sample of survivors of acute lymphoblastic leukemia (ALL), their siblings, and healthy controls.

Design/Methods: 24 survivors (54.2% male; mean age=11.12 years; time off treatment=4.71 years), 13 siblings of survivors (56.3% male; mean age=12.00 years), and 60 healthy controls (63.3% male; mean age=11.07 years) completed seven consecutive days of actigraphy, from which TST was calculated. Parents reported if their children had media in their bedroom (y/n), and how many days per week their children used media in the hour before bedtime. An ANOVA was used to examine differences in media use between survivors, siblings, and controls. Generalized estimating equations were used to evaluate the relationship between media use and objective TST.

Results: Media use did not statistically differ by group; however, reduced TST was significantly associated with children having media in their bedroom ($\chi^2(1,36)=15033356.17$, $p<.001$) and media use in the hour before bedtime ($\chi^2(1,40)=38981.80$, $p<.001$), controlling for age and gender.

Conclusions: These data extend the current literature by demonstrating that media use is associated with objectively assessed TST. These findings underscore the need for reduced media use in the bedroom and before sleep and are particularly important for children impacted by childhood cancer, for whom sleep is critically important.

V660 SIOP19-1154 | Social Attainment in Adolescent and Young Adult Survivors of Cancer: A Yacprime Study

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Background/Objectives: The purpose of the current study was to examine relationship, student, and employment status in a national cohort study of survivors of cancer diagnosed as an adolescent/young adult (AYA) (i.e., 15-39 years of age).

Design/Methods: AYA's (n = 438; 15.5% male; median age = 34 years, range 20-64; median years from treatment completion = 2 years, range 0-47 years) reported on their relationship status (i.e., in a relationship, single), student status (i.e., yes, no) and employment status (i.e., yes, no) as part of the YACPRIME study. YACPrime is a cross-Canada survey for AYA survivors. Data from AYA's were compared to population data from the Canadian Community Health Survey completed in 2014 (n = 36,956, 46% male).

Results: Chi square analyses conducted across 9 age categories (i.e., 20-24; 25-29; 30-34; 35-39; 40-44; 45-49; 50-54; 55-59; 60-64 years) revealed a significant difference in relationship status for AYA survivors between 25-29 ($X^2 = 10.82$, $p = .001$) and 30-34 years ($X^2 = 7.97$, $p < .01$) where survivors were less likely to be in a relationship compared to the Canadian population. Employment status revealed a significant difference for AYA's 20-24 ($X^2 = 20.65$, $p < .000$), 25-29 ($X^2 = 6.06$, $p < .001$), 30-34 ($X^2 = 25.07$, $p < .000$), and 35-39 years ($X^2 = 13.52$, $p < .000$) with AYA's less likely to be employed. No significant difference in student status was found across any of the age categories ($p > .05$).

Conclusions: AYA survivors of cancer are less likely to be in a relationship and to be employed compared to the general population but may catch up with their peers on these milestones later in life.

V661 SIOP19-0543 | Factors Associated with Abandonment in Pediatric Patients, with Diagnosis of Childhood Cancer in the Guadalajara Hospital of Mexico

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Background/Objectives: Abandonment of treatment in pediatric oncology patients is one of the principle causes of treatment failure, along with reduced livelihood in children with cancer in middle and low -income countries. The prevalence of such abandonment has not been registered in any Mexican hospital.

The objective of this study was to examine the prevalence and factors associated with treatment desertion in pediatric patients with a cancer diagnosis in a third attention level center in Guadalajara

Design/Methods: Sociodemographic and clinical data from Guadalajara Mexico on children with cancer diagnosis's between January of 2006 and December of 2018 was retrospectively reviewed. The definition of treatment desertion followed the recommendation from the international society of pediatric oncology. Frequency charts, percentages, and central tendency measurements were used to describe the results.

Results: Data between 2006- 2018 from 1812 children oncological diagnosed, 163 (8.9%) abandoned treatment. The median age was 6 years (1 month – 20 Years). The solid tumors were neoplasia with more desertion 94 (21.3%), the most frequent was bilateral retinoblastoma 40 (5.5%), osteosarcoma 14 (8.6%), Ewing sarcoma 9 (5.5%). The mothers' education level was evaluated 72 (44.2%) had up to a basic secondary education. The identified causes for abandoned included; fear of treatment aftermath 10 (6.1%), parental denial of treatment 9 (5.5%), disbelief in chemotherapy effectiveness 8 (4.9%), lack of economic resources 6 (3.7%), transportation difficulties 5 (3.1%) homeopathic medicine 5 (3.1%), side effects of medical treatment 2 (1.2%). The patients were from municipalities distant from Guadalajara 85 (52.1%), displacement time was <2 hours 106 (65%), 84 (51.5%) of the mothers were between the ages of 18-30.

Conclusions: The prevalence of treatment abandonment in oncological patients from the hospital of Guadalajara Mexico, is high and is narrowly associated with socio-demographic factors, especially to educational factors and to the aftermath of the treatment itself. Treatment results can be substantially improved with strategies that help reduce treatment desertion, based on these results.

V663 SIOP19-1274 | “Family First” Programme: Understanding the Psycho Social Needs of Families with Cancer-Experience from a Tertiary Care Centre In India

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Background/Objectives: A diagnosis of cancer almost always throws patients and their families into uncharted territories. They face a gamut of emotions and have different mechanisms to express the same. Our hospital is tertiary multispeciality children's hospital which initiated a “Family first” programme with the view to look at the psycho social needs of the families & provide holistic care.

Design/Methods: The children and their families were assessed by a clinical psychologist at the request of the pediatric oncologist. This is retrospective analysis to identify their concerns and mechanism of expression of concerns thus identified.

Results: 30 family units were evaluated from 01/01/2017 to 15/03/2019. The age range was 2 years-16 years. Only 5/30 children had age- appropriate behaviour. The common concerns of the children were fear of injections/procedures or hospital staff (10/30), isolation from peers (12/30), body image changes (5/30), dislike for hospital food (5/30) and fear of death or disability (4/30). These usually manifest as aggressive behaviour like temper tantrums/hitting out at parents (15/30) or withdrawal into self and a refusal to talk (10/30). 17/30 parents expressed concerns such as anxiety related to the diagnosis or treatment (15/17), difficulty in setting boundaries (9/17), managing behavioural issues (5/17), withholding age appropriate information to child (5/17), a lack of support from the extended family and managing siblings (3/17) and preparing for the terminal event (2/17). Other parents did not voice their feelings.

Conclusions: All families go through a tumultuous journey when dealing with cancer; but only some express their emotions. We plan to include all families coming to the pediatric oncology unit in the “Family first” services from outset & start volunteer programmes looking into the major concerns like distraction techniques around procedures, sibling days in the hospital, rewards programmes and support groups for the parents.

V664 SIOP19-1137 | Health-Care Providers’ Communication about Complementary Alternative Medicine in Childhood Cancer in Indonesia

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Background/Objectives: Complementary alternative medicine (CAM) usage in childhood cancer is common. Effective communication about CAM is a keystone in successful conventional childhood cancer treatment. This study explored communication about CAM of health-care providers (HCP) involved in childhood cancer care.

Design/Methods: A cross-sectional study using semi-structured questionnaires in HCP of childhood cancer patients at an Indonesian academic hospital.

Results: Altogether, 168 HCP (response rate 80%) participated. Only 2% of HCP describe their view on CAM as enthusiastic. Most HCP (90%) think that their cancer patients use CAM. HCP (94%) find it important that parents inform them if their child with cancer uses CAM. Yet, only 6% of HCP always ask parents whether they use CAM. Most HCP think that parents are afraid to disclose their CAM use to doctors (78%) and subsequently do not inform their doctors (76%). Main concerns about CAM of HCP are: giving false hope to vulnerable patients (87%), lack of evidence that CAM works (87%), and their own limited CAM knowledge (80%). Significantly more pediatric residents (88%) than nurses (68%) are concerned about doctor's inadequate knowledge of CAM ($P=0.003$). Almost all HCP (98%) think that parents should receive guidance by doctors in hospital about potential beneficial and harmful effects of CAM. Doctors and CAM-practitioners never communicate about childhood cancer patients (66%), although this communication is required (86%). CAM-practitioners could help with the doctor-patient dialogue about the usefulness of conventional cancer treatment (62%).

Conclusions: HCP should update their knowledge about CAM and openly discuss CAM with parents and CAM-practitioners.

V665 SIOP19-0788 | My Máxima Plan: Evaluation of an App with Tailored Information about Wilms Tumor Treatment

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Background/Objectives: It has become more and more common to provide patients with information in an online patient portal or with other types of e-health. In the Princess Máxima Center we are developing a new patient portal in which we want to include innovative utilities, such as a timeline and information customized to the characteristics of the child with a childhood cancer treatment. We developed My Máxima Plan: an app aimed to provide tailored information to families about the treatment of their child with a Wilms Tumor (WT). Providing information adjusted to family is an addition to family centered care, helps families with coping stressful situations and adds to prevention of medical traumatic stress. We aimed to study the feasibility of this first prototype of the app from both parents as well as health care providers.

Design/Methods: A mixed method design with interviews and assessment of questionnaires was used. Parents were interviewed before and after the use of the app for four weeks, and questionnaires about need for information, experienced stress, distress thermometers and communication were administered. Additionally, professionals were interviewed on their expectations and experiences with the app in 2 groups (specialized nurses and psychosocial team).

Results: We interviewed parents of 7 children with a WT ($M=33$ years old) before start of their post-operative treatment. A total of 13 parents filled in both questionnaires. The families reported different needs for information. Parents were positive about the information in the app but it contained too much text. Professionals and parents both want the treatment schedule automatically connected to the medical record instead of manually.

Conclusions: E-health provides great opportunities for providing customized information to parents of children with cancer. Parents express a need for an overview about the complete treatment, including appointments with a concrete timeline and information about all treatment elements during their patient-journey.

V666 SIOP19-0518 | The Exploration of Psychosocial Needs Among Children Diagnosed with Cancer and Their Parents in Singapore: A Pilot Cross-Sectional Study

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Background/Objectives: The management of psychosocial functioning in paediatric patients and their families is an important aspect of cancer treatment. However, there is a paucity of such information in Singapore. This cross-sectional study explored the psychosocial needs of both the children

with cancer and those of their parents. The findings will inform the development of future psychosocial interventions.

Design/Methods: Twenty-six children ($M = 7.99$ years, $SD = 4.80$) diagnosed with blood cancer, solid- or brain tumour, and their main caregiving parent ($n = 26$; $M = 39.96$ years, $SD = 6.86$) were recruited in this cross-sectional study. Children and parents were administered with the Distress Thermometer and Paediatric Quality of Life Inventory (PedsQL) including, Generic Core Scale, Cancer Module, and Family Impact Module, at 1-year post-cancer diagnosis. One-way analysis of variance (ANOVA) and Pearson's correlation analysis were used to analyse the data.

Results: Cancer type had no significant influence on the distress level reported by both children and parents ($p > 0.05$). However, emotional functioning did differ among cancer types ($p = 0.02$). A post-hoc test ($p = 0.03$) revealed that children with solid tumours ($M = 53.25$, $SD = 16.10$) reported significantly poorer emotional functioning compared to those with brain tumours ($M = 91.67$, $SD = 2.89$). Additionally, moderate to large correlations (r range = -0.41 to 0.69 , r^2 range = 0.16 to 0.48 , $p < 0.05$), were found between children's quality of life and parental distress.

Conclusions: This cross-sectional study identified psychosocial needs previously unreported for paediatric-oncology patients in Singapore. Specifically, children who rated more problems such as, experiencing physical pain, nausea, and anxiety about medical procedures, the more parents reported poorer emotional coping. This mutually-inclusive relationship suggested that a targeted psychosocial intervention need to involve both children and their parents. The results informed the development of a prospective psychosocial program in Singapore.

V667 SIOP19-0757 | Teenage and Young Adult Information and Support Needs When Active Treatment Ends

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Background/Objectives: The end of active treatment is known to be a period of high stress for young people despite this little is known about young people's information and support needs during this phase. We aimed to identify young people's information and support needs when active treatment ends.

Design/Methods: Semi-structured interviews were conducted with 11 young people aged 19-26yrs with a range of

cancer diagnoses within one year of completing treatment. Framework analysis was used to analyse the data.

Results: Young people struggled to manage their own expectations of how they thought they would feel at the end of treatment versus the reality of how they felt both physically and emotionally. They experienced conflicting feelings of excitement about finishing treatment versus anxiety about what comes next, changes in their routine, and the loss of the perceived security of regular hospital visits and contact with healthcare professionals. This was also described as a period of uncertainty as young people took steps to move forward in terms of education/careers, relationships, health and well-being.

The expectations of others were described as challenging, with surrounding networks (family, friends, employers) expecting young people to be happy and 'normal' after treatment, while often they felt far from that. Young people described feeling uncertainty around their future care with many unanswered questions, including: who to call when they had concerns, what, why and how long their side-effects would last, and how long it would take for them to return to 'normal'.

Conclusions: The findings from young people have shown that the experience of ending active cancer treatment can be complex, challenging and full of emotion. The development of more specific, tailored and age-appropriate resources are needed to assist healthcare professionals to provide adequate information and support to young people in an appropriate and timely way.

V668 SIOP19-0436 | Pediatric Hematology/Oncology Physician Burnout: Associations with Workload and the Second Victim Experience

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Background/Objectives: Burnout is a syndrome of emotional exhaustion, depersonalization, and reduced personal accomplishment that has become a widespread problem for physicians. A 2011 study found that 38% of pediatric hematology/oncology physicians were burned out. Increased workload and the second victim experience (personal trauma due to a patient adverse event) have been associated with propensity for burnout. We describe the rate of burnout in physicians taking care of pediatric hematology/oncology patients,

and examine whether the rate of burnout has changed since 2011. We describe associations with workload and the second victim experience to help identify targeted interventions to reduce burnout.

Design/Methods: Physicians (N=53) caring for pediatric hematology/oncology patients at a single institution were surveyed using the Maslach Burnout Inventory, the National Aeronautics and Space Administration (NASA) Task Load Index, and validated questions regarding second victim encounters. The total clinic patient volumes were measured as an objective metric of physician workload.

Results: Thirty four percent of physicians surveyed met criteria for burnout. Burnout was associated with increased temporal demand ($p<0.01$), effort ($p<0.05$), and frustration ($p<0.01$) on the NASA Task Load Index. Burnout was also associated with physicians reporting second victim feelings ($p<0.05$). There was no association between burnout and clinic patient volumes.

Conclusions: The rate of burnout reported here is similar to past studies of burnout in pediatric hematology/oncology physicians indicating more effective interventions are needed to prevent and treat burnout in this population. The association of burnout with specific aspects of workload and the second victim experience gives guidance for targeted interventions to reduce burnout. The lack of association between burnout and clinic patient volumes suggests physician burnout is not associated with objective workload alone, but related to the perception of workload.

V669 SIOP19-0369 | Fine Motor Skills in Pre-School Children with Acute Lymphoblastic Leukemia Compared with Healthy Peers: A Preliminary Study

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Background/Objectives: CNS-directed leukemia therapies can adversely affect the acquisition of new skills, such as motor skills (Taverna et al., 2017), with schooling difficulties (Tremolada et al., 2018) and self-esteem problems (Tremolada et al., 2017). The goal of the present study is to assess fine motor skills in pre-school children with leukemia during the acute phase of first year of treatment and comparing their performance with those of matched healthy peers.

Design/Methods: Participants were 13 children, with a mean age of 58.31 months (SD=9.09; range: 44-70), including 7 females and 6 males. All participants were affected by acute lymphoblastic leukemia (ALL), 7 with a high risk leukemia and 6 with a standard risk leukemia. Children were assessed with the manual dexterity scale of the MABC-2.

Results: A series of non-parametric Wilcoxon tests were run to identify the possible significant mean ranks differences between pediatric patients and healthy peers in the several scales of the motor development skills. Results showed a significant difference between the two groups in: 1. posting coins standardized score when using the non-preferred hand ($Z=-3.11$, $p=0.002$) with patients obtaining lower scores (Mean=7.69, SD=3.19) than the control group (Mean=11.38; SD=1.89); 2. in the thread beads standardized task ($Z=-2.72$, $p=0.006$) with the clinic group with a worse performance (M=9.31, SD=3.27) than the healthy one (M=13.23, SD=2.94); 3. in general manual dexterity standardized score ($Z=-2.32$; $p=0.02$), lower in patients (M=8.92, SD=3.09) than controls (M=11.53, SD=1.66). ALL participants' age was negatively significantly correlated with the grapho-motor task performance ($\rho = -0.74$; $p=0.004$).

Conclusions: Children with ALL showed a poorer fine motor skill's general performance than healthy controls and older age of pediatric patients was associated with higher risk of impaired grapho-motor abilities. Occupational therapy intervention is needed children with leukemia in order to improve their fine motor abilities.

V670 SIOP19-0880 | Working Together with Designers to Support Families at Home During Childhood Cancer Treatment: A Pilot Study

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Background/Objectives: A diagnosis of cancer in a child has significant impact on the whole family. Everyday routines change, family relationships are challenged, and social activities are hampered by the distress that comes along with the disease and its treatment. This loss of normality is among the consequences causing the large impact on the child and family. Therefore, it is important to support families dealing with this distress, and to safeguard normality in everyday family life. We developed a tool to help families engage in behavior that supports their normal family life at home. We describe the experiences with this new tool, and the usability and potential effectiveness.

Design/Methods: In collaboration with design researchers we developed a tool called "Mr. Verrassing" (Mr.V; i.e. "Mr. Surprise" abbreviated in Dutch). Mr.V is an interactive dispenser that looks like a small astronaut and proposes family activities. These activities are suggested by family members themselves and dispensed by the machine at unexpected moments. Semi-structured interviews and questionnaires were used to evaluate the experiences of the families, which were analyzed using descriptive statistics.

Results: In this pilot study, ten families with a child between 4 and 12 years old ($Mage=6.7y$) and in active cancer treatment (mixed diagnoses) participated ($N=35$; $nchild=10$, $nmother=9$, $nfather=7$, $nsibling=9$). Families reported high satisfaction with the tool, especially regarding usability (how easy the tool was to use; 94%) and potential effectiveness (that it positively impacted the whole family, 88%; and that it helped to do more activities together in stressful times, 88%).

Conclusions: Mr.V is a promising tool for families dealing with childhood cancer to support their normal family life. Collaborating with designers has proven to be an opportunity to create an innovative tools to address family-centered care. Future research should further investigate the effectiveness of this tool and possibilities to use the tool at the hospital.

V671 SIOP19-1268 | Addressing Anxiety as a Means of Non-Pharmaceutical Pain Management for Children with a Haematology/Oncology Diagnosis

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Background/Objectives: Background: Anxiety is closely associated with the perception of pain. The emotional context of children with a haematology/oncology diagnosis can influence their perception of the intensity of pain. Developmentally appropriate psycho-education, preparation and distraction are effective as methods of anxiety regulation and can positively influencing the child's perception of pain.

Within the context of middle to low income counties – such as South Africa - where there is frequently a lack of pain medication it is imperative to explore the implementation of anxiety regulation as a means of non-pharmaceutical pain management in children with a haematology/oncology diagnosis.

Objectives: To explore and describe the connection between anxiety and the perception of pain. To explore and describe developmentally appropriate psycho-education, preparation and distraction as methods of anxiety regulation that positively influencing the child with a haematology/oncology diagnosis' perception of pain.

Design/Methods: Methods: Developmentally appropriate psycho-education combined with cognitive activities such as alternate focus, relaxation and imagery tend to deter the sensory transmission of pain. This form of non-pharmaceutical pain management when implemented with children with a haematology/oncology diagnosis can address their perception of pain and promote their adaptive coping. This method of non-pharmaceutical pain management has proven very effective in the context of South Africa as a low-income country where the access to pain medication is often limited.

Results: By addressing children with a haematology/oncology diagnosis' anxiety, their perception of pain can be positively influenced.

Conclusions: By attending this session the delegate will attain deeper understanding on the relationship between anxiety and pain in children with a haematology/oncology diagnosis. The delegate will gain a deeper understanding as how to implement developmentally appropriate psycho-education, preparation, alternate focus and play techniques as forms of non-pharmaceutical pain management in children with a haematology/oncology diagnosis.

V672 SIOP19-1270 | The Implementation of Children's Rights as Well as Unesco Bio-Ethical Decision-Making Framework Towards Delivering Child Centered Health Care for Children with a Haematology/Oncology Diagnosis

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Background/Objectives: Background: The aim of the UNICEF Child Friendly Health Care Initiative is to provide the best possible health care to children and families. This denotes the promotion of the emotional and psychological well-being of the child and the protection against unnecessary fear, anxiety, pain and suffering during and because of a health care experiences. How can the ideals of child- and family centered health care be realized for children with a haematology/oncology diagnosis in low-income countries with a context of socio-economic conditions of poverty, violence and child-headed households?

Objectives: The objective is to explore and describe the implementation of the Child Friendly Health Care Initiative as well as the UNESCO Bio-Ethical decision-making framework towards attaining child- and family centered health care for children with a haematology-oncology diagnosis.

Design/Methods: Methods: This presentation will focus on the provision of "best possible care" to children as stipulated by the Child Friendly Health Care Initiative as well as the

implementation of the UNESCO Bio-Ethical decision-making framework during health care service delivery to children and families affected by a haematology/oncology diagnosis.

Results: The implementation of the Child Friendly Health Care Initiative as well as the UNESCO Bio-Ethical decision-making framework can serve as tools that empower health care workers and psychosocial support staff with concrete actions towards attaining the ideals of child- and family-centered health care for children with a haematology/oncology diagnosis.

Conclusions: By attending this session the delegate will attain a deeper understanding of the Child Friendly Health Care Initiative as well as the UNESCO Bio-Ethical decision-making framework. The delegate will gain deeper understanding in the implementation of these tools towards the realization of child- and family-centered health care in their daily interaction with children and families affected by a haematology/oncology diagnosis.

V673 SIOP19-0208 | Impact of Sustainable Financial Support Through Indian Cancer Society - Cancer Cure Fund (ICS-CCF) for Treatment of Cancer Patients – A Model from a Developing Country

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Background/Objectives: Lack of finances for treatment of cancer is a major hindrance for improving outcomes on a national level. ICS-CCF, has demonstrated a robust, successful & an innovative approach for addressing this problem.

Design/Methods: HDFC AMC in collaboration with ICS launched 3 phased Mutual Fund Scheme (2011 to 2019), where investors donated the dividends for treatment of underprivileged cancer patients from 16 hospitals across India. Curative intent and optimal treatment strategies were ensured by the ICS-CCF Due Diligence Team and the Governing Advisory Council to provide a substantial, and timely financial aid to cancer patients. We analysed patients aided financially from inception of ICS-CCF till 31st December 2013 to know the long-term outcomes.

Results: During this period, 598 patients applied and 516 (86.3%) received financial aid. Males were 345/516 (67%), age at diagnosis was ≤ 15 years in 190/516 (37%) and 16-30 years in 232/516 (45%) patients. Diagnosis was solid tumour

(ST) in 116/516 (22%) and rest-400/516 (78%) had hematolymphoid (HL) malignancy.

At a median follow up of 5.7 years, 250/516 (48%) patients are alive and without disease, 16 (3%) are alive with disease, 128 (25%) are dead due to disease, 34 (7%) are dead due to other causes and 88 (17%) patients have been reported as lost to follow up.

The outcomes did not differ between gender ($p=0.8$) or diagnoses (ST Vs. HL, $p=0.5$). The lost to follow-up proportion varied widely (5.8%-58%) between institutes. On an average 46.5% of total treatment cost (across diagnosis and institutes – range 31%-62%) was supported by ICS-CCF.

Till 31st December 2018, 7,305 patients, from 34/36 states & union territories of India, have applied for ICS-CCF funding, and 6,805 (93.9%) approved, for whom a total of Rs.196.78 crore (~US \$ 28 Millions) were sanctioned.

Conclusions: ICS-CCF has significantly impacted lives of substantial number of cancer patients Pan-India. This sustainable model of financial aid for cancer patients can be replicated across resource constrained countries.

V674 SIOP19-1559 | Development of a Standardised, Evidence and Consensus Based Psychological Intervention Tool: “Mein Logbuch – ICH KENNE MICH AUS!” (“My Logbook, I Know My Way Around!”)

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Background/Objectives: As a basis for interventions to achieve defined psychosocial goals, guidelines and standards systematically describe stressors and resources in particularly challenging situations (Schröder et al. 2013, Wiener et al. 2015). Despite fundamental principles on psychosocial methods, considerable differences exist due to setting, provision and profession. The purpose of the study is to develop an intervention method and to illustrate psychological processes in a standardised way, resulting in a practical guide (“My Logbook”) to accompany the child throughout all stages of treatment.

Design/Methods: In an evidence based set-up, critical disease related issues for “My Logbook” were selected. Booklets for individual issues (e.g. “diagnosis-shock”, preparation for chemotherapy) were developed based on clinical and paediatric psychological considerations and by a multidisciplinary approach. To define key intervention elements for each issue, face-to-face discussions and telephone conferences were held

with multidisciplinary experts of German speaking countries ($n=12$). Moreover, in a consecutive developmental phase, experts ($n=47$) took part in a delphi-survey. In a two stage procedure all booklets were rated on content, method and design. The specialist group for quality assurance of the psychosocial working group in the Society for Paediatric Oncology (PSAPOH) concluded with a final agreement.

Results: The developmental phase resulted in 10 booklets and a supplementary handbook for professionals. The level of consensus ranged from 66% to 97% and can be defined as “acceptable”. Every booklet provides practical materials with enhanced stimulating elements to encourage the child to explore actively. The booklets are structured in two face-to-face sessions covering psychoeducational, activity & practice and reflective aspects. Finally, previously omitted but essential issues for booklets were identified.

Conclusions: A core set of practical intervention methods was implemented. The results emphasize that psychological support can be standardised enabling an evaluation and optimisation of psychosocial care. Next step is to draft a multi-centre, randomized controlled clinical trial.

V675 SIOP19-1576 | “ABC of Chemotherapy”: Preliminary Results of a Psychological Preparation for Chemotherapy - A Multi-Level Pilot Study

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Background/Objectives: Although chemotherapy is an established treatment option in paediatric oncology, methods for a standardised psychological preparation are rare. Nevertheless, chemotherapy implicates many stressors for the affected family, e.g. invasive medical and differentiated applications, long lasting treatments, frequent appointments at the hospital, and physical and psychological side effects. We propose a psychological tool addressing these aspects.

Design/Methods: Children ($n=5$) aged between eight and twelve years receiving chemotherapy underwent the program “ABC of Chemotherapy” – an evidence- and consensus-based tool for a psychological preparation for chemotherapy. The program consists of a psychoeducational, an activity & practice as well as a reflection component. It aims at dealing with challenging situations in a resource-oriented and creative way (e.g. (side) effects of chemotherapy, coping-strategies, empowerment for medical consultations). Sample

specifications on IQ (WISC-IV) and cognitive control strategies ("Health Competence scale", Weiler-Wichtl et al. 2018, adapt. Grootenhuis & Last, 1998) were administered as baseline. A multi-level approach was used for evaluating feasibility, level of information and emotional wellbeing, including the rating of medical and psychological staff, but also by the child itself.

Results: The first results focus on the individual perspective and emotional well-being of patients related to chemotherapy treatment and highlight the variability between and within subjects. Differences in the rating depend on the level of information provided or the achievement of psychological goals by the child itself or the interdisciplinary treatment team. Feasibility and manageability of the psychological preparation are remarkable.

Conclusions: The psychological preparation for chemotherapy is feasible. The pilot study illustrates the necessity of also including patients in the evaluation process to meet their needs best. A greater sample is required to illustrate and improve psychological processes of preparation, derive practical implementations for ongoing psychological support during chemotherapy, detect age or sex related differences and help to identify risk subsamples.

Treatment and Care - Radiation Oncology (PROS)

V676 SIOP19-0925 | Evaluation of Hippocampal Dose for Children Undergoing Intensity Modulated Radiotherapy for Nasopharyngeal Cancer

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Background/Objectives: Radiation therapy is the locoregional treatment of choice of pediatric nasopharyngeal carcinoma (NPC). Intensity modulated radiotherapy (IMRT) is frequently used because it improves conformity with target dose and limit the exposed dose of the organs at risk. Due to the importance of the hippocampus in respecting memory and cognitive functioning, we conduct a study is to analyze the radiation dose of the hippocampus in children treated by IMRT for NPC.

Design/Methods: From 2016 to 2018, seven children were treated at Salah Azaiz Institute for a NPC. Five patients had a locally advanced disease. The prescribed dose on the high risk planning target volume (PTV) and on the intermediate risk PTV was 70 Gy and 59.4 Gy, respectively. Radiation was delivered in 33 fractions with the integrated boost. For each patient, we made a fusion of his CT obtained at the time of simulation, with a T1 sequence MRI. The hippocampus was retrospectively delineated on axial images according to the

recommendations of the RTGO. Then, a dosimetric analysis was done.

Results: The mean hippocampus volume was 5.6 cm³. The average maximum dose to the hippocampus was 25.2 Gy (ranged from 5.9 to 53.46 Gy) and the average mean dose was 6.3 Gy (ranged from 3.16 to 12.2 Gy). The patient with the maximum dose, had a T4 tumor with extension at the temporal lobe. The Planning organ at risk volume (PRV) was defined as the hippocampus +5mm. The average maximum dose to the PRV was 34.3 Gy (ranged from 12.3 to 69.3 Gy) and the average mean dose was 7.45 Gy (ranged from 3.5 to 15.38 Gy).

Conclusions: The dose received for the hippocampus may be significantly high. More precise delineation and long-term follow-up is desired in order to seek for neurocognitive sequelae.

V677 SIOP19-0956 | Intensity Modulated Radiotherapy for Pediatric Nasopharyngeal Cancer: Oar Tolerance and Acute Side Effects

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Background/Objectives: Pediatric nasopharyngeal carcinoma (NPC) is a rare pediatric disease. Radiotherapy is the optimum local treatment for this cancer. With the technical progress, the disease control and the quality of life of adult and pediatric patients are enhancing. The aim of our study was to evaluate the doses to organs at risk and acute toxicity of pediatric patients treated by intensity modulated radiotherapy (IMRT) for NPC in the radiotherapy department in Salah Azaiz Institute, Tunisia.

Design/Methods: Data from 7 pediatric patients treated for pathologically confirmed NPC between 2016 and 2018 were retrospectively analyzed to determine delivered doses to spinal cord ($D_{max} \leq 45$ Gy), brainstem ($D_{max} \leq 54$ Gy), chiasma ($D_{max} \leq 54$ Gy) and optic nerves ($D_{max} \leq 54$ Gy). All patients had neoadjuvant chemotherapy followed by concomitant radio-chemotherapy. Radiation was delivered with IMRT with integrated boost. Patients were followed weekly during treatment to determine the acute toxicities which were graded according to the Common Terminology Criteria for Adverse Events (CTCAE) v.4.

Results: Chiasma and the brainstem limit doses were respected in all cases with a median $D_{max} = 33.7$ Gy (15.5-45.2) and 50.9 Gy (48-51.9) respectively. Spinal cord limit dose was respected for 6 patients (87.7%) with a median $D_{max} = 38.4$ Gy (33-46). For optic nerves, D_{max} for the left optic nerve was respected in all cases with a median $D_{max} = 44.2$ Gy (24.5-49.4) but was respected in only 6 patients (87.7%) in the right optic nerve with a median $D_{max} 44.1 =$ Gy

(20.7-67.1). During treatment, all patients developed acute mucitus and dysphagia grade I. Radio-epithelitis grade I was occurred in 3 patients (42.8%). Two patients had weight loss and xerostomia that were $\geq$ grade II (28.5%).

Conclusions: Treatment plans with IMRT technique allows good protection of organs at risk. However, it is often associated with acute toxicity requiring monitoring during treatment.

V678 SIOP19-0959 | Radiotherapy for Pediatric Brain Tumors: Dose to the Hypothalamus-Pituitary Axis

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Background/Objectives: The hypothalamo-pituitary (HP) axis is frequently included within the irradiation field used for treatment of central nerve system tumors in children. Data concerning the dose constraints of the HP axis and the evolution of radiation-induced hypopituitarism are limited. The aim of this study is to evaluate the dose of the HP axis in children with brain tumors treated by radiotherapy in Salah Azaiz Institute.

Design/Methods: Data from 20 pediatric patients treated for CNS tumors between 2015 and 2018 were retrospectively analyzed to determine delivered doses to the HP axis. The mean age was 10.2 years and the sex-ratio was 4. Nine patients had supra-tentorial tumor (45%). All patients received 3-dimensional conformational radiotherapy. Medulloblastoma was the most frequent histological type (30%) followed by astrocytoma (25%). The mean dose was 52.6 Gy (extremities ranged from 36 to 60 Gy). The daily fraction was 1.8 Gy in all patient. The hypothalamus and pituitary were contoured on planning CT scans with MRI coregistration for generation of dose statistics.

Results: The average maximum dose to the pituitary axis was 33.2 Gy (ranged from 2 to 52.4 Gy) and the average mean dose was 30.7 Gy (ranged from 1.5 to 51 Gy). Five patients had a mean dose inferior to 20 Gy (25%). For patients with medulloblastoma, the mean dose was 34.2 Gy. Mean Dose was higher in patients with supra-tentorial tumors. Among the patients, we found GH deficiency in eight. The incidence of hypothyroidism, ACTH deficiency, and gonadotropin deficiency couldn't been determined because no one of the patients underwent hormonal dosage.

Conclusions: The doses received by the HP axis depend on the localization of the tumor. Prospective study are needed to determine the restricting HP axis dose and minimize the risk of post radiotherapy neuroendocrine dysfunction. Regular monitoring with hormonal dosage should be done to diagnose the deficiency.

V679 SIOP19-0211 | Results of a Collaborative Network for the Organization of Proton Therapy in Pediatric Malignancies in the South of France

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Background/Objectives: Proton therapy technique is used in some indications to decrease the risk of side effects and/or improve tumor coverage. In order to facilitate the access to this technique, a collaborative network was created in the South of France we describe the proton therapy collaborative network

Design/Methods: From 12/09/16 to 12/12/18 we use 3 different agreements between Centre Antoine-Lacassagne (CAL) of Nice, Centre Léon Bérard of Lyon (CLB), Assistance-Publique-Hopitaux of Marseille (APHM) and Institute du Cancer de Montpellier. The present study describes the ongoing procedures between these centers.

Results: Technical validation of the feasibility of proton therapy is made by the Comity Technic of Protontherapy (CTP) through teleconference with the CLB, APMH and the ICM. During the CTP, the patient can be: a- validated, b- refused for technical reasons, c- compared with another photon technique in order to confirm the superiority of protons (regarding protection of organ at risk and/or better tumor coverage). 4-The child is seen by the radiation oncologist from Nice, together with a pediatric medical oncologist. 5-The dosimetric CT-scanner is realized, then the dosimetry (CAL-CLB-APHM), and finally the treatment. 7-Post-therapeutic consultation (3-6 months according to initial pathology) by the referring doctor (CAL-CLB-APHM-ICM). From September 12, 2016 to December 31, 2018, a total of 284 patients were presented to the CTP including 69 children, 3 in 2016, 33 in 2017 and 33 in 2018. During the CTP, 48 were directly validated, 14 were rejected and 2 need a comparison against conventional RT; in these 2 cases protontherapy was better.

Conclusions: The collaborative network in the South of France using agreements between CAL, CLB, APMH and ICM, was an effective way to offer protons to a large region. This approach may represent an optimal model to rationalize costs while allowing easy access to protons-candidate patients

V680 SIOP19-0714 | First Short-Term Results of Pulsed Proton Beam Treatment

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Background/Objectives: We present the first short-term results for our pediatric patients treated with a pulsed proton beam (Proteus One - IBA) at the Institute Mediterenan for Proton Therapy (IMPT) in the Center Antoine Lacassagne (CAL) in Nice.

Design/Methods: We conducted a review of our database since the start of our installation. All patients were treated with pulsed proton beam in IMPT. In case of suspicion of anatomical modification during treatment, we performed an evaluation CT-scan, if a change was found, we performed an MRI. If the geometric modification was confirmed on the MRI, a new dosimetry was performed. Depending on the summation dose with the previous dosimetry, a change in treatment planning was proposed.

Results: From 12/09/16 to 31/12/18, 49 children were treated. The median age was 9.6 years [mean: 8.5, min: 2.8, max: 21.8]. The median dose delivered was: 50.4 Gy [mean: 42.6, min: 14.4, max: 59.4]. median number of fractions were 28 [mean: 23.6, min: 8, max: 33]. During pulsed beam proton treatment, we observed an objective improvement of 10% [5] in clinical symptoms. The median follow-up is 10 m [average: 9 m, min: 0 m, max: 24], we find 20% [10] of progression and 3 deaths. One patient had a progression under treatment. In two cases, we modify the treatment planning for an anatomical modification detected at the evaluation CT-scan and MRI. We notice 16 immediate toxicities; 4 grade 1, 11 grade 2 and 1 grade 3. It was: 9 epithelitis, 3 nausea/vomiting, 1 mucitis and 1 headache.

Conclusions: Immediate tolerance pulsed proton beams for children is good. Further evaluation needs to be done for clinical results and long term tolerance

V681 SIOP19-1381 | Assessing the Impact of the Irradiation of Metastatic Sites in Children and Young People with Metastatic Rhabdomyosarcoma and Ewing Sarcoma

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Background/Objectives: Outcomes for children and young people with metastatic rhabdomyosarcoma (RMS) and Ewing sarcoma (ES) remain poor, despite intensive multimodality therapy. Current guidelines recommend systematic irradiation of all metastatic sites that can feasibly be treated, despite a lack

of strong evidence to support this strategy. Irradiation of multiple metastatic sites requires frequent hospital visits, and can potentially result in significant toxicity.

Design/Methods: Following institutional approval, we performed a retrospective review of children and young adults aged 1-24 years with metastatic RMS and ES, treated in our centre from 2012-2016. Clinical, radiological and outcome data were analysed.

Results: Seventeen patients were identified (13 RMS, 4 ES). Median age was 16 years (range 1 - 22 years); median number of metastatic sites was 2 (range 1 - 5). Seven (41%) were long term survivors (6 RMS, 1 ES), with median overall survival of 22.0 months (range 8.1 - 74.5 months). Six of 7 survivors had a single site of metastasis, most with lung/pleural deposits. Of 10 patients with relapse/progression, median time from start of radiotherapy to event was 5.1 months (range 1.7 - 8.1) and 5 progressed at an irradiated metastatic site. Of the 17 patients, only 2 experienced grade 3 or 4 radiotherapy related toxicity.

Conclusions: This small single centre study has shown that systematic metastatic irradiation can achieve long-term disease control for selected metastatic RMS and ES patients, and is well tolerated. However, relapse still occurs for the majority of patients and further studies are required to fully assess the impact of this, particularly in patients with extensive metastatic disease.

V682 SIOP19-1698 | Pediatric Quality of Life (PEDSQL) and Adverse Events (CTCAE) During Proton and Photon Radiation Therapy: Results of a Prospective Registry in a Large-Volume, Multi-Site Practice

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Background/Objectives: While patient-reported outcomes (PROs) such as becoming commonplace, utilization in clinical decision-making is often limited. In 2015 we instituted a patient outcomes registry to capture PROs, clinician-rated toxicities, and clinical outcomes in a large, multi-site practice. Herein, we evaluate the association between patient demographics and treatment with the pediatric quality of life inventory (PedsQL) and clinician-rated adverse events (CTCAE), as well as the relationship between PedsQL and CTCAE.

Design/Methods: Eligible patients were treated by RT with a curative intent between April 2015 and April 2019. PedsQL and CTCAE at baseline and post-RT were collected from date of diagnosis throughout follow-up. PedsQL scores were inversely linearly transformed and baseline adjusted generalized linear models were implemented for analysis of

overall score. We implemented a baseline adjusted method for CTCAE; a CTCAE grade of 3 or 4 after baseline that was higher than its grade at baseline was considered treatment related adverse (CAE). Logistic regression was used to investigate predictors of toxicity.

Results: Of 104 eligible patients, 76 (83.7%) had PedsQL and CTCAE recorded at baseline and at least one post-RT time point. Most common disease sites (%) were; Brain (52), Lymph Nodes (6.1), Bone (5.7), and Nervous System (5.7) with CAE rates for Brain of 15.79% and all other sites of 25.71%. Proton use was significantly associated with improved QOL with an average increase in 6 points across time ($p=0.0351$). Adjusting for disease site and tumor cell category; protons remained associated with an average QOL difference of 11.9 ($p=0.0853$). PedsQL was not significantly associated with CAE. Protons non-significantly decreased risk of grade 3 with odds ratio of 0.66 (95% CI: 0.12, 3.7).

Conclusions: Proton therapy is significantly associated with improved QOL throughout treatment and follow-up, and appears to decrease toxicity. There does not appear to be a significant association between PedsQL and clinical toxicity (CAE).

V683 SIOP19-0666 | Retrospective Analysis of Clinical Outcomes of Pediatric Tumors after Whole-Lung Irradiation

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Background/Objectives: Although whole-lung irradiation (WLI) is an effective tool for controlling residual lung metastases of major pediatric cancers, limited data are available to ascertain the eligibility and efficacy of the treatment.

Design/Methods: We selected patients who underwent WLI as definitive treatment between January 2006 and May 2017 in a pediatric cancer hospital. The clinical records and radiotherapy reports of the patients were reviewed. The patients' pretreatment characteristics and treatment parameters were analyzed as factors that influence disease control and sequelae.

Results: Of 9 selected patients, 6 had Wilms' tumor and the remaining 5 had different pediatric tumors (Ewing sarcoma, rhabdomyosarcoma, hepatoblastoma). WLI was delivered with total doses of 10.5–21.0 Gy in 6–14 fractions.

The median follow-up time after WLI was 42 months. Five patients remained alive without evidence of disease within the follow-up period. Three patients died of disease recurrence. All those patients had a bulky lesion other than in the lungs at the time of WLI. Recurrence in the lungs was observed only in one patient who had a massive chest wall lesion. All patients without residual disease other than in the lungs survived without evidence of disease for more than 42 months. None of the patients developed interstitial pneumonitis with apparent symptoms or radiological findings indicative of the disease.

Conclusions: WLI is an effective treatment to reduce the risk of early pulmonary recurrences. Long-term disease-free survival durations were expected for patients without bulky lesions other than in the lungs. Even though the whole lungs and heart were irradiated, the lower doses seem to preserve pulmonary function.

V684 SIOP19-0042 | Re-Irradiation of Pediatric Central Nervous System Tumours

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Background/Objectives: In adults, re-irradiation of central nervous system (CNS) tumors is frequently applied as an effective treatment. However, there are only a few studies evaluating the late side effects and survival in pediatric patients.

Design/Methods: The pediatric patients <18 years of age at the initial diagnosis who underwent CNS re-irradiation between 2014-2018 with the diagnosis of recurrent central nervous system malignancies were examined retrospectively.

Results: A total of 7 patients were included in the study. All of the patients received second line radiotherapy (RT) with the diagnosis of medullablastoma in three patients (42%), pons glioma in 2 (29%) and ependymoma in 2 (29%) patients. The median age at first RT was 5 (1-3) yrs, while the mean age for re-irradiation was 7.5 (2-22) yrs. The median time between RT sessions was 21.5 months (11.3-102.3 months). The median radiation dose and fractionation in equivalent 2-Gy fractions (EQD2) was 53.1 Gy (range 49.6-58.4) for initial RT and 21.2Gy (range 10.5-40) for re-irradiation. Recurrences were seen in 5 patients in the primary tumor region, while regional recurrence was observed in 2 patients. After recurrence, 58% of the patients underwent total/subtotal resection. The techniques used in secondary irradiation were volumetric arc therapy (VMAT) in 6 patients, and intensity-modulated radiotherapy (IMRT) in 1 patient. Median overall survival after secondary irradiation was calculated as 5.46 months.

Conclusions: No side effects were observed due to the short follow-up period of the patients. Re-irradiation in pediatric patients is particularly feasible because other treatment options are limited, although there is a need for prospective large series to observe local control and toxicity.

V685 SIOP19-0960 | ORPEDIA-01: Optimizing Radiotherapy in Pediatric Tumors: Normal Tissue Radiation Dose-Volume Response, a Biological Model for Optimal Management in Pediatric Cancer Patients

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Background/Objectives: Multidisciplinary therapeutic strategies lead to cure 78% pediatric cancers, resulting in an increasing number of long-term survivors. The evaluation of chronic treatment-related toxicities remains therefore crucial. Although Radiation therapy (RT) plays a central role in the local control, it causes developmental and functional impairments. The introduction of intensity modulated RT (IMRT) has not eliminated these risks. In this context, Proton therapy (PT) is an appealing technique, but with still limited access. Currently, the relative merits of rival IMRT and PT plans are based on dose-volume histograms intercomparisons. This approach disregards biological aspects, although the Normal Tissue Complication Probability (NTCP) modelling has become increasingly popular, in adults. The goal of this study is to build a specific pediatric model (pedNTCP), based on long-term clinical evaluations confronted with initial dosimetric parameters.

Design/Methods: We propose a sequential two-step study. Firstly, building an initial pedNTCP based on the Lyman-Kutcher-Burman (LKB) model by collecting available data (mostly adult) through literature, and then adjusting it to late toxicities recorded at least twice, with a minimum 3 years follow-up, in a prospective cohort of children. Secondly, evaluating the potential benefit of PT based on this model, through a systematic in-silico IMRT vs PT plannings intercomparison, and provide statistical significance for the panel of analysed toxic events.

Results: A cohort of two hundred children irradiated nationally, between 2010 and 2017, should be available for evaluation, along with comparative IMRT/PT treatment plans with associated NTCP, in each of them. This project will be supported clinically by the Groupe Français de Radiothérapie Pédiatrique (GFRP), and financially by the national Programme Hospitalier de Recherche Clinique (PHRC-2019).

Conclusions: This project will develop the first specific pediatric NTCP model which might represent a major innovation towards a rational approach for selecting optimal technologies, both in cohorts enrolled in clinical trials, and in individual situations.

V686 SIOP19-1652 | Identifying Potential Normal Tissues of Interest for the Paediatric Radiotherapy Population

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Background/Objectives: The QUARTET project from SIOPE and the EORTC aims to standardise radiotherapy in order to improve outcomes in tumour control and quality of life (QoL) for childhood, adolescent and young adult cancer survivors. Variation in the selection and delineation of normal tissue structures can have significant implications for both target coverage and organ at risk (OAR) sparing. Guidelines are required for more homogenous datasets, which are essential to yield meaningful conclusions from clinical trials. **Objectives:** To produce a list of recommended OARs specifically adapted to the paediatric radiotherapy population. This list will inform delineation guidelines for improved consistency in structure contouring and will be implemented within the QUARTET radiotherapy quality assurance (RTQA) guidelines.

Design/Methods: Two lists of OARs were produced, compared and simplified: list one was sourced from the recent ASTRO consensus paper (Wright, 2019) and list two was produced by correlating likely originating structures to effects highlighted within international long-term follow-up guidelines for paediatric, adolescent and young adult cancer survivors.

Results: A total of 132 structures were identified, of which 50 were common to both the adult and paediatric lists. Of the unique structures, 13 were associated with the adult, and 69 with the paediatric list. Major additions were observed in the identification of nervous (20), cardiovascular (17), and musculoskeletal (16) structures.

Conclusions: There are additional considerations for paediatric cases owing to the long-term follow-up care plan. Identifying the required structures of concern and/ or interest is the first step to ensure that we can standardise the delineation of structures and collect dose data that informs paediatric specific constraints and improves QoL for childhood cancer survivors. The QUARTET group will evaluate this list for clinical relevance and practicality; a consensus on structures of

interest, alongside delineation guidelines will be released and implemented in studies undergoing prospective RTQA under the SIOPE QUARTET project.

V687 SIOP19-1618 | Optimized Pulse-Dose Rate Brachytherapy Benefits in Multimodal Conservative Treatment for Bladder-Prostate Rhabdomyosarcoma: Magnetic Resonance Imaging–Based, Dose Volume Histogram Comparative Analysis

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Background/Objectives: In bladder-prostate (BP) rhabdomyosarcoma (RMS) conservative strategy is based on chemotherapy then surgery (partial cystectomy/prostatectomy) combined with brachytherapy (BT), low-dose rate (LDR, Iridium wires) or pulse-dose rate (PDR). To evaluate the benefits of PDR, we performed a comparative dosimetric study between PDR and two LDR BT modalities, in a retrospective cohort.

Design/Methods: Four boys with BP RMS, median age 2.5 years [1.4–4.3y.] were treated with PDR BT at Centre Leon Bérard from 05/2014 to 01/2018. All received neoadjuvant chemotherapy according to RMS 2005 protocol. The implantation of the vectors for BT, 2 plastic loops, was carried out during surgery with a transperineal approach. Clinical target volume (CTV) (residual tumor) and organs at risk (OARs) were delineated on a postoperative magnetic resonance imaging co-registered with a scanner. The prescribed dose to the CTV was 60 Gy (50 cGy/h). An optimized PDR plan was generated and applied for the treatment. For each patient, 2 theoretical non optimized plans based on the Paris system were generated with 2 referent dose rates: issued from the ‘Paris system’ calculation (LDR1) or applying the same dose rate as the PDR plan (LDR2).

Results: The median dose rate received by 95% of CTV was respectively 50.80 [47.4–76.6], 43.10 [40.4–61.1] and 48.25 cGy/h [45.5–74] with optimized PDR, LDR1 and LDR2. The median maximum dose rate received by 0.1 cc of the urethra was respectively 65.4 [56–73.5], 82.45 [80.2–98.9] and 96.30 cGy/h [90.4–105.9] with optimized PDR, LDR1 and LDR2. The median maximum dose rate received by 0.1 cc of the rectum was respectively 62.15 [52.1–70.6], 65.05 [60.9–74.5] and 72.95 cGy/h [68.7–86.4] with optimized PDR, LDR1 and LDR2.

Conclusions: The use of optimized PDR in BT treatment for BP RMS allows an improvement in the CTV coverage (versus

‘Paris system’) and a decrease of the dose received by urethra and rectum.

V688 SIOP19-0331 | Pencil Beam Scanning Proton Beam Therapy for Paediatric Patients with Neuroblastoma: Outcomes and Early Clinical Experiences of Motion Mitigation at the Paul Scherrer Institute

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Background/Objectives: Clinical data on patients with neuroblastoma (NB) treated with pencil-beam-scanning proton-beam-therapy (PBS-PBT) is limited. PBS-PBT can be prone to dose degradation from interplay effects due to respiratory motion. We report the outcomes of paediatric patients treated at the Paul Scherrer Institute (PSI) and our early clinical experiences of motion mitigation.

Design/Methods: Nineteen patients with high-risk (n=16) and intermediate-risk (n=3) NB received PBS-PBT. Median age at PBS-PBT was 3.5 years (range, 1.2–8.6) and median PBS-PBT dose was 21Gy (RBE, Relative-Biological-Effectiveness). Most children (89%) were treated under general anesthesia, all of whom were under 5 years old. Seven patients (37%) underwent a planning 4-Dimensional-Computed-Tomography (4DCT) for motion assessment and were treated with volumetric rescanning technique to mitigate motion effects. The number of rescans was guided by 4D-dose-calculations (4DDC) for four of the plans (57%). The number of rescans used were 2 (n=2), 4 (n=3) and 8 (n=2).

Results: The mean result of maximum organ motion was 3.21mm (cranial-caudal), 1.23mm (left-right), 0.94mm (anterior-posterior). The mean deterioration or improvement to the coverage of 95% of dose to the Planning-Target-Volume (PTV-V95%) compared to static 3D plans were: 4DDC with no rescan, -0.58%; 2 rescans, +0.3%; 4 rescans, +0.26%; and 8 rescans, +0.08%. With a mean follow-up of 15.2 months (range, 2.7–49), there were no local recurrences. The actuarial 2-year overall survival was 95% and distant progression free survival was 80%. The acute toxicity rate for Grade 1 and Grade 2–4 was 36.8% and 11%, respectively. There were no late toxicities.

Conclusions: Our preliminary data suggest that PBS-PBT is safe and efficacious in NB, with outcomes comparable with published passive-scatter proton cohorts. The clinical use of 4DCT, 4DDC and volumetric rescanning in our cohort has shown that there is minimal dosimetric impact of respiratory interplay effect, especially in those under 5 years treated under general anesthesia.

V689 SIOP19-0806 | Dedicated Illustrated Booklet before Radiotherapy in Children: Interest in Term of Better Understanding?

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Background/Objectives: Explanation for radiotherapy (RT) modalities is a key point in the children's care management. An illustrated booklet was written in collaboration with multi-disciplinary radiotherapy team, patient associations and child editor. All the steps of RT are explained, including the different RT techniques. The purpose of this study is to prospectively evaluate the child's level of comprehension with or without the booklet.

Design/Methods: 30 children (4-16 y.) treated for the first time by RT are included or will be included soon. The first 10 patients did not receive the booklet and "only" had an oral explanation. In contrast, the booklet is now used during the medical consultation, explained and given to the patients for the 20 following children. Self-administered surveys are completed by the children after the consultation. Ten multiple-choice questions about RT purposes, practical aspects and adverse effects are answered. Information is considered as well, middle or poorly understood if the rate of correct answers is > 80%, between 33% and 80% and < 33% of the patients respectively.

Results: For the first ten patients who did not receive the booklet, goals of RT, duration and number of RT fractions are well understood. The comprehension for planning-CT modality is mildly understood as well as painless aspects of RT. Acute adverse RT effects, life modalities between RT fractions, and radiation modalities (who perform the treatment, what you can bring during RT.) are poorly understood. Inclusions are ongoing for the last 20 patients who received the booklet, and the results will be compared and available for the congress.

Conclusions: Key messages delivered to children and their families before RT are not easy to bring. Some of them remain misunderstood despite oral information. The use of a dedicated illustrated booklet before RT in children is simple and may help provide better information.

V690 SIOP19-0705 | A Dosimetric Comparison of Proton and VMAT for Pediatric Ewing Sarcoma of Pelvis and Spine

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Background/Objectives: To compare the dosimetric results of proton radiation with volumetric modulated arc therapy (VMAT) for pediatric Ewing Sarcoma of pelvis and spine. The goal was to assess the potential advantage of proton over VMAT planning in pelvis and spine Ewing's sarcoma.

Design/Methods: Ten patients with Ewing sarcoma of the pelvis and spine treated with proton beam at Protontherapy center (CPO) at Institut Curie. VMAT plans had generated and analyzed. To facilitate dosimetric comparisons, clinical target volumes and normal tissues volumes were held constant. Plans were optimized for target volume coverage and normal tissues sparing.

Results: The average dose coverage values for CTV were comparable in PROTON and VMAT plans. Whereas the Proton plans achieved a higher conformity index compared to the VMAT plans (conformity index 1.2 ± 0.2 vs. 1, $p=0.009$), The index of homogeneity (IH) did not differ significantly. For the bladder, Kidney, head femoral and testis Dmean were significantly reduced in Proton plans. For the bowel and rectum, there was no significant difference in Dmean. The volume of normal tissue receiving at least 5 Gy (V5) was significantly higher in VMAT plans compared with Proton, whereas at high dose levels (V30) it was significantly lower.

Conclusions: Compared to VMAT, Proton showed significantly better results regarding dose conformity ($p=0.009$), mean Dose of bladder ($p=0.004$) and kidney ($p=0.01$). Proton delivered a lower healthy tissue dose than VMAT. Thus, dose escalation in the radiotherapy of pelvic and spine Ewing's sarcoma can be more easily achieved using proton.

V691 SIOP19-1635 | Clinical Outcomes in a Large Pediatric Cohort of Ependymoma Patients Treated with Proton Radiotherapy

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Background/Objectives: To report mature outcomes, patterns of disease progression and predictors of relapse in patients treated with proton radiation (PRT) for pediatric ependymomas.

Design/Methods: One-hundred-seventy-two pediatric patients (<22 years) with ependymoma were treated between 1/2001 and 1/2019 at Massachusetts General Hospital. Patients were excluded for <2 months follow up ($n=2$) or if tumors were WHO grade I (myxopapillary, $n=16$). Demographic, tumor, and treatment related characteristics were analyzed. Rates of local control (LC), event free survival

(EFS) and overall survival (OS) were assessed using the Kaplan-Meier method.

Results: One-hundred-fifty-four eligible patients had a median follow-up of 5.7 years (0.2–18.7 years). Fifty-nine (40%) and 90 (60%) had WHO grade 2 and 3 histology. One-hundred-sixteen patients (78%) had gross total resection (GTR) and 38 (22%) had subtotal resection (STR). LC, EFS, and OS for the cohort at 5 and 7 years is 80.5 and 76.6, 68.4% and 64.0%, and 86.6% and 81.7%. LC, EFS and OS at 5 years for GTR and STR is 85.0% and 64.3% ($p=0.001$), 73.8% and 50.2% ($p=0.0001$), and 94.2% and 50.2% ($p=0.0003$). Fifty-four patients failed: 27 (18.1%) patients experienced a local failure (LF), 21 (14.1%) had a distant failure (DF) and 6 (4.0%) had both LF+DF. Posterior fossa (PF) and supratentorial patients had 5/7-year EFS of 64.3/58.1% and 76.3/76.3% ($p=0.10$). 5/7-year EFS by WHO grade 2 and 3 is 72.5%/72.5% and 66.2%/56.9 ($p=0.19$). In a multivariate model including extent of resection, grade, and location, STR was the only prognostic factor (HR: 3.7 $p=0.002$). One patient developed a secondary malignancy (glioblastoma) 9 years from treatment and 1 patient developed Grade 2+ radiation necrosis after first PRT course.

Conclusions: Proton RT was associated with excellent EFS and OS. A GTR was associated with improved EFS, LC and OS. However, failures can occur late, suggesting the need for long-term monitoring.

V692 SIOP19-0305 | Tolerability and Acute Toxicity of Craniospinal Irradiation in Pediatric Patients in a Developing Country

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Background/Objectives: The purpose of this study was to evaluate the tolerability and acute toxicity of craniospinal irradiation in pediatric neuro-oncology patients.

Design/Methods: This cross-sectional descriptive study included 23 patients within age of 3 to 14 years who received craniospinal irradiation (CSI) from January 2017 to December 2018 in Radiotherapy Department of Yangon General Hospital, Myanmar. Radiotherapy was given with conformal technique in 2 phases; Phase 1 CSI (36 Gy) or low dose CSI (23.4 Gy) followed by phase 2 posterior fossa or tumor boost up to 50.4 Gy or 54 Gy, according to nature of disease, age of patients and performance status. Toxicity assessment was done during RT, then 6 weeks and 3 months after RT.

Results: Median age was 6 years (range= 3–14 years) and male to female ratio was 2:1. Twenty-three patients received

craniospinal irradiation; of these, ten patients (43%) with medulloblastoma, five patients (22%) with ependymoma, five patients (22%) with intracranial germ cell tumor (Germinoma) and three patients (13%) with pinealoblastoma. Three patients less than 4 years and five patients with Germinoma (35%) received low dose CSI 23.4 Gy followed by boost up to 50.4 Gy. Fifteen patients (65%) were given with 36 Gy CSI followed by posterior fossa or tumor boost up to 54 Gy. All 23 patients completed radiotherapy. Acute hematologic toxicity was mild and self-limiting. Grade 3 neutropenia seen in 3 patients (13%), of whom 1 child (4%) was documented as treatment interruption due to febrile neutropenia. Two children (10%) experienced Grade 2 thrombocytopenia during CSI. There was no disease progression on follow-up 3 months clinically and radiologically. 5 patients got complete response and others showed good partial response.

Conclusions: Craniospinal irradiation is safe, well tolerated and associated with mild and self-limiting acute toxicities. Abandonment of CSI treatment in pediatric patients of developing country might be reduced.

V693 SIOP19-0082 | Utilization of Paediatric Radiotherapy Services at Uganda Cancer Institute: Baseline Results of a Quality Improvement Project

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Background/Objectives: Introduction: Radiotherapy is life saving for most childhood solid tumors. Radiotherapy access in Africa, patient preferences, experiences and sociocultural influences can affect adherence to treatment protocols and treatment outcomes. A radiotherapy QI project was initiated and a dedicated clinical follow up team was formed at the Uganda Cancer Institute (UCI) Pediatric Service in March 2018 to improve access to radiotherapy.

Purpose: To report on the baseline assessment of radiotherapy utilization and patient reported challenges in UCI Paediatric Department following radiotherapy QI project initiation.

Design/Methods: We conducted a file review of all children who had been recommended for radiotherapy from March 2018 to December 2018. We collected data on patient demographics, cancer diagnosis, radiotherapy treatment. To assess challenges, we utilized semi-structured clinical interviews either on a one on one or telephone interviews.

Results: A total of 56 patients files were reviewed indicating 31/56 (55.4%) were male with mean age of 64.8 months (5.4years). The commonest radiotherapy referral diagnosis were Wilms Tumor 27/56 (48.2%), Retinoblastoma 15/56 (26.8%) Rhabdomyosarcoma 13/56 (23.2%) Hodgkin 1 (1.8%). A total of 49/56 (87.5%) completed radiotherapy

sessions while 7 (12.5%) were lost to follow up. From phone call or one on one clinical interview 53/56 (94.6%) were reached of whom 47/53 (88.67%) reported having completed radiotherapy. 3 patients could not be reached. Shared challenges reported by patients who had completed radiotherapy and those lost to follow up were delays or recurrent postponement of radiotherapy 43/53 (81.1%), pre-radiotherapy starving 40/53 (75.4%) and sociocultural reasons 5/53 (9.4%). Concurrent traditional medicine and religious reasons were cited.

Conclusions: The baseline results show that while majority patients completed radiotherapy sessions significant challenges were reported. We recommend follow up assessments to quantify impact of radiotherapy access to treatment outcomes which is critical for cure of children with solid cancers in resource limited settings.

V694 SIOP19-0083 | Adolescent and Young Adults Treated Curatively with Proton Therapy: The Paul Scherrer Institute Experience

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Background/Objectives: The National Cancer Institute (NCI) and EUROCare-5 recognize adolescents and young adults (AYAs) with malignancies as a high priority population for research. This study aimed to analyze the demographics and cancer pattern among AYAs treated in a proton therapy center.

Design/Methods: A retrospective study from January 1997 to December 2018 was undertaken on AYA cancer patients (aged 15-39 years) treated with pencil beam scanning proton therapy during the study period.

Results: A total of 395 AYAs (mean age, 28.5 years; range, 15 to 39) years have been identified in our institutional database. The average annual number of AYAs treated during the study period was 18.8. Two hundred and sixteen females (54.7%) and 179 (45.3%) males were treated with pencil beam scanning proton therapy with or without chemotherapy. Conventional radiotherapy was delivered with PT to only a minority ($n=29$; 7.4%) of AYAs. The most common cancer was skull-base chordomas ($n=63$; 15.9%) followed by skull-base and spinal chondrosarcomas ($n=53$; 13.4%) and gliomas ($n=37$; 9.4%). The other cancers are detailed in the Table. Most AYA patients ≤ 18 years ($n=53$; 89.8%) underwent quality of life testing using a self-rating version (PedQoL). The percentage of AYA with cancer treated with PT remained stable during the years: 24.9% and 25.7% of all patients were AYAs during the period 1997-2012 and 2013-2018, respectively.

Conclusions: One cancer patient out of four treated with PT is an AYA. The most common tumors are skull-base/spinal rare tumors and gliomas. Cancer distribution patterns from AYAs treated with protons are thus distinct among AYAs treated with conventional radiotherapy. The percentage of AYA treated with PT has remained stable during these last years.

V695 SIOP19-0133 | Patterns of Referral of Children and Adolescents with Cancer to Proton Therapy in Switzerland

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Background/Objectives: Approximately 50% of the pediatric cancer patients are treated with radiation therapy (RT). Different studies suggest that proton therapy (PT) may decrease the radiation-induced toxicity compared to non-PT RT. The referral practice for PT varies however substantially in Switzerland. This study aims to analyze the geographical differences in referral practice for PT in Switzerland and assessed the predictive factors for referral to PT.

Design/Methods: Demographic data from Swiss children and adolescents (SCA) and those living in Switzerland treated with PT at Paul Scherrer Institute (PSI) from 1997 to 2017 were reviewed and compared with data from the Swiss childhood cancer registry (SCCR) treated with non-PT RT in the same period. The choice of therapy was also analyzed as a function of Swiss pediatric oncology group (SPOG) units, diagnosis and year of treatment in a binomial logistic regression.

Results: During the study period, 1,482 SCA were treated with RT in Switzerland, of which only 190 (13%) received PT. Most of the latter SCA patients were treated with PT only ($n=182$; 96%) and a few with combined PT-RT ($n=8$; 4%). The use of PT increased over time from <1% ($n=1$; 1997) to 35.4% ($n=102/288$; 2013-2017). Children treated with PT were on average 2.2 years younger, mostly with soft tissue sarcomas or low grade gliomas, were more commonly referred by one (1/10; 10%) specific SPOG unit and resided less than 100 km away from PSI.

Conclusions: The proportion of SCA with cancer being treated with PT has significantly increased from 1997 to 2017. Younger age, cancer type and shorter distance to the PT center were associated with higher likelihood of referral to the PT center.

Treatment and Care - Surgery (IPSO)

V696 SIOP19-1085 | Skeletal Muscle Mass Does Not Correlate with Disease Severity in Children with Wilms Tumor and Neuroblastoma

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Background/Objectives: Sarcopenia is the loss of lean skeletal muscle mass (SMM) and has been associated with poor outcomes in adults with malignancies. The effects of sarcopenia on outcomes for pediatric oncology patients are unknown. Our objectives were to: 1) examine differences in SMM between non-cancer patients and those diagnosed with Wilms tumor (WT) or neuroblastoma (NBL), and 2) longitudinally assess changes in SMM throughout cancer treatment and correlate changes with tumor stage.

Design/Methods: Children <18 years diagnosed with WT or NBL between 2007-2016 were identified at a single institution. Whole-body SMM was estimated using psoas muscle area (cm²) measured at the 3rd lumbar vertebra on axial, abdominopelvic CT scans at diagnosis and at time points throughout treatment. Healthy pediatric trauma patients who underwent abdominopelvic CT scans comprised the control cohort. One-way ANOVA was used to examine differences in SMM between groups at diagnosis, and paired samples *t*-tests were used to quantify changes in SMM over time.

Results: SMM measured at diagnosis was similar across the included non-cancer patients (mean, SMM, SD) (n=33, 4.88, SD=1.8), patients with WT (n=43, 5.06, SD=1.6) and patients with NBL (n=39, 4.45, SD= 1.2). Subgroup analysis revealed that patients with advanced-stage WT (stage III/IV) had significantly higher mean SMM at diagnosis (6.12; SD 1.7) compared to patients with advanced-stage NBL (4.55; SD 1.3) and cancer-free patients (4.88; SD 1.8)(*p*=0.018). Longitudinally, SMM did not change throughout the course of treatment in NBL over a median follow-up of 10.6 months (IQR 176-376). Patients with WT had a significant mean SMM increase of 1.03 over a median follow-up of 11.7 months (299-402)(*p*<0.0001).

Conclusions: Sarcopenia was not observed in WT or NBL patients at diagnosis or throughout treatment, even after stratifying by stage. This may relate to enhanced attention to nutritional status throughout therapy of pediatric patients with extracranial solid tumors.

V697 SIOP19-1109 | Diverse Evolution and Management of an Anusular Presentation of Non-Hodgkin Abdominal Lymphoma

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Background/Objectives: Besides the abdomen is the most common site of involvement in non-Hodgkin lymphoma (NHL), specially in the ileocecal region, jaundice is a very unusual presentation. The reported incidence in pediatric series is less than 1% and the management remains controversial.

Design/Methods: We report two cases of abdominal NHL presented with obstructive jaundice and had completely different evolution.

Results: Case 1 – 16 years-old male, previously treated for abdominal NHL, remained disease-free for 10 months. Presented to the hospital with a 2 weeks history of abdominal pain and fatigue. On physical examination, he had a mass in the superior abdomen and jaundice, with total bilirubin level of 5.11mg/dl. Common bile duct distal obstruction and dilation of extra and intrahepatic biliary ducts was demonstrated on CT scan. A biopsy was performed with histological diagnosis of Burkitt Lymphoma. No biliary drainage was necessary. After chemotherapy with according to St Jude's protocol the jaundice completely resolved. Case 2 - 14 years-old male, 3 weeks presenting abdominal discomfort and progressive jaundice. During examination, a superior abdominal mass, severe jaundice, fever and signs of sepsis, with total bilirubin level of 8.15 mg/dl. A magnetic resonance cholangiopancreatography demonstrated distal choledocal obstruction with intra and extrahepatic dilatation, associated to mass involving the head of the pancreas and the duodenum. The patient underwent a exploratory laparotomy in order to biopsy and, because of signs of cholangitis, a tube cholecystostomy was performed. After completing the same chemotherapy protocol, a cholangiography demonstrated still obstruction of common bile duct, without contrast in the duodenum. Two months after treatment, the patient still presented obstruction of biliary tract associated with principal pancreatic duct. After discussion with endoscopy team, the option was to perform a duodenopancreatectomy.

Conclusions: Jaundice is an unusual presentation of NHL, with diverse evolution and individualized management.

V698 SIOP19-1538 | Percutaneous Endovascular Removal of Fractured Port Catheters

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Background/Objectives: Port catheters are the main tools in the management of children with cancer. These devices can be used for many years. Rarely removal of catheters is complicated by fracture of catheter. This study is designed to determine outcome of endovascular retrieval of fractured port catheters.

Design/Methods: Fifteen children whose catheters were fractured during surgery for removal of port catheter between 2004 and 2019 were included.

Results: Female to male ratio was 6:9. Median age at time of insertion was 22 months (4–144). Initial diagnosis of patients were; acute lymphocytic leukemia (n=8), acute myeloid leukemia (n=1), non-Hodgkin lymphoma (n=1), neuroblastoma (n=1), primitive neuro ectodermal tumor (n=1), immature teratoma (n=1), Hodgkin lymphoma (n=1), optic glioma (n=1) and retinoblastoma (n=1). Median duration of retrieval was 60 months (19–120). All port catheters but one were inserted by venous cut-down technique and one was inserted percutaneously. Dysfunction was not encountered in any of the catheters during treatment course. Nine patients had catheter related sepsis at least once. The most common isolated bacteria were *Staphylococcus epidermitis*. Adhesions between catheter and vessel wall lead fracture of catheter and impaired safe removal during surgery. Thus, catheter remnants were retrieved by percutaneous endovascular technique through femoral access. No complications were observed during or after the procedure.

Conclusions: Fracture of port catheters during removal is an unusual complication. Previous infections or venous cut-down technique may be leading causes. Percutaneous endovascular removal of fractured catheter is a safe way to treat this complication.

V699 SIOP19-0217 | Sacrococcygeal Teratoma: A 10 Year Retrospective Review in a Tertiary Center in Johannesburg, South Africa

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Background/Objectives: Sacrococcygeal teratoma is the commonest tumour occurring in the neonatal period with an incidence of 1 in 35000 to 40000 live births. It has a female: male ratio of 4:1. Complete early resection of the tumour with removal of the coccyx is the main stay of treatment. Diagnosis during the early neonatal period is associated with an excellent prognosis following complete surgical excision. In recent

times multidisciplinary approach to management has significantly improved survival. The aim of this study was to review data on all sacrococcygeal teratomas presenting at the Chris Hani Baragwanath Academic Hospital from 2005 to 2015.

Design/Methods: We retrospectively identified patients with sacrococcygeal teratoma managed at the Chris Hani Baragwanath Academic Hospital (paediatric surgical and oncology units) from 2005 to 2015. Sex, age at diagnosis, intervention, histology, complications and recurrence were recorded.

Results: A total of 22 patients were managed during the study period. Of these, 20 were female (90.9%). Fourteen (63.6%) patients were diagnosed within the neonatal period, 4 (18.2%) patients during the first year of life and 4 (18.2%) patients during the first two years of life. Histology was mature (benign) in 12 (54.5%), immature in 6 (27.3%), and malignant in 4 (18.2%). Incomplete resection was found in 6 (27.3%) patients: 2 (9.1%) of which had positive margins and 4 (18.2%) in which the coccyx was absent at histology. Recurrence occurred in all 4 (18.2%) patients in whom the coccyx was not removed. 1 (4.5%) patient had a rectal prolapse post-surgical excision of the tumour. Mortality was seen in 1 (4.5%) patient whose histology showed yolk sac tumour.

Conclusions: Sacrococcygeal teratomas have an excellent prognosis when diagnosed in the early neonatal period following complete surgical resection. The incidence of malignancy increases with increasing age of presentation beyond the neonatal period. Resection of the coccyx is crucial in management.

V700 SIOP19-1756 | Upfront versus Delayed Resection of Pleuropulmonary Blastoma

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Objectives: Pleuropulmonary blastoma (PPB) is a rare and aggressive lung tumor found in children. The purpose of this study was to evaluate the outcome of diagnosis and treatment of PPB. **Methods:** This is a retrospective analysis of consecutive patients from 2001 to 2017 with a minimum follow-up from 6 months to 11 years. **Results:** Four patients were treated with PPB, three girls and one boy, aged from three months to seven years old. Symptoms presented were two with superior vena cava syndrome, and all patients had respiratory difficulties. A biopsy was performed prior to surgery on two. Pathology results after the surgery showed two patients with PPB subtype one and two with PPB subtype two all with a free borderline. Multiagent neoadjuvant chemotherapy was applied in two patients with symptoms of oncology emergency and one patient presented pneumatocele and pneumothorax after chemotherapy. Postoperative chemotherapy was applied in all

patients and radiotherapy in one with PPB subtype two. The surgical approach was posterior lateral thoracotomy on three patients and clamp shell thoracotomy on one. The weight of the tumor ranged from 70 to 1,500g. All three girls survived. One patient died fifteen months after being diagnosed with PPB subtype two because of progression of the disease. Conclusion: An aggressive surgery and subsequent chemotherapy was curative for all type one tumors. Symptoms of superior vena cava syndrome conditioned the form of treatment as multi-agent neoadjuvant chemotherapy, biopsy prior to surgery followed by post-surgical chemotherapy, and radiotherapy. The pathological outcome on the free-bound tumor in PPB type two was not an impediment to the reoccurrence of the disease.

V701 SIOP19-0792 | Surgical Emergencies in Paediatric Cancer at Diagnosis. The Difficulty of Deciding When to Operate or Not

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Background/Objectives: Some children with cancer associate life-threatening emergencies at diagnosis and in the first days of therapy. Clinical management is difficult, some patients need surgery but surgical risk is high. Sometimes recommendations aren't included in the protocols. Aim of the study: Analysis of the surgical emergencies observed in children diagnosed with malignancy, review of the procedures and evolution.

Design/Methods: We have revised the last two years' early emergency situations in children diagnosed with leukemia and solid tumor, their initial approach and the bibliography that supported the decisions. Central catheter complications were excluded. Clinical, laboratory and radiological data were analyzed.

Results: We found 6 patients with severe complications in the first 2 weeks after diagnosis: 2-neuroblastomas, 2-acute leukemias, 1-Askin tumor of the ribs, 1-Wilms tumor. In two patients the emergency situation (acute abdomen) was the initial symptom of neoplasia (Wilms tumor and appendicitis). Four suffered emergencies in the first days after chemotherapy start. Early complications were: 3 massive bleeding (neuroblastoma, Askin tumor, and Wilms tumor); massive hepatomegaly, ascytis and life threatening symptoms in an infant with neuroblastoma-MS; typhilitis with bowel perforation in ALL; appendicitis in AML patient. Emergency surgery was performed in 3 patients due to: massive hemothorax in Askin tumor, renal bleeding mass in Wilm's tumor, and bowel perforation (laparotomy and ileostomy). Three children were managed by conservative approach (pig

tail drainage placement in neuroblastoma-MS, antibiotics in AML patient with appendicitis and observation in other).

Conclusions: Early surgical complications of pediatric malignancies are rare and interdisciplinary management is recommended. Surgeons have to decide the benefits and risks of the surgical procedures and some life-threatening emergencies need fast decisions. Due to the lack of evidence about what the best attitude is, deciding when to make a surgery or when not to do is difficult and it is a handicap to the paediatric surgeon.

V702 SIOP19-1678 | Cementoplasty Reconstruction as a Simple and Effective Alternative for Chest Wall Reconstruction

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Background/Objectives: Chest wall reconstruction after Surgical resection of a malignant tumor in children can be done with various techniques described in the literature (prosthetics, GORE-TEX). However, they may[HF1] lead to complications like prosthetic material disruption or lung hernia. We report preliminary results of a new reconstruction technique that may avoid these complications.

Objectives: to describe the surgical technique and results of cementoplasty in chest wall reconstruction, including complications.

Design/Methods: Patients who underwent resection of a malignant tumor of the chest wall with cementoplasty reconstruction from 2005 to 2017 were investigated retrospectively.

Surgical procedure: After tumor resection, a Gore-Tex plate is sutured to the parietal pleural membrane. The hand made cement plate (ref 6196-9-001) is adapted to the chest wall defect. Holes created around its entire perimeter allowed fixation to the ribs with non resorbable stiches. It is then covered by muscles flaps and skin.

Results: Seven children were operated (6 Ewing sarcoma, 1 synoviosarcoma) at a mean age of 12.3 years (range 6 to 17 years. The mean follow-up period was 3,4 years (range, 8 months to 7,5 years). Surgical related complications that occurred were limited to a post-operative acute respiratory distress, an adjacent rib fracture, 2 restrictive syndromes, 2 scoliosis and no infections, hernias or dislocations. Disease related complications occurred with 3 local recurrences (all R1 resections), among which 2 also experienced distant recurrence leading to patient death. All patients were free of complaints related to function.

Conclusions: Cementoplasty seems to be a simple technique, well adapted to children chest wall reconstruction.

tion. It is well tolerated and leads to a small amount of complications.

V703 SIOP19-1690 | Paediatric Teratoma: 25 Years of Experience

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Background/Objectives: Teratomas are unique tumours with variable behaviour. This paper describes presentation, management and outcome of paediatric teratomas treated in one centre, with management coordinated via an oncology multidisciplinary team.

Design/Methods: Patients were identified from the pathology database, and a retrospective case note review conducted from 1993-2018. Analysis was by teratoma site. Primary outcome was survival. Secondary outcomes included: age at presentation; pathology; management; recurrence and follow up.

Results: 53 patients were identified. Sites of teratoma were: ovary (n=22, 42%); sacrococcygeal (SCT) (n=15, 28%); testicular (n=6, 11%); mediastinal (n=4, 8%); head and neck (n=3, 6%); retroperitoneal (n=2, 4%) and abdominal (n=1, 1%), with 100% survival in 25 years.

Overall median age at presentation was 2 years (1 day – 16.8 years), with a significant wide variation (One-way ANOVA $F=8.485$, $P<0.001$). 17% (n=9) teratomas were immature. All patients had surgical resection. Four patients had adjuvant chemotherapy (n=3 SCT, n=1 head and neck teratoma).

Overall median follow up was 2.6 years (2 months – 14 years). There was no difference in length of follow up between tumours (One-way ANOVA $F=1.234$, $P=0.3079$). Surveillance is ultrasound and tumour markers until 16 years, then transition into adult care.

There were 2 recurrences (3.8%), both in SCT, where malignant yolk sac tumour was found 2-3 years after original diagnosis.

Conclusions: Teratoma occurs at various sites; ovarian the most common and abdominal the rarest. Surgical resection is usually curative, with a select group requiring adjuvant or salvage chemotherapy. Low recurrence (3.8%), associated with SCT, and an unusual phenomenon of progression from benign to malignant or germ cell tumour progression observed.

V704 SIOP19-0016 | Intravenous Patient-Controlled Fentanyl Analgesia With and Without Quadratus Lumborum Block in Pediatric Patients Post Oncology Abdominal Surgery

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Background/Objectives: The aim of this prospective hospital-based comparative study was to compare the postoperative analgesic efficacy of intravenous fentanyl patient-controlled analgesia (IVPCA) with and without quadratus lumborum block (OLB).

Design/Methods: 34 patients undergoing abdominal surgery were randomly divided into two groups for postoperative analgesia, ie, an IVPCA group receiving a 10 µg/mL fentanyl bolus of 15 µg with a 10-minute lockout and a maximum hourly dose of 90 µg, and an IVPCA + OLB group that additionally received QL block (0.3 mL per kg of 0.375% bupivacaine) on both sides via a posterior approach with ultrasound guidance before skin incision. Postoperatively, bolus injections of bupivacaine 0.375% were given every 8 hours through a QLB catheter.

Results: Age, weight, and sex were comparable between the groups ($P>0.05$). The visual analog scale score was significantly lower at 12, 18, 24, 48, and 72 hours ($P<0.01$) in IVPCA + QLB group. The Ramsay sedation score was lower only after 72 hours in the IVPCA + QLB group when compared with the IVPCA group (1.79 ± 0.63 versus 2.34 ± 0.52 , respectively, $P<0.01$). Heart rate, systolic blood pressure, and fentanyl consumption were lower in the IVPCA + QLB group at 24, 48, and 72 hours ($P<0.05$). Intensive care unit stays were significantly shorter with QLB (2.74 ± 0.38 days versus 4.27 ± 0.77 days, $P<0.01$).

Conclusions: Combining QLB with IVPCA improved postoperative pain management and reduced fentanyl consumption, with a shorter stay in intensive care. OLB block can be included as part of a balanced multimodal postoperative pain regimen in children.

V705 SIOP19-0017 | Anterior Rectus Sheath Blocks in Children with Abdominal Wall Pain Due to Anterior Cutaneous Nerve Entrapment Syndrome after Laparoscopic Oncology Surgery

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Background/Objectives: Chronic abdominal pain in children may be caused by the anterior cutaneous nerve entrapment syndrome. Local nerve blocks are recommended as an initial treatment in adults. Evidence on effectiveness and safety of such a treatment in children is lacking. Our aim was to study outcome and adverse events of anterior rectus sheath

blocks in childhood anterior cutaneous nerve entrapment syndrome.

Design/Methods: Patients <18 years of age receiving anterior rectus sheath blocks were prospectively followed. Injections were administered using a free-hand technique in the outpatient department.

Results: A total of 18 children were included (median age 15 years, range 8–17, 67% female). 11 children reported immediate pain relief following a single bupivacaine block and 6 achieved long-term success. Another 7 children were successfully treated with additional blocks combined with steroids. A total 49.4% success ratio was attained after a median 17-month follow-up (range, 4–39). Pain intensity and diagnostic delay were not associated with a beneficial outcome. However, young age predicted success. An infrequently occurring adverse event was temporarily increased pain some 6 h post injection.

Conclusions: Anterior rectus sheath blocks using local anesthetics and steroids are safe and long-term successful in more than one-third of children suffering from abdominal pain due to anterior cutaneous nerve entrapment syndrome after laparoscopic oncology surgery.

V706 SIOP19-0470 | Clinico-Pathological Pattern and Outcome of Pediatric Adnexal Masses: Institute Experience

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Background/Objectives: Adnexal abnormalities in pediatric patients are uncommon but not rare. It may be an infective, purely benign or a malignant condition. Diagnosis may be more difficult, even delayed or missed, because of low index of suspicion and nonspecific complaints.

The aim of this study is to analyze the clinico-pathological pattern of adnexal masses at presentation; and its management and outcome in children and adolescents.

Design/Methods: Retrospective study included all girls presented with adnexal masses from January 2014 to December 2018 in our department. Data were collected from patients' records including initial presentation, diagnosis (tumor markers and imaging), surgical staging and pathological types. Management (surgical and chemotherapy details) and outcomes were also analyzed.

Results: 22 patients aged between 5 to 17 years (median 10 years) presented with adnexal mass during study period were included. The most common presenting symptoms and signs

were Abdominal/Pelvic mass (21), abdominal Pain/Heaviness (18), Fever (6), Vomiting (6) and feature of Sub-acute Bowel Obstruction (3). Final diagnoses were Tubercular (1; managed with anti-tubercular treatment); benign Cystadenomas (1-serous, 1-mucinous); Dysgerminoma (1); Mixed Germ Cell Tumor (2); Yolk Sac Tumor (3); Teratoma {13; Mature-7; Immature-6 (grade II in 4 and grade III in 2 patients)}. Surgical interventions in most patients were unilateral salpingo-oophorectomy (n=21). 2 patients had bilateral disease. Early stages I and II were reported in 1 and 8 patients respectively, while 12 patients had stage-III disease. 16 patients were treated with chemotherapy. Local recurrence occurred in one patient with grade II immature teratoma; treated successfully by re-excision and chemotherapy. 3 patients were lost in follow-up. Follow-up period ranged from 6 – 60 months (median 30 months).

Conclusions: Fertility sparing surgery and chemotherapy provides excellent survival but careful evaluation of adnexal masses is necessary to save ovary in cases of benign and chronic infective diseases especially in endemic areas.

V707 SIOP19-1679 | Interventional Radiology in Paediatric Oncology – The Nottingham Experience

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Background/Objectives: Attached to one of the largest major trauma centres in Europe, Nottingham Children's Hospital, unlike most of the other UK paediatric oncology centres, benefits from twenty-four hour access to interventional radiology (IR). Surgeons routinely use ultrasound to biopsy under anaesthesia, but over the last five years we have used IR for awake biopsies in children that are unstable for an anaesthetic, or where there is life threatening bleeding. Focussing on acute management and diagnostics, we explore our local usage of IR over the last five years in Paediatric Oncology.

Design/Methods: Patients were identified searching the local paediatric oncology database between January 2014 and January 2019. Medical records and imaging were accessed for each patient and reviewed from their initial presentation onwards.

Results: 5 children were identified with mean age of 12.3 years (3 – 16.8 years). 80% had solid tumours, 20% had leukaemia, with 50% of the solid tumours presenting with widely metastatic disease. Awake ultrasound guided biopsy was used in two cases with large mediastinal masses, who were unfit for general anaesthesia, and vascular embolisation or angioplasty performed in three cases (aorto-enteric fistula, arterio-venous malformation and intra-tumoural haemorrhage in a Wilms' tumour). 80% of cases were consultant led,

60% were performed out of hours, with 80% requiring a critical care admission following intervention. 100% of the cases achieved the desired outcome of the procedure. Sadly, one of the children died from complications relating to their underlying pathology.

Conclusions: IR has an evolving role in paediatric oncology. It has been used safely for many years for guided biopsies and central line insertions, but its use in the acutely unstable child is much newer in our centre. We believe that it is a modality worthy of expanding, and have shown that it can have a lifesaving role in high-risk scenarios.

V708 SIOP19-0545 | A 10-Year Retrospective Review of Paediatric Surgical Oncology at Chris Hani Baragwanath Academic Hospital

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Background/Objectives: In the paediatric population, there are few modifiable risk factors for solid tumours, and early diagnosis and treatment are important in improving survival. There is paucity of literature on the incidence, prevalence, demographics, treatment and the outcomes of paediatric solid tumours in Low to Middle Income Countries (LMICs). The aim of this study was to present, describe and interpret the disease burden, demographics, and stages at presentation of paediatric solid tumours at Chris Hani Baragwanath Academic Hospital (CHBAH), the world's 3rd largest hospital, which registers more than 150 000 inpatients and 500 000 outpatients each year.

Design/Methods: A retrospective review of medical records of children below 16 years with solid tumours treated at CHBAH from 1 January 2007 to 31 December 2016 was carried out. Central nervous system, eye, bone, and medically managed tumours were excluded.

Results: There were 387 solid tumours, accounting for 33% of all paediatric oncology cases. Eighty-five percent were malignant and only 3% of these tumours occurred in children with a predisposing condition. Nephroblastoma was the commonest tumour, accounting for 28%, followed by rhabdomyosarcoma at 15.5%, neuroblastoma at 12.5%, germ cell tumours at 12%, and hepatoblastoma at 4%. Peaks in occurrence were seen in nephroblastoma, rhabdomyosarcoma and neuroblastoma within the 1 to 5 years age group. Late presentation was common with 52% presenting with advanced disease. Over the 10-year period, 296 oncological surgeries were performed, averaging 30 operations per year, including surgeries performed for lung metastases.

Conclusions: The solid tumours studied accounted for a third of all oncology cases encountered in children at CHBAH

with over 50% of the malignant tumours presenting late with advanced disease. Programmes put in place to create awareness on signs and symptoms of paediatric solid tumours, encourage early presentation, early referral and prompt management will improve survival in paediatric solid tumours at CHBAH.

V709 SIOP19-1418 | Multidisciplinary Management of Rare Diaphragmatic Germ Cell Tumor

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Background/Objectives: Diaphragmatic Germ Cell Tumors (GCTs) in children are rare, only six cases reported in the English literature.

We present challenges in pre/intra/post-operative multidisciplinary management of a two years old patient with large GCT of Diaphragmatic origin.

Design/Methods: The patient presented with abdominal pain and weight loss. Preliminary CT demonstrated a 13cm*7.5cm left upper abdominal/retroperitoneal mass (image-1). Pathology of the true-cut biopsy reported GCT, Revised radiological report raised question of chest origin.

Central line couldn't be inserted safely due to significant mediastinal large vessels shift, Thus it was postponed until regaining normal anatomy.

Neoadjuvant treatment with CEB-protocol was initiated through peripheral IV-access and had remarkable impact on the tumor size.

Central Line was inserted and the patient underwent surgery by left postero-lateral thoracotomy. Firm solid tumor, 10cm in diameter (image-2), originating from the diaphragm was separated from Left-Lower-Lobe without damage to the bronchial tree and with minimal air leak. Total resection was done with part of the diaphragm reconstructed.

Results: Pathology demonstrated yolk sac tumor, with tumor free margins (image-3). Alpha-Feto-Protein (AFP) was 465,000ng/ml at diagnosis and <1ng/ml following surgery. Complex post-op admission of twenty one days in PICU included prolonged period of mechanical ventilation for severe respiratory distress with left "white" lung and SIRS (image-4). Bronchoscopy demonstrated open bronchial tree and small amount of mucus. She was gradually weaned from ventilation and discharged home at day twenty eight post-op in good general condition. Follow-up PET/CT ten months post-op demonstrated complete remission (image-5) with no respiratory symptomatology and AFP of 4ng/ml.

Conclusions: Questions regarding the medical treatment, surgical approach and post-op management were discussed ret-

respectively in detail by local multidisciplinary team. Most probably, neoadjuvant chemotherapy protocol, which was chosen in regard of misinterpretation of tumor origin (abdominal vs. chest) in preliminary imaging, included Bleomycin that induced severe diffuse lung injury in the early post-operative period.

V710 SIOP19-1754 | Acceptance of Enucleation in the Management of Retinoblastoma in a Unit of the Franco-African Group of Pediatric Oncology (GFAOP) of Lubumbashi

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Objective: to evaluate the rate of acceptance of enucleation, indications, operative incidents and the evolution of patients with retinoblastoma in Lubumbashi. **Methodology:** This is a descriptive, retrospective data-gathering study focusing on 68 cases of children with retinoblastoma who consulted at the Ophthalmology Department of University Clinics in Lubumbashi, for a total of 7224 children's files, collected by sampling, during the period from 1 January 2011 to 31 December 2018. **Results:** The retinoblastoma frequency was 0.94%; the mean age of the children was 3 ± 3.7 years, for a median of 3 (2-5) years and a 2 years mode. The male sex was predominant in 56% of patients, a sex ratio of 1.3 in their favor. The unilateral involvement was 83% and bilateral 17%. Class E was predominant in 70% of patients. Stage IV of IRSS was in 34%, stage III in 20% and I in 27% of patients. The acceptance of enucleation was 26% and the refusal and discontinuation of treatment in 74% of patients. Enucleation without incident was 85%. The section of the optic nerve with the 7mm node clamp in 9%, 6mm 13% and 5mm 4%. The complete remission after enucleation was 7%, the patients died 39%, the discontinuation of treatment 2.9%, 6% progressing and the loss of sight (refusal of treatment) was 45%. **Conclusion:** Retinoblastoma diagnosed and treated early with the acceptance of enucleation gives a good life prognosis for children with this pathology in our developing countries.

V711 SIOP19-1736 | Surgical Management of Ovarian Neoplasms in Children and Adolescents: A Developing Country Experience

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Background/Objectives: Ovarian tumors are uncommon, estimated to occur in 2.6 per 100 000 girls per year, and malignant neoplasms account for 1% of all childhood cancers.

This study analyzes clinical, diagnostic, and surgical features for the treatment of ovarian neoplasms in children and adolescents at a developing country pediatric hospital with specific oncological pediatric surgery unit.

Design/Methods: A retrospective analysis of all patients diagnosed with ovarian tumor and submitted to surgical treatment in a pediatric oncology surgery unit at a single institution from a developing country between July 2014 and October 2018. Demographic and clinical features, diagnosis, surgical procedure, complications and survival follow-up were reviewed.

Results: Twenty-nine patients, ranging from 11 to 222 months of age, were surgically treated for 29 ovarian tumors: 19 (65,5%) malignant and 10 (34,5%) benign lesions. Median age at surgery was 12 years (13.4 years in patients with malignant tumors, 9.3 years in patients with benign ones). Nine patients with malignant and none of patients with benign ovarian lesions had elevated serum level of tumors markers. Primary surgical approach was done in our hospital in 16 of cases, 50% laparotomic, those not primarily managed 4 cases were laparoscopically reevaluated with our team. Most frequent tumor stage were FIGO IA in 51,7% of cases (36,8% in malignant tumors). The most frequent surgery (89,6%) was unilateral oophorectomy. 25/29 patients are alive and disease-free.

Conclusions: The high number of malignant cases may be explained because we are one of the main centres of pediatric oncological surgery at Brazil, so cases from all country are send to our hospital. The application of laparoscopic techniques to pediatric cancer patients is a safe and effective diagnostic, staging and treating modality.

V712 SIOP19-0805 | Application of 3D Scanner Reconstructions and Printing for Complex Pediatric Solid Tumors Surgery

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Background/Objectives: In the last years we have been involved in a great technological change that has reached most surgical procedures. Scanners and 3D printers are better, faster and much more precise. The 3D reconstruction simulation and printing has become a valuable tool for paediatric surgeons who must deal with complex solid tumor surgeries. The aim of the study is to share our experience with this inno-

vative techniques and its contribution to surgical procedures in childhood.

Design/Methods: This is a retrospective case series of patients between 2017-2019 in who 3D scan techniques or print were used for planning surgery.

Results: We show our experience in 4 patients diagnosed with cancer. We have used this technique for surgery planning, design a better approach and therefore reach better surgical results. We have used 3D scan reconstruction in a bilateral Wilms tumor to perform a nephron sparing surgery, a synovial sarcoma of the psoas to get an R0 surgery preserving homolateral kidney and rectum, and two adrenal tumors located close to the hepatobiliary area and inferior vena cava. As inconvenient, they need long time to get the reconstruction and are expensive, as they are designed by high quality 3D printers and materials.

Conclusions: 3D reconstruction is a helpful tool for oncological pediatric surgeons and contributes to a precise design of the surgical procedure and better results. Our experience in pediatric solid tumors located in abdomen is very positive. However it is necessary to carefully define the criteria for its use and to select the cases that may benefit more by this innovative approach.

V713 SIOP19-1289 | A 12-Year Retrospective Review of Primary Adrenal Neuroblastomas in Paediatric Patients at a Tertiary Academic Hospital in South Africa

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Background/Objectives: To describe the demographics, clinical presentation, management and outcome of patients under the age of 18 years who presented with a primary adrenal neuroblastoma to a tertiary academic hospital in South Africa between 1 January 2006 and 31 December 2017.

Design/Methods: The study is a retrospective study. Demographic information, symptoms at presentation, histology, blood results, radiology, treatment received, associated morbidities, and outcomes of patients were recorded. Ethics clearance to conduct the study was obtained from the local ethics committee.

Results: Thirty-six patients were included in the study, 61.1% (n=22) of whom were female. The median age at presentation was 33 months (IQR: 14.75-52.50). Median duration of symptoms was 30 days (IQR: 14-60). Fifty-six percent of patients presented with abdominal distension or a mass and 66.7% of patients presented with symptoms secondary to increased catecholamines. Seventy-two percent of patients were categorised as high-risk. Surgical resection was

performed in 67.4% of patients. The most frequent morbidity was neutropenic sepsis due to chemotherapy, occurring in 42.2% of patients. Surgical morbidity occurred in 3 patients (8.3%). The overall 5-year survival was 22%. We could not demonstrate a significant difference in mortality when low, intermediate, and high-risk groups were compared (p=0.542), or between N-Myc positive and N-Myc negative patients (p=0.852). Survival was better in patients with a Haemoglobin of more than 7g/dl (p=0.038), a normal Ferritin level (p=0.016) and in patients with a LDH of less than 1500 u/L (p=0.016).

Conclusions: There was a female preponderance in patients in the study. The median age of presentation was 33 months. Surgical morbidity occurred in 8.3%, but the overall 5-year survival was 22%. We could not show a significant improvement in survival in patients who had N-Myc negative tumours. Survival was however significantly better in patients with a normal Haemoglobin, Ferritin and LDH less than 1500 u/L.

V714 SIOP19-0391 | Use of Indocyanine Green Fluorescence in Assisting Pediatric Laparoscopic Resection of Hepatocellular Carcinoma

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Background/Objectives: Recent advances in surgical techniques have resulted in the use of minimally invasive technique for liver resection in many centres. However, the resection margin is often difficult to define intra-operatively, even with the help of ultrasound. As indocyanine green (ICG) is preferentially uptaken by hepatocytes and retained much longer by liver tumor cells, its use maybe applicable in intra-operative localisation of tumor and defining the resection plane.

Design/Methods: We here report a 9-year old girl with 4x3x5cm hepatocellular carcinoma at segment 6, admitted for laparoscopic resection of tumor. One day prior to surgery, 5mg of ICG was given intravenously for intra-operative imaging.

Results: At the operation, the tumor mass was clearly shown up by ICG fluorescence. Resection margin could thus be delineated. Laparoscopic segmentectomy was performed uneventfully. Total operative blood loss was 290mls. The child made an excellent recovery and was discharged on post-operative day 7.

Conclusions: Both the safety and accuracy of laparoscopic liver resection for HCC has been enhanced by the use of ICG.

V715 SIOP19-0376 | Pediatric Mediastinal Teratomas: A Review of 22 Cases from a Single Center

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Background/Objectives: Mediastinal teratomas are rare and usually located in anterior mediastinum. They are mostly mature teratomas (MT). Surgical resection is the mainstay of treatment. We aimed to review our institutional experience with these rare tumors.

Design/Methods: Hospital files of 22 children diagnosed with mediastinal teratomas between 1973 and 2018 were reviewed for demographic characteristics, clinical, radiological and other laboratory data, surgical practices, histopathological features, treatment approaches and outcomes.

Results: Median age was 5.5 years (1 day to 15 years) (male/female: 8/14). Most common presenting complaints were respiratory distress followed by cough, chest pain, anorexia and wheezing. Two cases had incidental diagnosis. The ages were <12 months in eight and >11 years in 7 cases. Two newborn cases had immature teratomas (IT) (one with prenatal diagnosis, one with pneumothorax). In 21 cases primary tumors were located in the anterior mediastinum, one had tumor over the sternum. The maximum diameter of the tumors ranged between 4 cm and 15 cm (median 8 cm). Four cases, including two newborns, had ITs (18%) and 18 had MT (82%). Serum alpha-fetoprotein and beta-HCG were normal for age in 21 cases. All cases with MT underwent gross total/total tumor resection (10 thoracotomies, 9 sternotomies, 3 data unavailable) and were under follow-up with no further treatment. A 13-year-old girl with an IT and elevated serum alpha-fetoprotein had tumor recurrence and received chemotherapy following second surgery with no further events at a follow-up of 11 years. A newborn with an IT received chemotherapy postoperatively and is disease-free. Another newborn with IT is tumor-free after surgery. At a median of 136 months (1-521 mo.) 3 cases were lost to follow-up, 19 were alive.

Conclusions: Mediastinal MTs have favorable prognosis following complete surgical resection and recurrences are uncommon. Chemotherapy might be indicated for ITs and careful follow-up after surgery is needed for possible recurrences.

V716 SIOP19-0454 | Pediatric Appendiceal Carcinoid Tumors: A Review Of 27 Cases from a Single Center

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Background/Objectives: Carcinoid tumors (CT) are quite rare neoplasms of neuroendocrine origin in children which are mostly appendiceal. Most children undergo surgery with the initial diagnoses of appendicitis. We aimed to review our experience with pediatric appendiceal carcinoid tumors.

Design/Methods: Records of children with appendiceal CTs were examined and data concerning demographic characteristics, initial clinical and laboratory findings; surgical procedures and histopathological findings; management approaches and overall outcome were recorded.

Results: Between 1985 and 2018 we identified 27 cases with appendiceal CTs whose median age was 12.8 years (range, 8.4-16 years; male/female= 9/18). At initial presentation, all but one patients experienced abdominal or right lower quadrant pain, 5 had vomiting and 4 had fever; none had carcinoid syndrome findings. Abscess drainage and appendectomy was performed in a 16-year-old girl who presented with vomiting, pallor and fatigue with preoperative diagnosis of right ovarian mass, and tumor was positive in the omentum. All remaining 26 cases with initial clinical diagnosis of acute appendicitis underwent simple appendectomies. Histopathological diagnoses was carcinoid tumor in all cases. In patients with adequate data, median tumor size was 0.8 cm (range 0.1-3.5 cm) and various degrees of appendix wall invasion were noted as: submucosa 8/23, tunica muscularis 12/23, subserosa 5/23, serosa 5/23 and mesoappendix 2/23 cases. Urinary 5-HIAA levels were normal in all patients following diagnoses. Three cases were lost to follow-up, 24 cases were alive at a median follow-up of 64 months (1-310 mo.).

Conclusions: No clinical or laboratory findings suggestive of CT were evident in our cases. None of our patients required further surgery. Pediatric appendiceal CTs mostly measure <2 cm in diameter and postoperative further interventions or treatment are almost never required despite invasion of layers of the appendix wall. Slow growth and symptoms resulting in appendectomy and early removal may explain the favorable prognosis.

Treatment and Care - Transdisciplinary Tumor Genomics and Biology and Cancer Predisposition

V717 SIOP19-1659 | Development of a Cancer Genetics/Paediatric Oncology Service for Solid Tumour Patients: Establishment of Referral Guidelines and Results of the First Year

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Background/Objectives: Identification of cancer predisposition syndromes (CPS) is essential for cancer patients and their families. Identifying a CPS provides information on why cancer has occurred, opportunity for individualised cancer management and discussion of future cancer risks and surveillance. Childhood cancer should raise suspicion of a CPS. Collaboration between geneticists and oncologists is crucial to identify and counsel those at risk. In our Centre we developed and implemented local guidelines for referrals to Cancer Genetics.

Design/Methods: We reviewed the number of referrals to Cancer Genetics in the period January–December 2018

Results: 142 patients were diagnosed with non-haematological malignancies in our Centre during the study period, 38/142 (26.7%) were referred to genetics. Genetic testing (single gene or panel) was discussed with 30 patients. One family (whose child was diagnosed with choroid plexus carcinoma) refused genetic testing. In 5 patients (13%) a pathogenic variant was identified: *WT1* in a patient with Wilms tumour, *TP53* in 3 patients (one with medulloblastoma SHH-subtype, one with adrenocortical carcinoma, one with known family history) and a likely pathogenic variant in *SMARCE1* in a child with meningioma and relevant family history. A list of 43 indications for referral to cancer genetics was generated based on literature review and the national genomic test directory. All patients identified with a CPS will be offered surveillance based on their diagnosis: annual brain/spine MRI for *SMARCE1*, annual renal ultrasound for *WT1* and in line with new UK Cancer Genetics Group recommendations, *TP53* carriers will be offered yearly whole body MRI, brain MRI, skin evaluation, and abdominal US and physical examination every three months.

Conclusions: Multidisciplinary collaboration improves diagnosis of CPS, development and implementation of surveillance protocols and cascade genetic testing of family members. Increased genetic testing through the new Genomic Medicine Service will improve CPS detection and strengthen our collaboration.

V718 SIOP19-1231 | Grafting Human Tumoral Cells in an Avian Embryo to Model Pediatric Malignancies in an Immature Organism

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Background/Objectives: Pediatric malignancies share the unique particularity to occur in developing organisms. Half of them even arise at embryonic stages, thus concomitant to morphogenetic processes characterized by intense cell proliferation and migration. To which extent cancer cells exploit and hijack the embryonic programs to widely spread and colonize particular developing tissues is a fundamental question. It has long remained inscrutable, mainly due to the lack of models recapitulating prenatal tumoral events and allowing experimental manipulations. Based on our recent achievements on neuroblastoma, we aimed to develop additional models recapitulating the embryonic environment and adapted to patient-driven analyses.

Design/Methods: We focused on three pediatric malignancies with migration specificities: neuroblastoma (NB), medulloblastoma (MB) and germ cell tumors (GCT). Graft of cell lines and patient samples in avian embryos were performed in selected tissue sites and developmental stages to reproduce and study the etiological steps of primary tumor formation and/or secondary dissemination modalities.

Results: We analyzed by 3D imaging using light sheet confocal microscopy the sequence of events and physical pathways leading to NB secondary metastasis to distant organs such as the bone marrow. In the same line, grafting MB cells in selected brain territories revealed stereotypic migratory patterns. At last, placing GCTs cells in the migratory path of their cells of origin successfully led to the formation of tumors in gonadal sites, opening the possibility to challenge the hypotheses underlying their etiology.

Conclusions: Thus, our in vivo paradigm consisting in confronting tumoral cells to microenvironments specific to the developing organism and selected according to the territories of tumor occurrence, appears as a powerful in vivo paradigm to model pediatric malignancies. The data obtained on three major pediatric indications pave the way to a range of embryonal malignancies with yet no available or suitable in vivo models.

V719 SIOP19-1444 | P53 Modulates MYC-Mediated Cell Competition in Cancer Backgrounds

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Background/Objectives: MYC-Mediated Cell Competition (MMCC) is a phenomenon of fitness comparison occurring between adjacent cells showing different levels of MYC activity. It describes a mechanism, conserved from *Drosophila melanogaster* to mammalian development, through which cells characterised by high expression of MYC (*winner* cells) induce apoptotic death of neighbouring low MYC-expressing cells (*loser* cells) and acquire an advantage in space occupancy. In *Drosophila*, p53 protein resulted necessary in MYC-overexpressing cells to sustain their competitive advantage.

Malignant cells often upregulate MYC and MMCC has been demonstrated to be at work in human epithelial cancer context: it selects cells undergoing clonal expansion, so shaping tumour progression and evolution. p53 is one of the most frequently mutated genes in human cancers, but the function of its several mutant products and dominant negative forms is not clear.

Design/Methods: Through IHC investigations on several kinds of human carcinomas, *in vitro* co-culture assays and *Drosophila* experiments, we observed that loss of p53 in the winner cells is sufficient to make them unable to grow and out-compete the neighbours, thus suggesting a functional cooperation between MYC and p53 in cancer-associated MMCC.

Results: Our results show an oncogenic side of the p53 *wild-type* protein that appears to help shape cancer progression through selection of the most competitive cells.

Conclusions: Altogether, our findings indicate that, such as it happens during organ development, human malignant cells may use transient expression of MYC activity and p53 to expand at the expense of less fit neighbours, suggesting an important role for both p53 and MYC during cell competition in cancer evolution.

V720 SIOP19-1369 | What's Next? Should Next Generation Sequencing in Healthcare Lead Us to Reassess Basic Ethical Concepts Guiding Practices in Research?

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Background/Objectives: Next generation sequencing (NGS) is deploying. After the United-Kingdom (100K genomes project), France is developing a programme for genomic medicine (FMG2025) and starts to operate two platforms in Paris and in Lyon regions in 2019. Looking at similar inter-

national programs, FMG2025 coins genomic medicine as a “hybrid care/research system”, leading to the definition of 12 “pre-indications”, including one in paediatric oncology. Should this lead to reassess the basic concepts guiding genetic research ethics reflection?

Design/Methods: We revisit different empirical materials from previous field survey work relevant to this topic, from consultations at the European level on “confidentiality in biobanks” in the EU-FP7 ENCCA project (2011-2015) and from semi-structured interviews conducted in France that scoped a social sciences and humanities project financed by INCa (2018-2021) on ethical, legal and psychological issues raised by NGS.

Results: There is consensus on some key issues (status of samples, social value of research, public awareness), but we identified two areas of uncertainties about research practices, based on ENCCA consultations with parents'/patients' representatives (n=39) and professionals' representatives (n=22): firstly, between the two populations (e.g. child's refusal, de-identification, length of storage), secondly, between what is acceptable but may be difficult to implement (timing of consent, child's refusal, reconsent). The two consultations were inconclusive on other topics (deceased donors, care/research boundaries). Interviews with French professionals (n=22) allowed further evaluation of recurring key topics (reuse, reconsent, return of results) and how they are dealt with in clinical practice and research contexts, from a multidisciplinary view and the broader perspective of NGS.

Conclusions: Triangulating results obtained in different field surveys in paediatric oncology avoids duplication and optimises the updates that need to be done in the light of rapid evolution towards precision medicine and NGS. We identify remaining and novel areas of uncertainty to prioritise future research.

V721 SIOP19-1082 | Prevalence and Spectrum of Germline Mutations in Children with High-Risk Cancer

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Background/Objectives: Zero Childhood Cancer's National Precision Medicine for Children with Cancer Study (PRISM) utilises novel technologies to guide individualized management of children with high-risk cancer (expected overall survival less than 30%). Germline DNA is utilised to distinguish cancer-specific somatic variants from constitutional variants or polymorphisms, allowing identification of clinically relevant germline mutations. The prevalence of cancer predisposition syndromes in paediatric cancer may range from 8.5% to as high as 33%.

Design/Methods: PRISM combines molecular genomic analysis (WGS and RNASeq) with *in vitro* high-throughput drug screening and patient-derived xenograft drug efficacy testing. A Molecular Tumour Board of Oncology and Genetics professionals convenes to determine the significance of genomic analysis as curated by bioinformaticians and molecular scientists.

Results: Between September 2017 and March 2019, 170 children aged under 21 years have been enrolled in PRISM (35.3% with central nervous system (CNS) tumours; 48.2% with non-CNS solid tumours and 16.5% with haematological malignancies). Thirty-seven reportable germline variants were detected in 30 participants (detection rate: 17.6%) comprising of 25 pathogenic and 12 likely pathogenic variants, across 23 cancer predisposition genes. The most frequently affected gene was CHEK2 (n=6) followed by SMARCB1 (n=4) and BRCA2 (n=3). In one out of three participants with germline mutations (10/30), somatic analysis revealed a double hit in the same gene altered in the germline. Distribution of participants with germline mutation per group were: 20% of patients with CNS tumours (12/60), 24.3% of patients with non-CNS solid tumours (20/82), and 21.4% of patients with haematological malignancies (6/28).

Conclusions: Germline mutation detection rate in cancer predisposition genes was higher than expected (17.6%), however it may result from selection bias (i.e. cohort of high-risk cancers). Although genomic sequencing has expanded our understanding of paediatric cancer predisposition and presented opportunities for genetics-mediated care, identifying children at-risk remains a clinical challenge for paediatric oncologists.

V722 SIOP19-0904 | Multiple Primary Malignant Tumors in Children, Analysis of Sporadic and Hereditary Forms

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Background/Objectives: Over the past decades, there has been a growth of multiple primary tumors (MPT) throughout the world, in both adults and children. The aim was to study the features of the clinical presentations of multiple primaries sporadic and hereditarily determined malignant tumors in children.

Design/Methods: From 1998 to 2012 among 5875 patients were revealed 104 children who had multiple primary malignant tumors (MPMT). The analyses of clinical data such as: the frequency of occurrence of second tumors, the interval of their appearance from the primary diagnosis was carried out both in the group as a whole and in separate types of cancer. Using methods Next Generation Sequencing (NGS) and Multiplex Ligation-dependent Probe Amplification (MLPA) allowed to reveal germinal mutations in 12 children with MPMT.

Results: The second primary tumor detected in 104 (1.8%) children. The age of patients at the time of occurrence of the second malignant tumor ranged from 2.8 to 28 years. The second tumors occurred significantly more frequently in the group of primary hematopoietic tumors, compared with the group of solid tumors - 8.7% versus 3.4%, respectively (p < 0.0001). In children with MPMT were found tumors that occur in common the most frequency, such as retinoblastoma patients have an increased risk of developing sarcoma, patients with Hodgkin's lymphoma have an increased risk of developing leukemia. The germline mutations in *TP53*, *RBI*, *CHEK2*, *FANCN/PALB2*, *MLH1*, *PMS2* genes identified in 12 patients. They were associated with hereditary syndromes and an increased risk of developing second tumors, among which: sarcomas, brain tumors, hematopoietic tumors were the most frequent. It was shown that the second tumors can appear at the any age.

Conclusions: Children who survived the treatment of the first tumor in later life should be monitored annually. Clinical management of children with MPT requires a multidisciplinary approach.

V723 SIOP19-0557 | Zero Childhood Cancer: A Comprehensive Precision Medicine Platform for Children and Adolescents with High-Risk Cancer

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Background/Objectives: The Australian Zero Childhood Cancer (ZERO) program aims to assess the feasibility of a comprehensive precision medicine approach to improve outcomes for patients with high-risk (HR) paediatric cancer.

Design/Methods: We combine comprehensive molecular profiling (whole genome sequencing, deep targeted DNA sequencing, whole transcriptome sequencing, DNA methylation profiling) with *in vitro* high-throughput drug screening and patient-derived xenograft drug efficacy testing. Results are curated and recommendations made by a national Multidisciplinary Tumour Board (MTB). Recommendations consist of targeted therapy, change of diagnosis or genetics referral for a germline cancer predisposition gene mutation.

Results: The ZERO national trial (PRISM) is open in all 8 paediatric centres around Australia and has enrolled 183 patients over 18 months to date, predominantly those with brain tumours or sarcomas and patients with relapsed or progressive disease. The unique ZERO testing platform has resulted in at least one recommendation being issued for 69% of patients with a median turnaround time of 9.1 weeks from enrolment to post-MTB recommendation report. The most highly mutated genes/pathways include TP53, MAPK pathway, CDK/cyclin family and PI3K/mTOR pathway. Mutation signatures and tumour mutation burden assessment support targeted treatment recommendations (e.g. PARP inhibitors or immunotherapy). *In vitro* and *in vivo* drug efficacy studies were attempted in 69% of the samples and provide corroborating evidence. Of the first 18 patients who received a MTB recommendation therapy, 28% have a partial response to therapy, 28% have stable disease and 44% have progressive disease.

Conclusions: ZERO demonstrates the feasibility of a comprehensive precision medicine platform to identify treatment recommendations in HR paediatric cancer patients. The national trial is planned to run for 3 years, recruiting ~400 patients. In addition, ZERO is partnering nationally and internationally to conduct parallel research studies in immunoprofiling, liquid biopsy, psychosocial impact of precision medicine, health economics and health implementation.

V724 SIOP19-0285 | Discovery of Actionable Genetic Alterations with Targeted Panel Sequencing in Children with Relapsed or Refractory Solid Tumors

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Background/Objectives: Advances in genomic technologies and the development of targeted therapeutics are making the use of precision medicine increasingly possible. In this study, we explored whether precision medicine can be applied for the management of refractory/relapsed pediatric solid tumors by discovering actionable alterations using targeted panel sequencing.

Design/Methods: Samples of refractory/relapsed pediatric solid tumors were tested using a targeted sequencing panel covering the exonic DNA sequences of 381 cancer genes and introns across 22 genes to detect clinically significant genomic aberrations in tumors. The molecular targets were tiered from 1 to 5 based on the presence of actionable genetic alterations, strength of supporting evidence, and drug availability in the Republic of Korea.

Results: From January 2016 to October 2018, 55 patients were enrolled. The median time from tissue acquisition to drug selection was 29 d (range 14-39), and tumor profiling was successful in 53 (96.4%) patients. A total of 27 actionable alterations in tiers 1-4 were detected in 20 patients (36.4%), and the majority of actionable alterations were copy number variations. The tiers of molecular alterations were tier 1 (clinical evidence) in 4 variants, tier 2 (preclinical evidence) in 8 variants, tier 3 (consensus opinion) in 2 variants, and tier 4 (actionable variants with a drug that is available in other countries but not in the Republic of Korea) in 9 variants.

Conclusions: Using a targeted sequencing panel to discover actionable alterations in relapsed/refractory pediatric solid tumors was practical and feasible.

V725 SIOP19-0561 | Shallow Whole Genome Sequencing on Circulating Cell-Free DNA in Pediatric Cancer Patients

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Background/Objectives: Liquid biopsies (LQB) have gained much attention in cancer research. They provide broader insight into tumor heterogeneity and offer an alternative to painful and invasive tumor tissue biopsies. For adult cancers, studies have proven that circulating cell-free DNA (cfDNA) can be used for copy number aberration profiling and mutation analysis at diagnosis, monitoring treatment response and prediction of relapse. In contrast, the use of cfDNA in the context of pediatric cancer patients has not been systematically documented.

Design/Methods: In a retrospective study, we performed shallow whole genome sequencing (sWGS) on cfDNA from 100 pediatric patients representing different tumor entities including osteosarcoma (17), Ewing sarcoma (8), rhabdomyosarcoma (19), Wilms tumor (17), various brain tumors (13) and neuroblastoma (26). Copy number profiles of cfDNA were compared with the matching tissue data. Capillary electrophoresis was performed and concentration of the cfDNA measured to correlate with the copy number profiles.

Results: A good concordance (64.2%) was obtained between the copy number profile of the primary tumor and the cfDNA. The concentration of cfDNA varied significantly and success rate depends on the amount of cfDNA present in the plasma, which may be influenced by disease stage and tumor entity. Blood plasma from osteosarcoma patients contained the lowest cfDNA concentrations. Furthermore, we show that the method of plasma separation and storage can influence the results. For brain tumor patients, comparison of plasma cfDNA versus cfDNA isolated from cerebrospinal fluid (CSF) indicated the latter being the most suitable source.

Conclusions: We will extend the present study with more samples for each tumor entity to strengthen the conclusion if cfDNA could serve as an alternative for tissue DNA. In a prospective study, standardized sampling and analysis will be tested. Furthermore, longitudinal sampling of material will be performed for the visualization of treatment response and follow-up.

*TL and NVR are shared last authors

V726 SIOP19-0642 | Molecular and Immunological Characterisation of High Risk Cancer at Diagnosis, During Treatment and Follow-Up in Children, Adolescents and Young Adults: The French Micchado Study

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Background/Objectives: The prospective MICCHADO study (NCT03496402) aims at characterizing genetic alterations and immunological features of high-risk (HR) cancers in paediatric/adolescent/young adult patients.

Design/Methods: This non-therapeutic study will enroll 600 patients ≤ 25 years from all SFCE centers (n=30) over 3 years. Patients with HR or with non-HR cancers, (cohort of comparison) are eligible if cryopreserved and formalin-fixed paraffin-embedded tumour samples at diagnosis are available. Molecular and immunological Tissue characterization will be performed by WES (100x, tumor/paired germline), whole RNAseq and immunohistochemistry for description of the tumor microenvironment. Blood flow cytometry will evaluate the host immune profile. WES and targeted sequencing of circulating tumor DNA (ctDNA) will sequentially study tumor specific genetic alterations. Performed in a research setting, results will only be to patients' physicians in specific cases after validation in a molecular tumour board.

Results: With centers having opened to recruitment progressively, from April 2018 to March 2019, 64 patients have been enrolled in 5 centers. Median age at diagnosis was 7 years. 23 patients had neuroblastoma (HR, n=16), 8 osteosarcoma (HR, n=3), 9 Ewing sarcoma (HR, n=4) and 9 rhabdomyosarcoma (HR, n=3). 1 and 14 patients with HR leukemia and other solid cancers have also been included, respectively. Analysis of tumor samples by WES, RNAseq and immunohistochemistry is ongoing for these first patients, and flow cytometry has been performed for 32. (Sequential) ctDNA samples are available for all patients. A feedback on results has been requested for 4/64 patients with primary refractory disease with a request to identify the overall mutational burden or targetable genetic alterations.

Conclusions: Data integration within this cognitive study will provide further insight into occurrence of infraclinic recurrence as well as mechanisms of disease progression and treatment resistance, and will contribute to the development of future novel frontline therapeutic approaches.

V727 SIOP19-1046 | Liquid Biopsies in Paediatric Patients with Solid Tumours: An Attractive Approach to Determine Therapy Response and Disease Progression

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Background/Objectives: In recent years, the analysis of tumour-associated copy number variants (CNV) in cell-free tumour DNA (ctDNA) in peripheral blood plasma has gained interest as a non-invasive cancer screening tool. Here, we explored CNV detection in paediatric patients with solid tumours during the course of treatment and follow-up.

Design/Methods: We prospectively performed CNV analysis in ctDNA by genome representation (GR) profiling (median coverage across the whole genome 0.23x) in 25 patients [with neuroblastoma (NB; n=5), Ewing sarcomas (ES; n=4), osteosarcomas (OS; n=5), rhabdomyosarcomas (RMS; n=5) and others (n=6)]. In patients where an abnormal GR profile was detected at diagnosis, the testing was extended to blood samples collected during routine follow-up in the consecutive 6-24 months from the start of treatment (surgery/chemotherapy/radiotherapy). Molecular data were linked to the clinicopathologic tumour characteristics and clinical follow-up of the disease.

Results: All of the ES, OS and NB had an abnormal profile GR at diagnosis, as did 5 patients with other solid tumours. During therapy, the fraction of the genome affected by CNV decreased and the GR profile 'normalized'. A normal GR profile during follow-up was associated with clinical remission at these time points. In 4 patients, we observed an increase in the fraction of the genome affected by CNV at time of disease progression or relapse. In one patient with ES, the detection of an abnormal GR profile after previous normalization during follow-up even indicated relapse before the clinical diagnosis was made. Two patients had inconclusive data.

Conclusions: Our results indicate that the serial analysis of ctDNA in liquid biopsies offers a promising approach for the evaluation of treatment response and disease progression in paediatric patients with solid tumours, both during treatment and routine follow-up. Especially in ES, OS and NB, this technique seems to be a valuable approach.

V728 SIOP19-0717 | The Validation of a Clinical Screening Instrument For Tumor Predisposition Syndromes in Childhood Cancer Patients (TUPS): A Prospective, Observational, Multi-Center Study

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Background/Objectives: Up to 10% of children with cancer has a tumor predisposition syndrome (TPS). Identification of a TPS in a child with cancer is of clinical relevance. Previous studies have shown that half of TPSs are not recognized prior to treatment. To increase diagnostic accuracy and clinical efficiency we developed a screening instrument, ensuring evaluation for a TPS in all children with cancer.

Design/Methods: TuPS is a prospective, observational, multi-center study including children newly diagnosed with cancer in the Netherlands from 2016-2019 in whom no TPS was previously diagnosed. The screening instrument consists of a clinical assessment, 2D and 3D pictures, and integrated digital assessment by two independent clinical geneticists. If a TPS was suspected by at least one clinical geneticist (positive assessment), the patient was referred to clinical geneticists for genetic counseling. In addition negative assessed patients are randomized for genetic consultation as control group. Primary outcome is the clinical value and acceptance of the instrument.

Results: Results of 315 patients show a positive assessment rate of 57% (180/315) (25% by one assessor, 32% by both assessors). The reason for positive assessment was based mainly on type of cancer (54%) and family history (38%). In 17% (30/180) the clinical geneticist would not have assessed the child positive if pictures would not have been available. Hundred-seventy-one patients were evaluated by genetic consultation thus far. In the positive assessed group three (3/145) patients were diagnosed with a TPS and in four (4/145) patients a germline variant of non-conclusive significance was found. In the negative control group (26/135) no TPS was diagnosed. In 11 patients further analysis is still ongoing.

Conclusions: Preliminary results indicate the screening instrument seems feasible in routine care. No false negative results were identified in the negative control group, indicating that negative assessments by the screening instrument were justified.

V729 SIOP19-1061 | Clinical Tumor Exome Sequencing for Pediatric Non-CNS Solid Tumor Patients—Results from the Baylor Advancing Sequencing in Childhood Cancer Care (BASIC3) Clinical Sequencing Study

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Background/Objectives: Tumor exome sequencing (ES) has the potential to impact clinical management of children with non-CNS solid tumors; however data regarding clinical utility are limited. To investigate this topic, enrollment onto the BASIC3 clinical exome sequencing study was offered to children with newly-diagnosed solid tumors.

Design/Methods: ES was performed on tumor and blood specimens in a clinical laboratory, with genetic variants categorized by perceived clinical relevance and reported to the electronic health record. Somatic variants were subsequently annotated per recent consensus guidelines (Li et al. J Mol Diagn 2017). ES was performed on 158 non-CNS solid tumors, including neuroblastoma (n=26), Wilms tumor (n=25), germ cell tumors (n=15), and sarcomas (Ewing sarcoma=11; osteosarcoma=11; soft tissue sarcomas=31).

Results: Analysis revealed that 28% (45/158) of tumors harbored a somatic variant of either “Strong” (Tier 1) or “Potential” (Tier 2) clinical significance, including 13% (20/158) with therapeutic implications (all of which were Tier 2 variants). This latter group of targetable mutations primarily involved the MAPK pathway (BRAF, HRAS, KRAS x 2, FGFR1, NRAS x 2), PI3K/MTOR pathway (TSC2 x 2, PIK3CA x 2, MTOR), and SWI/SNF family (SMARCB1). Other genes with alterations included BRCA1, GNAS, NF2, PTPN11, and KIT. The rate of clinically relevant mutations differed by histology, with frequent variants in hepatoblastoma (4/7, 57%), Wilms tumor (12/25, 48%), and soft tissue sarcomas (9/31, 29%). Fewer variants were detected in neu-

roblastoma/ganglioneuroblastoma (4/30, 13%), and Ewing sarcoma (1/11, 9%).

Conclusions: These data highlight the promise of clinical genomic testing for pediatric non-CNS solid tumor patients and the need for further development of molecularly targeted agents.

V730 SIOP19-1581 | Selective Screening for Genetic Cancer Predisposition Syndromes Results in High Detection Rate

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Background/Objectives: It is estimated that 10-29% of pediatric hematology-oncology patients have an underlying Cancer Predisposition Syndrome (CPS). Investigation of a possible underlying predisposition is significant not only for the patients, but also for their relatives in terms of prevention and genetic consultation.

Design/Methods: Since 2012, all newly-diagnosed patients (pts) with hematologic-oncologic malignancy and patients with CPS were prospectively registered and studied in our Department. All pts with family history or clinical findings compatible with possible CPS, as well as, pts with tumors known to be associated with specific syndromes were genetically tested for CPS.

Results: During the study period, 649 pts (age range: 10 days-17 years) were evaluated in our unit; 214 with brain tumors (32.9%) and 145 with acute leukemia (22.3%). Genetic testing was performed in 112 of them, and cancer predisposition syndrome was diagnosed in 90 pts (13.5%). In 41 out of 90 pts with confirmed CPS, suspicion was raised after diagnosis of malignancy in the propositus, with the main type of malignancy being optic pathway glioma (25 pts, 28.4%). Specifically, 65 pts were genetically diagnosed with Neurofibromatosis type-I and 4 with type-II, 5 pts with tuberous sclerosis, 3 pts with Li-Fraumeni syndrome, 3 with Myelodysplastic syndromes, 2 with s. Beckwith-Wiedemann, 2 with Fanconi-anemia, 2 patients with rhabdoid predisposition syndrome, 2 pts with Hereditary Gastric Cancer Syndromes, 1 patient with s. MEN1, 1 patient with familial retinoblastoma, while gene testing is pending in 22 pts. CPS was confirmed in 7 siblings of our pts. Subsequently to the diagnosis, all pts were placed under regular monitoring, according to standard recommendations for follow up of the respective syndrome.

Conclusions: Evaluation for underlying CPS is expected to improve mortality and morbidity in patients with CPS.

Appropriate screening criteria need to be established for optimal outcome.

V731 SIOP19-1200 | Deciphering the Genetic Etiology of Pediatric Cancers Through an Integrative Gene Network Approach

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Background/Objectives: Cancer is the leading cause of disease-related mortality in children beyond fourteen years of life. Major advances have been made in onco-pediatric research but additional studies are needed to achieve a comprehensive understanding of the genetic etiology of pediatric cancer.

Design/Methods: Our work addresses this challenge by analysing the transcriptome data provided by the Treehouse Childhood Cancer Initiative. We constructed a co-expression network composed of modules gathering genes having functional relationships in pediatric cancers and performed a deep multi-layer examination of these modules.

Results: Pediatric cancer genes gathered in 6 modules associated with cancer-histotype specific functions. Interestingly, numbers of these processes were developmental pathways, underlying the close tie between organogenesis and tumorigenesis in childhood cancers. Childhood cancer predisposition genes were enriched in a particular module associated with common oncogenic process, such as DNA repair and cell cycle regulation. Additionally, we reveal over-representation of clinically actionable genes in this particular module, as well as in two other modules tightly related to leukemogenesis. In pediatric acute leukemias, the driver genes were co-expressed in another module related to epigenetic and post-transcriptional processes, underlying the critical role of these pathways in the progression of hematologic malignancies. Topological analyses highlight that numbers of the key regulators of these cancer-histotype specific modules were known pediatric cancer predisposition genes (e.g. *PHOX2B*, *PAX5*).

Conclusions: This integrative pan-cancer study offers detailed information about the genes and modules that drive childhood tumorigenesis, and provides a comprehen-

sive understanding of the genetic architecture in pediatric cancers.

V732 SIOP19-0594 | Extracranial Malignant Rhabdoid Tumor Associated with Rhabdoid Tumor Predisposition Syndrome Type 1. Experience of the Russian National Center

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Background/Objectives: analysis of clinical and genetic characteristics of extracranial malignant rhabdoid tumors (MRT) associated with rhabdoid tumor predisposition syndrome type 1 (RTPS1).

Design/Methods: from 12.2012 to 01.2019 (84 months) 45 patients with extracranial MRT were diagnosed and treated in Dmitry Rogachev NRC PHOI. Four (8.9%) had RTPS1. The diagnosis was established by histology and absence of *SMARCB1*/INI1 nuclear expression. RTPS1 was confirmed by Sanger sequencing or FISH. Therapy was given according to the European Rhabdoid Registry (EU-RHAB) guidelines.

Results: the median age at the moment of the diagnosis was 2 months (range 0.5-5.0). The male:female ratio - 0:4. The primary tumor was localized in kidney in 3 (75%) cases, soft tissue of gluteal region and pelvis in 1 (25%). Two (50%) patients had localized disease and 2 (50%) patients had distant metastases in lungs, brain, skin. RTPS1 was detected by sequencing in 3 (75%) patients with MRT of kidney. Point mutations/deletion p. 843 G-A, c. 157 C-T, C. 669_670del were found. One (25%) patient with soft tissue MRT had *SMARCB1* deletion detected by FISH. All the patients underwent intensive chemotherapy. Radical surgery could be done in 1 (25%) case, non-radical (R1/R2) in 3 cases (75%), 2/3 (50%) had tumor rupture. Radiotherapy (RT) was performed in 1 (25%) case with kidney MRT (flank RT, 10.8 Gy). Therapy was completed in 1 (25%) case, 3 (75%) patients progressed on therapy. Outcome: 1 (25%) patient is alive, 3 (75%) died (2/3 – disease progression after 4 and 5 courses, 1/3 – metachronous tumor of the posterior cranial fossa 1 year after the end of the therapy. Median time to the event was 3 months (range 2-12).

Conclusions: MRT associated with RTPS1 is presented in early age, characterized by prevalence of metastatic/locoregional disease and high probability of developing metachronous tumors.

V733 SIOP19-1366 | Reduced Penetrance for Malignant Neoplasms in Non-Proband *DICER1* Mutation Carriers; A Nationwide Retrospective Study from The Netherlands

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Background/Objectives: *DICER1* syndrome is a rare autosomal-dominantly inherited disorder that predisposes to a variety of malignant and non-malignant tumors of mostly pediatric and adolescent onset. Pleuropulmonary blastoma (PPB), cystic nephroma (CN), ovarian Sertoli-Leydig cell tumor (SLCT), multi nodular goiter (MNG) and differentiated thyroid cancer (DTC) are the hallmark tumors of *DICER1* syndrome. Disease penetrance has been estimated to be low to moderate.

Design/Methods: We performed a nationwide retrospective cohort study in the Netherlands including all *DICER1* mutation carriers until 2018. Age-related penetrance of *DICER1*-related malignant and non-malignant tumors was estimated using the Kaplan-Meier method.

Results: We included 75 individuals with germline pathogenic *DICER1* variants from 16 families. Probands (n=16) were diagnosed with PPB (n=3), thyroid neoplasms (MNG n=5, DTC n=3), CN (n=1), pineoblastoma (n=1), embryonal rhabdomyosarcoma (n=1) and other (n=2). By age 10 years, 8.5% (95%CI, 0.5% to 16.5%) of non-probands *DICER1* carriers had developed a *DICER1*-related neoplasm (females, 8.5%; males, 8.7%). By age 35 years, 46.9% (95%CI, 31.6% to 62.2%) of non-probands had developed a neoplasm (females, 77.7%; males, 13.2%). Most frequent were benign thyroid disease (n=17) or PPB type I in regression (n=3). In total four non-probands were diagnosed with malignant disease, all DTC. The estimated penetrance for malignant *DICER1*-related neoplasms by age 10 and 35 years was respectively 0% and 10.4% (female 19%, male 0%). In total 10 affected family members (MNG n=6, SLCT n=3, PPB n=1) declined DNA testing.

Conclusions: This nationwide cohort study showed reduced penetrance for malignant neoplasms in 59 non-probands with *DICER1* syndrome. Although penetrance for benign thyroid nodules is high, only a small percentage progressed to (often low risk) DTC. Larger series are needed to determine the optimal age at which surveillance should be initiated and the best

monitoring intervals to capture the different *DICER1*-related manifestations as they develop.

V734 SIOP19-0297 | Non-Invasive Classification of Pediatric Tumor Types Using Reduced Representation Bisulfite Sequencing of Cell-Free DNA: A Proof-of-Principle Study

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Background/Objectives: In the clinical management of pediatric solid tumors, a biopsy remains the gold-standard to establish a diagnosis. The DNA methylation pattern of a tumor is known to correlate to the histopathological diagnosis across cancer types and thus might be of value in the diagnostic workup of tumor samples. It has previously been shown that this methylation pattern can be detected in cell-free DNA (cfDNA). Currently, the most well-established method to detect the cfDNA methylation signature is whole-genome bisulfite sequencing. However, this technique is not cost-effective.

Design/Methods: Here, we provide proof-of-concept that classification according to the histopathological diagnosis is possible using a novel and affordable method called “cell-free reduced representation bisulfite sequencing” (cfRRBS) from plasma and cerebrospinal fluid. Our retrospective cohort (n = 60) consists of a diverse set of pediatric patients with extracranial and intracranial tumors.

Results: Using matrix decomposition and a reference set composed of publicly available methylation profiles from primary tumors, we were able to correctly classify 49 samples (81.6%) according to their histopathological diagnosis. In contrast to adult cancers, the estimated ctDNA tumor fraction did not correlate with metastatic disease. Misclassified samples were more frequently contaminated with high molecular weight (HMW) DNA originating from white blood cell lysis, which reduced the estimated tumor fraction. After excluding samples with moderate to high HMW contamination, classification accuracy increased to 94%.

Importantly, the cfDNA methylation profile allows us to distinguish nephroblastoma and malignant rhabdoid tumor of the kidney or clear cell sarcoma of the kidney, and medulloblas-

toma from an atypical teratoid-rhabdoid tumor. These clinical entities often pose a diagnostic challenge.

Conclusions: Although there are still several limitations to our methods, our findings open up the perspective of developing a cost-effective blood-based diagnostic assay for non-invasive diagnosis and subtyping of pediatric cancers.

V735 SIOP19-1570 | Germline Mutations of TP53 Gene Among Children with Cancer from Russia

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Background/Objectives: Germline mutations of *TP53* are associated with Li-Fraumeni syndrome (LFS). LFS is characterized by early onset of multiple tumors, the most common are bone and soft-tissue sarcomas, brain tumors, leukemia, adrenocortical carcinoma (ACC) and choroid plexus carcinoma (CPC). Patients with *TP53* germline mutation have a poor survival rates and increased risk of second malignancy developing.

Design/Methods: DNA was isolated from the peripheral blood of 83 patients (29% females, 71% males) with various malignant tumors. The age of patients ranged from 5 months till 18 years (median 5 years). Since 2013 samples have been analyzed for *TP53* mutations by Sanger sequencing. The vast majority of tumor types were rhabdomyosarcomas (RMS) – 30 patients (67% embryonal RMS, 27% alveolar RMS, 6% spindle cell RMS); 10 medulloblastomas (MB); 7 CPC, 4 ACC, 4 high grade gliomas, 3 acute myeloid leukemia (AML) and other tumors. Twelve patients developed synchronous and methachronous primary tumors.

Results: Germline mutation of *TP53* was identified in 16 patients (19%). The spectrum of tumors in patients who carried *TP53* mutation was 4 RMS, 4 CPC, 4 ACC, 1 MB and 3 patients had two primary tumors each (MB and AML, osteosarcoma and embryonal RMS, Burkitt lymphoma and ACC). We detected 10 missense mutations, most of them localized in the DNA-binding domain, 2 truncated and 1 splicing variant. Specific for Southeastern Brazil population R337H was found in a patient with ACC, whose father and sister harbored the same mutation. Novel heterozygous deletion c.749_762del, P250Hfs*9 was detected in a patient with alveolar RMS and his mother.

Conclusions: Our results demonstrate the strong association of germline mutations of *TP53* with core spectrum of LFS tumors in cohort of Russian patients and report a new genetic variant in *TP53* gene that was not described before.

Treatment and Care - Treatment Toxicity and Supportive Care

V736 SIOP19-0759 | Venous Thromboembolism (VTE) Incidence in Childhood Cancers – A Retrospective Analysis from Kingdom of Saudi Arabia

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Background/Objectives: Incidence of venous thromboembolism (VTE) in patients with cancers is a complication believed to have a negative prognostic impact, however limited information is available of the same in pediatric patient population. Pediatric Hematology section of King Faisal Specialist Hospital and Research Centre, Riyadh, manages several cases of childhood cancers with VTE.

Design/Methods: Retrospective chart review of newly diagnosed patients with malignancies during 2012 to 2016 was conducted.

Results: A total of 1775 children with cancers [Solid tumors: 54% (962); Leukemia: 22% (387); Neuro-oncology: 16%(277); Lymphoma: 8%(149)] were reviewed with an overall VTE incidence of 8% (146/1775) observed, 12%(77/962) in leukemia followed by 8% (77/962) in solid-tumors; 7% (12/277) in neuro-oncology and 4%(10/149) in lymphomas, respectively observed over a median follow-up of 3 years. Majority of Children with leukemia developed VTE in Non-Central Nervous System (CNS): 70%, defined by central venous catheter (CVC) - associated upper or lower –extremity deep venous thrombosis (DVT); while 30% developed in CNS related to Asparaginase-associated cerebral venous thrombosis, whereas in solid-tumor cases 60% presented with upfront tumor-thrombus and staged accordingly while 40% developed DVT during treatment. Non-CNS VTE observed in 60% of Neuro-oncology cases and 100% lymphoma cases. Three-Year overall survival (OS) of the cohort was 80.1%, upon comparison of Non-VTE to VTE cases an OS of 80.3% and 76.6% was observed, respectively statistically not-significant (P-value >0.05); however a longer follow-up is warranted.

Conclusions: A five-year VTE incidence of 8% observed in our cohort is comparable to published thrombosis risk of 1% - 37% in children. In leukemia, risk factors for VTE remained CVC and Asparaginase therapy while in the solid-tumors, tumor-thrombus at disease presentation emerged as a

factor worth exploring as early treatment offered to the patient might determine better outcomes, reduce treatment delays and improve survival.

V737 SIOP19-1133 | Secondary Neoplasms in Children Treated in the Civil Hospital Juan I. Menchaca. Experience Since Year 1993 to 2019

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Background/Objectives: Secondary neoplasms (SN) represent a serious complication of oncological treatment and represents a poor prognosis. The objective is to determine the incidence of SN and the associated factors in children who received treatment for different types of neoplasms.

Design/Methods: A retrospective study of patients treated from november 1993 to january 2019, between 4 months and 14 years old. Of a total of 2507 patients in this period of time 21 (0.83%) patients developed SN.

Results: Of the 21 patients developed SN the primary neoplasm was ALL (n=6), Non Hodgkin lymphoma (n=4), Hodgkin lymphoma (n=1), CNS tumors (n=2), hepatoblastoma (n=2), neuroblastoma (n=2), rhabdomyosarcoma (n=2), retinoblastoma (n=3). The SN were ALL (n=3), Non Hodgkin lymphoma (n=1), Hodgkin lymphoma (n=1), sarcoma (n=3), PNET (n=2), AML (n=4), Osteosarcoma (n=4), LGC (n=2), Adenocarcinoma (n=1). Median latency was 44 (rango 1 to 168) months. Of patients with SN 42.8% were treated with radiotherapy, and 90.4% chemotherapy. Among the received chemotherapeutics we find etoposide, alkylating agents and anthracyclines. Of the 21 patients with SN 13 (61.9%) died, all of them during therapy, 4 (19%) are in treatment, and 4 (19%) are in surveillance.

Conclusions: AML and osteosarcoma were the most frequent SN. A correlation was found between the use of radiotherapy, and cumulative doses of chemotherapeutics such as etoposide, alkylating agents and anthracyclines with the development of SN as in similar studies. The 61.9% mortality in patients with second neoplasms corroborates the poor prognosis of these patients. A follow-up of the surviving children is needed to determine the total impact of the treatment and other factors for the risk of developing second neoplasms.

V738 SIOP19-0818 | Virtual Visits and USB Flash Drives can Provide Electronic Information to Reduce Oncology Treatment Toxicity

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Background/Objectives: Treatment toxicity is a common problem for patients with childhood cancer. Face-to-face and visual communication tools can provide high quality information. Because of our treatment team's interest in preventing and ameliorating treatment toxicity, we increased our efforts using audio-visual and media tools including virtual visits to address treatment toxicity issues.

Design/Methods: Patients on active treatment currently get chemotherapy calendars, a summary which includes a problem-list ("Opportunities to Improve Health"), and additional information on a USB flash drive. Since 2017 virtual visits have also become common for patients throughout North America. For patients outside of North America we offer Cleveland Clinic's MyConsult with a follow-up summary via email, then in some cases phone and/or FaceTime. "Opportunities to Improve Health" includes an anticipation and reduction of side effects section. We analyzed virtual visit trends in age, diagnosis, location, and information shared to reduce toxicity.

Results: In 2017-2018 we conducted 223 virtual visits; 51.3% were ≤ 18 years old, 33.2% 19-30 years old, and 16% were 31+ years old. Diagnoses included Ewing sarcoma (37%), osteosarcoma (36%), desmoplastic small round cell tumor (DSRCT, 11%), other sarcomas (8%), and paragangliomas (3%). Areas served were midwest (68); south (62), west (37), northeast (28), and southwest (12). At least 3 common opportunities to reduce toxicity were addressed in 100% of virtual visits. The most common were nutrition, nausea, and hematologic toxicity. Other topics included pain, monitoring and reducing lung, cardiac, and GI toxicity, infection prevention, fatigue, activity guidelines, and neurocognitive function.

Conclusions: Supportive care and treatment toxicity can be addressed visually using electronic educational approaches including pdf calendars & articles, summaries, virtual visits, FaceTime, email, and USB flash drives. Hopefully our efforts will inspire others to use virtual visits and other media resources to improve supportive care and to more effectively reduce treatment toxicity in pediatric oncology.

V739 SIOP19-1144 | Successful Implementation of a Pediatric Early Warning System (PEWS) in 10 Resource-Limited Pediatric Oncology Centers in Latin America and the Caribbean

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Background/Objectives: Pediatric Early Warning Systems (PEWS) are clinical assessment tools for early identification of clinical deterioration in hospitalized patients. PEWS are used to improve care for pediatric oncology patients in high-resource settings; however, it is unclear if they can be implemented in hospitals of varying resource levels. We describe the successful implementation of PEWS in 10 resource-limited pediatric oncology centers in Latin America and the Caribbean.

Design/Methods: In April 2017, we created the EVAT Program to improve hospital outcomes for children with cancer through implementation of PEWS. Each center participated in a mentored, 3-phase quality improvement program to: 1) create a prospective registry of clinical deterioration, 2) pilot and implement PEWS, and 3) achieve programmatic sustainability. Regional and international PEWS implementation experts trained local leadership teams in standardized PEWS implementation methodology. The local team then trained all clinical personnel and monitored quality of PEWS implementation via three process measures: omissions, errors in calculation, and non-adherence to the PEWS algorithm. Implementation "success" was defined by 2 consecutive months with <15% errors in these measures.

Results: Participating centers included 2 oncology, 6 pediatric, and 2 general hospitals in 7 countries, with a combined 6000 annual pediatric oncology hospital admissions. Nursing:patient ratios ranged from 1:3 to 1:10. Centers began phase 1 between April and June 2017, were sequentially trained in program methodology, conducted a pilot, and implemented PEWS. All 10 centers met criteria for successful implementation requiring a median of 5.5 months (range 3 to 10) from pilot start to implementation completion. Combined, over 700 nurses and physicians were trained in PEWS.

Conclusions: PEWS can be quickly and successfully implemented using a mentored quality improvement approach across pediatric oncology centers in hospitals of varying organization and resource-levels, resulting in high program qual-

ity and excellent adherence to established standards. We now focus on programmatic sustainability and evaluating impact.

V740 SIOP19-0081 | Iron Overload in Children Treated for Hematological Malignancies

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Background/Objectives: Iron-overload leads to oxidative stress. A mild/moderate degree of iron-overload may be concerning; immune dysfunction has been reported. Indications for estimation of liver/myocardial iron concentration (LIC/MIC) or iron chelation in cancer survivors are not described.

Design/Methods: The cross-sectional study was performed in children treated for hematological malignancies. Patient's ≥ 6 months from therapy completion, who had received ≥ 5 red-cell transfusions were enrolled. Patients with relapsed disease or hematopoietic transplant were excluded. T2*-weighted magnetic resonance imaging (T2*MRI) and serum ferritin were performed.

Results: Four-hundred and thirty-one patients were screened. Forty-five patients, including, B-ALL: 32 (72%), T-ALL: 5 (11%), AML: 4 (9%), T-NHL: 3 (7%) and MPAL: 1 (2%) were enrolled. The median age at diagnosis and enrolment was 7 and 11 years, respectively. The median number of red-cell units transfused was 8 (IQR: 7, 10). The mean serum ferritin was 581 ± 454 ng/ml (range: 32-2115) and was >1000 ng/ml in 5 (11%) patients. The elevation in LIC was mild (2-7 mg/g) and moderate (7-15 mg/g) in 18 (41%) and 2 (4.5%) patients, respectively. The MIC was elevated in 2/44 (4.5%) patients. All patients with serum ferritin >1000 ng/ml had an elevated LIC. The LIC correlated with ferritin ($r=0.49$, $p<0.001$). The MIC did not correlate with either serum ferritin or LIC. The number of red-cell units transfused correlated with ferritin ($p=0.001$) and LIC ($p=0.012$). A serum ferritin >500 ng/ml predicted an elevated LIC with sensitivity/specificity of 80%/79%, respectively. A cut-off of 8-units of red-cell transfusions predicted an elevated LIC with sensitivity/specificity of 95%/49.8%, respectively.

Conclusions: The prevalence of an elevated LIC and MIC was 45.5% and 4.5%, respectively. No patient had severe iron overload. We suggest screening by serum ferritin for patients who have received >8 transfusions. A T2*MRI may

be avoided in patients with serum ferritin >1000 ng/ml, as all the patients had an elevated LIC.

V741 SIOP19-1182 | Developing an Intensive Care Assessment Tool (PROACTIVE) to Improve Care for Hospitalized Pediatric Oncology Patients with Critical Illness Using A Modified Delphi Consensus

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Background/Objectives: Hospitalized pediatric oncology patients are at high-risk for critical illness, especially in resource-limited settings. Hospitals in low- and middle-income countries (LMICs) manage this high-risk population with limited resources, affecting quality of care and outcomes. The objective of this study was to identify the most relevant quality indicators for inclusion in PROACTIVE (Pediatric Oncology cApaCity Assessment Tool for Intensive Care), a tool to assess the capacity and quality of pediatric critical care services offered to pediatric oncology patients in resource-limited settings.

Design/Methods: A comprehensive systematic literature review identified the most relevant quality indicators capturing gap priorities in the areas of structure, performance, and outcomes. An international expert focus group (n=11) reviewed and sorted potential indicators using the framework of domains (e.g. personnel, service capacity) and subdomains (e.g. general laboratory, medications). A three-round modified Delphi was executed among a group of 36 experts from 18 countries to reach consensus. Experts had diverse experience in pediatric oncology and critical care in resource-limited settings. Quality indicators were ranked on relevance (captures key aspects in the clinical process) and actionability (can be acted upon to improve patient care) via electronically distributed surveys.

Results: The focus group generated a list of 290 indicators and narrowed it to 175 potential indicators subject to expert ranking. Only indicators with high median importance in both relevance and actionability and $\geq 80\%$ evaluator agreement

were included in the final PROACTIVE tool, which contained indicators among 9 domains and 25 subdomains.

Conclusions: PROACTIVE is a consensus-derived tool to assess baseline capacities and quality of pediatric oncocritical care in resource-limited settings. Future work will involve utilization of this tool by institutions to identify service delivery gaps amenable to improvement, thereby its ability to influence inpatient quality of care and outcomes.

V742 SIOP19-0699 | Impact of Providing Holistic Care Outside the Hospital During Intensive Chemotherapy on Outcomes of Hematolymphoid Malignancies: The St Jude India Childcare Centres (SJICC) Experience

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Background/Objectives: In India, with comprehensive pediatric cancer units being located in major cities, many families travelling from far off places for treatment have to refuse or abandon therapy because of lack of accommodation. SJICC (<http://www.stjudechild.org>) run by an NGO came forward to bridge this gap and provide along with free accommodation, a hygienic environment, healthy nutrition and vocational activities.

Design/Methods: To evaluate the impact of such holistic care on the outcomes of children <15 years with hematolymphoid malignancies, we retrospectively analysed the survival of children registered with Tata Memorial Hospital from January 2013 to December 2016 staying at SJICC (Cohort A) versus those residing elsewhere (Cohort B).

Results: Out of 2368 patients treated, 344 (14.5%) stayed at cohort A whereas 2024 (85.5%) stayed at cohort B. The 5 year EFS for Cohort A and B was $62.5 \pm 4.3\%$ and $60.4 \pm 1.4\%$ whereas OS was $83.3 \pm 2\%$ and $73.8 \pm 1.4\%$ respectively. While the EFS was tending towards significance ($p = 0.051$), OS was highly significant (0.001). In disease specific EFS, there was a statistically significant difference in EFS between the cohorts for AML ($p = 0.02$) whereas for ALL, NHL and HL there was no statistical significance (p value ALL = 0.096 NHL = 0.123 HL = 0.14). In disease specific OS, there was a statistically significant difference in OS between the cohorts for AML, ALL (p value AML = 0.017 , ALL = 0.017) whereas for NHL and HL there was no statistical significance (p value NHL = 0.123 , HL = 0.14). In comparison to non relapse mortality, there was a statistically significant better survival for AML and ALL in cohort A ($p = 0.009$ and 0.005).

Conclusions: Environment plays a major role in outcomes especially of cancers requiring intensive treatment like acute

leukemia which was proved by improvement in non relapse outcome of children residing at SJICC where along with clean hygienic environment, children also got nutritional and emotional support.

V743 SIOP19-1706 | Longitudinal Assessment of Central Line Associated Blood Stream Infection (CLABSI) Education in Vietnam

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Background/Objectives: CLABSI are highly preventable complications associated with pediatric oncology patient care. LMIC's often do not focus on care delivery models to improve overall patient morbidity and mortality. In Vietnam, a generation of healthcare providers also struggle with limited experience and a lack of formalized education. Subsequently, 6.8-7.6 CLABSIs/1000 central line-days have been documented in Vietnam compared to 1.14 infections/1,000 central line-days in the U.S.A.

The purpose of this study is to develop an education module on CLABSI prevention and evaluate its effectiveness. Using the PDSA model for improvement, our global aim is to improve pediatric cancer care in Vietnam by addressing healthcare delivery models with a smart aim of improving CLABSI nursing education. Specifically, 70% of participants will demonstrate good comprehension/retention and none will demonstrate poor comprehension/retention following a 6 month interval.

Design/Methods: We provided formalized didactic and hands-on education to nursing staff regarding the importance of CLABSI prevention and identified practical protocols for policy implementation over two years. An educational module on CLABSI prevention was developed using guidelines from CDC, The Joint Commission, and APHON. Comprehension/retention was measured using a 9-question survey testing the content of the educational module before and after the intervention. Good comprehension/retention was defined as missing one question or less and poor comprehension/retention as missing four or more questions.

Results: Our 2017 assessment found that 40% of nurses after the intervention demonstrated good comprehension/retention. In 2018 we found that prior to the intervention 60% of nurses demonstrated good comprehension/retention while 10% demonstrated poor comprehension/retention. Assessments improved further after repeating the intervention after which 79% of nurses demonstrated good comprehension/retention and no nurses demonstrated poor comprehension/retention.

Conclusions: Based on these results, the educational module proved effective in increasing comprehension/retention. Participation and appreciation of CLABSI has improved between interventions suggesting appreciation and value for improved care delivery models within Vietnam.

V744 SIOP19-0512 | Implementation of I-Pass Standardized Handoff Communication System Across Clinical Disciplines at a Major Pediatric Cancer Center

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Background/Objectives: Hundreds of thousands of patients die each year due to medical errors of which communication failures are a common root cause. Standardized, structured handoff systems have been shown to improve communication, decreasing medical errors and preventable patient harm. I-PASS, a mnemonic for Illness Severity, Patient Summary, Action List, Situational Awareness, and Synthesis by Receiver, is a standardized patient handoff system that has been well-studied at numerous academic medical centers. The objective of this quality improvement initiative was to standardize handoff processes by adapting and implementing the I-PASS system across multiple handoff contexts within our institution.

Design/Methods: I-PASS was adapted and implemented using a phased approach across several handoff contexts within the hospital. Prior to implementation, researchers partnered with clinical staff from each discipline to appropriately adapt I-PASS for inpatient nursing bedside report, physician evening handoff, and handoffs that occur when admitted patients travel to other areas within the hospital (eg. Radiology). Clinician training was based on adult learning principles that allowed for modeling and constructive feedback. To ensure successful implementation and sustained use, peers were trained to audit handoffs, score performance, and provide reinforcing and formative feedback. The primary performance metric was percentage of observed handoffs that utilized all 5 components of the I-PASS mnemonic. Data were collected from 3/17-2/19 for inpatient nurses, 9/17-2/19 for physicians, and 11/17-2/19 for handoffs occurring when admitted patients traveled within the hospital.

Results: Across the study period, adherence to I-PASS structure was 87.9% for inpatient nurses (n=1299 observed handoffs), 72.8% for physicians (n=317 observed handoffs), and 91.6% for handoffs occurring when admitted patients traveled within the hospital (n=215 observed handoffs).

Conclusions: Our hospital's widespread implementation of the I-PASS handoff communication system demonstrates its adaptability. We plan to continue to expand our use of I-PASS to optimize clinician communication and enhance patient safety.

V745 SIOP19-1713 | Southeast Asia Pediatric Hematology Oncology (SEAPHO): Developing a Comprehensive Collaborative Longitudinal Paradigm for Global Pediatric Oncology in Vietnam

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Background/Objectives: Paradigms in global health have evolved from the single medical mission pioneered by Stanford's Interplast group in 1969 to more sustainable, longitudinal approaches in education and infrastructure for low-and-middle income countries (LMICs) today. Yet, these ventures generally remain singular in focus and support. Rarely, does more than one institution or foundation take on a collaborative, comprehensive approach to sustainable change. We present a new paradigm - collaborative, comprehensive development of pediatric oncology related-programs in Vietnam.

Design/Methods: Postulated to have a <5% 5-year survival rate, a local foundation approached UT Health San Antonio in 2011 seeking assistance to improve pediatric oncology care in Vietnam. Initially utilizing traditional methodologies including observerships to develop a frame-of-reference, in-country training, and communication, a relationship was nurtured on the basis of trust and beneficence. Differing from other twinning programs, this singular relationship has expanded to include multiple entities from other academic institutions including UCSF, global organizations, government entities, and NGOs, all working collaboratively with local foundations, treatment centers, and educational entities within Vietnam.

Results: While traditional measures of Vietnam's development remain forthcoming, advancement can still be documented. Initially siloed, institutions and leaders have unified to form the Vietnamese Pediatric Oncology Consortium (VPOC). Academic scholarship focusing on quality improvement has yielded multiple presentations and publications in both local and international arenas. Development of the first pediatric palliative care program and a renewed emphasis of

outpatient care has reduced hospital overcrowding and placed new relevance in cancer care delivery. Institutional survival rates are now also comparable to other LMICs. Beyond laying this foundation, Vietnam is now poised to develop a national training program, a national multi-institutional therapeutic protocol, while in parallel expanding into nursing and psychosocial arenas.

Conclusions: Global health paradigms have evolved significantly. New multi-institutional complex collaboratives such as that modeled in Vietnam illustrate innovative potential for other LMICs.

V746 SIOP19-0924 | Creatinine and Cystatin C- Can We Move Forward to Improve the Monitoring of Renal Function in Patients Undergoing Chemotherapy?

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Background/Objectives: Uncertainty surrounds the optimum method for estimated glomerular function rate (eGFR) in paediatric oncology patients. Newer methods, including the use of cystatin C, may improve current practice. It is unknown how prolonged nephrotoxic exposure effects the accuracy of the biomarkers and whether their accuracy declines during chemotherapy.

Design/Methods: A prospective, longitudinal study examined 132 combined isotope GFR (iGFR), creatinine and cystatin C measurements taken from 48 paediatric oncology patients at Leeds Children's Hospital. Correlation and agreement analysis at multiple time points was performed for biomarkers and multiple estimating equations. Sensitivity/specificity data, along with ROC curve analysis was performed for all biomarkers and estimating equations. Data from 3 patients was isolated, examining individual patient variation over time.

Results: Creatinine identified 1/32 patients with an abnormal iGFR and cystatin C identified 12/32. Creatinine and all estimating equations failed to change significantly over a period of declining iGFR, though cystatin C showed a significant inverse increase ($p < 0.05$). Bland Altman analysis for both the combined equation and creatinine alone showed poor agreement (mean difference -20mls/min/1.73m² and -64mls/min/1.73m² respectively). All biomarkers and equations showed poor sensitivity to detect an abnormal iGFR. Application of a transformation factor to the equations significantly improved their sensitivity. Analysis of 3 individual patients failed to show a constant relationship between their eGFR and iGFR over a period of chemotherapy.

Conclusions: Data from this study cannot support the use of creatinine or cystatin C as biomarkers to monitor renal

function in children undergoing chemotherapy. Newer cystatin C and creatinine combined equations do not offer the accuracy to replace iGFR or provide a tool for accurate dose calculations. A transformation factor can be applied to the estimating equations to significantly improve sensitivity to detect abnormal iGFR. Individual eGFR measurements do not remain constant in relation to the iGFR and individual transformation factors cannot be applied.

V747 SIOP19-1693 | Pneumatosis Intestinalis in the Pediatric Oncology Population: An Eleven Year Retrospective Review at Memorial Sloan Kettering Cancer Center

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Background/Objectives: Pneumatosis intestinalis (PI) is characterized by the presence of intramural gas in the gastrointestinal (GI) tract. The high incidence of PI in pediatric oncology patients has been well-documented in the literature, as this unique subset of patients become exposed to multiple factors which predispose to this intestinal pathology. The overall aim of this study was to review and lend analysis towards our experiences of pediatric oncology patients who developed PI.

Design/Methods: This was a single institution retrospective study from Memorial Sloan Kettering Cancer Center, a tertiary pediatric oncology center. Patients diagnosed with PI between 2007-2018 were identified from ICD10 coding of radiology reports. For each patient, the time-to-resolution (TTR), defined as the time elapsed between date of PI diagnosis to the first date of resolution (signified by absence of PI on imaging, advancement of diet, or de-escalation of antibiotics) was recorded.

Results: Forty-four patients were identified. Median age was 8.7 years (range 1.0-25.3 years). Twenty patients were females (45%) and 24 were males (55%). In 10 patients (23%), PI was diagnosed incidentally on imaging. Surgical intervention was required for three patients. Median TTR of PI was 3.5 days [95% CI: 3 to 7 days]. Two patients died without resolution of PI, though neither death was attributed to the PI. Antecedent stem cell transplant ($p=0.073$), concurrent pneumomediastinum ($p=0.071$), no change in diet at PI diagnosis ($p=0.090$) and steroid use in the past 30 days ($p=0.006$) were correlated with TTR in univariate analysis. In multivariate analysis, only administration of steroids in the past 30 days was significantly associated with higher chance of resolution of PI (HR = 2.54 [95% CI: 1.31-4.94], $p=0.009$).

Conclusions: Low rates of surgical intervention in this study support the success of conservative management in PI. A prospective study is warranted to define management guidelines for PI in the pediatric oncology population.

V748 SIOP19-1172 | Reduction in Blood Stream Infections after Intervention of Prephral Cannulation Practices at Peads Oncology Indus Hospital Karachi

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Background/Objectives: Pediatric cancer patients are immunocompromised and they are at high risk to obtain the Hospital Acquire blood stream Infections BSIs. Although there is a great risk of BSIs in pediatric oncology while using Central Venous Catheter PICC Line, porta - Cath despite of these used Peripheral venous catheter (PVC). PVC frequently used in hospitalized patient. It related to blood stream infections that is common cause of nosocomial bloodstream infection and also increase the morbidity, mortality. the objective of the study is to access the impact of education, and aseptic non touch technique on reduction in infection rates at oncology pediatric unit.

Design/Methods: We did an interventional study between Jan 2018 to December 2018, PLABSI data was collected from medical record and direct observation of care bundle. There are total 301 Nurses and 14445 patients of oncology were included in our study. Practices were observed after and before strategies. Education was provided based on WHO, CDC.

Results: Pre intervention PLABSI rate was 5.6 and post intervention rate was 2.45. The common organisms causing Catheter related BSI were *Staphylococcus aureus* (7%), *Klebsiella species* (14%), *Acinetobacter* (9%), VRE (3%), *E.coli* CRE (22%) and *Acinetobacter* spp (9%).

Conclusions: Bloodstream infections (BSI) are an important cause of morbidity and mortality. Most of the catheter related blood stream infections occurs due to lack of proper aseptic measures. Through education we can improve both compliance with safety steps for peripheral venous catheter insertion and performance of an optimum procedure was effective and was regarded helpful by healthcare workers.

V749 SIOP19-1293 | Evaluation of Late-Cardiotoxicity of Patients Treated for Hodgkin Lymphoma in Childhood by 3-Dimensional Echocardiography

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Background/Objectives: Patients with Hodgkin Lymphoma are at risk for long-term cardiac diseases because of the treatment methods applied. Early detection of cardiac changes in patients allows early intervention. For this purpose, 3-dimensional (3D) echocardiography is recommended for these patients.

In this study, it is aimed to determine long term cardiac changes by 3-Dimensional (3D) echocardiography method in patients with Hodgkin Lymphoma treated in childhood.

Design/Methods: The study included 50 patients with Hodgkin Lymphoma aged between 15- 54 years (median 25) who were treated with anthracycline and/or mediastinal radiotherapy at Hacettepe University. The median duration of remission was 14 years (3-39 years). Cardiac biomarkers were determined. Left ventricular ejection fraction (LVEF), and global and segmental strain and diastolic functions were evaluated with 3D echocardiography.

Results: Mean LVEF was $56.6\% \pm 5.12$. LVEF was detected lower than normal in ten (20%) patients. All but one patient who had low LVEF were asymptomatic. There was a statistically significant relation between low LVEF and mediastinal radiotherapy history ($p=0.029$). Only one patient's BNP level was higher than normal, however LVEF was normal. There was a statistically significant correlation between LVEF and global longitudinal strain (GLS) (mean GLS for low and normal LVEF were -8.90 and -13.23 respectively, $p<0.001$).

Conclusions: With 3-dimensional echocardiography, cardiac disorders can be detected more precisely before onset of symptoms. Mediastinal radiotherapy is a risk factor for cardiac disease development.

V750 SIOP19-0786 | Neutrophil Function in Cytotoxic Chemotherapy (NICC Study): A Prospective Cohort Study to Determine the Impact of Chemotherapy on Neutrophil Function in Paediatric Patients with Cancer

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Background/Objectives: Neutropenic fever is a common complication for children treated with chemotherapy. Early recognition and treatment are essential to successful management of neutropenic sepsis. To date, however there has been no focus on neutrophil function in addition to measuring cell count. A pilot study was conducted to measure neutrophil function pre- and post- chemotherapy administration compared to healthy controls. Ultimately, our aim is to determine if this assay could be used to predict patients at risk of infection and direct personalised, empirical antimicrobials.

Design/Methods: Pilot prospective cohort study to recruit children with oncological conditions requiring chemotherapy. Paired samples were taken before chemotherapy and 5-8 days later. A comparator population of healthy children was recruited. We used a flow cytometric citrated whole blood phagocytosis assay to measure neutrophil association and oxidation of standardised intraphagosomal-reporter beads. This assay had previously been validated in adult and paediatric healthy and sepsis patient populations. NHS REC and HRA approvals were obtained. Data reported as median [IQR] and appropriate non-parametric statistical tests applied (STATA V13).

Results: We collected paired samples for 15 oncology patients, and 10 single samples from control patients. Neutrophil oxidation of intraphagosomal reporter beads was significantly lower in pre-chemotherapy oncology (0.21 [0.15-0.27]) compared to control samples (0.36 [0.27-0.44]), $p=0.027$. This occurred despite significantly increased expression of neutrophil maturity markers CD16 (32178 vs. 18834, $p=0.005$) and CD66B (2475 vs. 1580, $p=0.021$) in oncological samples. We observed a non-significant trend to decreased neutrophil function in paired post-chemotherapy samples (phagocytic index 0.46 vs. 0.71, $p=0.156$).

Conclusions: Measurement of neutrophil function is feasible in paediatric oncological patients. We observed decreased neutrophil function in oncological patients compared to healthy controls. This pilot study demonstrates proof of concept and supports further work to determine if impaired neutrophil function can predict neutropenic sepsis and guide personalised antibiotic therapy.

V751 SIOP19-0798 | Optimal Rasburicase Dosing for Prophylaxis of Tumour Lysis Syndrome (TLS)

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Background/Objectives: The British Committee for Standards in Haematology (BCSH) recommends a single dose of 0.2mg/kg Rasburicase for children at high risk of tumour lysis syndrome (TLS), followed by close monitoring. Whereas a capped dose of 3mg is suggested for adults, there is insufficient evidence to guide nationally divided paediatric practice.

Design/Methods: To investigate rates of TLS in lymphomas and leukaemias with different prophylactic Rasburicase dosing strategies, we retrospectively examined (through case-note review) practice at our tertiary paediatric oncology centre over the past two years (22 cases). 50% (11 patients) received 0.2mg/kg; 50% received a capped 3mg dose.

Results: Five patients (23%), all with acute lymphoblastic leukaemia (ALL) or lymphoblastic lymphoma (LBL),

developed TLS despite prophylactic Rasburicase (two laboratory TLS, three clinical TLS with acute kidney injury). All had received a capped dose, i.e. 46% of patients developed TLS after a capped dose, versus 0% with 0.2mg/kg ($p=0.01$, 2-tailed $\square$ 2).

Rates of TLS may have been confounded by the increased numbers of ALL or LBL in the capped and lysing group (9/11 = 82%) versus the uncapped group (4/11 = 36%) – rates of TLS were significantly higher in patients with ALL/LBL versus other diagnoses ($p=0.03$, 2-tailed $\square$ 2).

Conclusions: We considered using a two tier Rasburicase dosing strategy for patients at high risk of TLS (uncapped for ALL/LBL, capped for others) but later chose a unified approach, recommending an initial uncapped dose (0.2mg/kg) for all high risk patients, as the risk and cost of established TLS with capped dosing outweighed any savings from using less Rasburicase.

V752 SIOP19-0969 | Varicella Post-Exposure Management for Immunocompromised Patients in Pediatric Hemato-Oncology: A French Prospective Regional Multicentric Study (VARIFHOP)

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Background/Objectives: The occurrence of varicella in a child receiving chemotherapy is a challenging situation. Literature evaluating varicella post-exposure management (VPEM) in this situation is scarce. Our regional care network for pediatric hematology-oncology (RIFHOP) recently published VPEM recommendations. The main objective of the VARIFHOP study is to prospectively evaluate health care

providers' adherence to these recommendations as well as overall VPEM in the Île-de-France area.

Design/Methods: VARIFHOP is an observational, prospective and multicentric study for patients aged 0-18 years, receiving care in a RIFHOP centre for a malignancy, and presenting with significant varicella exposure.

Results: From 01/2017 to 01/2019, 51 patients from 15 RIFHOP centres were enrolled after 52 episodes of varicella exposure. Median age at exposure was 5 years. Most common malignancy was leukemia (60%). Anti-VZV immune status in the patients' close family circle was inadequate for 73% of patients, leading to 38% of all significant exposures. Prophylactic treatment consisted in specific anti-VZV immunoglobulins (V-ZIG) ($n=19$) or in oral aciclovir ($n=15$). Eighteen pts did not receive any prophylactic treatment as they were known to be immunized against VZV. Adherence and tolerance of prophylactic treatment were 97% and 94%. RIFHOP recommendations were respected in 47/52 (90%) of episodes; VPEM was then effective in 39/47 episodes (83%) versus in 2/5 (40%) when recommendations were not followed. V-ZIG proved to be efficacious in 70% of cases, aciclovir efficacious in 87% and absence of prophylaxis appropriate in 83%. Eleven patients presented with post-exposure varicella, with a simple course in all cases. Chemotherapy had to be held for a median time of 7 days (range 5-12).

Conclusions: RIFHOP recommendations have been widely respected. Our current VPEM guidelines are efficient for our immunocompromised patients. Anti-VZV immunization of seronegative close family members needs to be encouraged. We do not report any complicated VZV infection after VPEM.

V753 SIOP19-0762 | Machine Learning Approach to Forecast Chemotherapy-Induced Haematological Toxicities in Patients with Rhabdomyosarcoma

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Background/Objectives: Major adverse effects of Ifosfamide-Actinomycine-Vincristine (IVA) treatment for rhabdomyosarcoma are haematological toxicities such as neutropenia. Among individual patients, the severity of these effects varies but their dynamic profiles are similar. A non empirical adjustment of the initial dose to avoid severe levels of these toxicities could be beneficial for patients. We developed a machine-learning approach to forecast the IVA induced haematological toxicities.

Design/Methods: Patients with rhabdomyosarcoma were treated with up to 9 cycles of IVA chemotherapy. Before and during each cycle, routine multiple blood cell counts were performed allowing for a dynamic study of the haematological toxicities. We developed a machine learning analysis using gradient boosting regression techniques to compute dynamic models (decision tree based) for neutrophil and platelet levels. Several regression parameters were optimized using a grid search technique. To validate models' accuracy, we performed a cross-validation and compared predicted and observed neutrophil and platelet levels.

Results: 21 patients were included (mean age 7). The first four cycles have been modeled as a function of neutrophil and platelet initial levels and the initial dose of ifosfamide. Among all cycles, the mean absolute error between predicted and observed neutrophil (platelet) levels was 1.2 G/L (67.3 G/L). During the first cycle, the mean absolute error on neutrophil (platelet) levels was 0.48 G/L (43.4 G/L). In addition, our dynamic models are capable of predicting neutrophils and platelets aplasia duration.

Conclusions: The dynamic profiles of haematological toxicities of patients with rhabdomyosarcoma were modeled using a machine learning technique. Adjusting a patient's ifosfamide dose based on the predicted haematological toxicity levels at the end of a treatment cycle could enable a tailored follow-up during the treatment.

V754 SIOP19-1095 | Metronomic Chemotherapy: Experience of a Subsaharan Center of French-African Pediatric Oncology Group (GFAOP)

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Background/Objectives: Treatment of childhood cancers remains undeveloped in sub-Saharan Africa. According to WHO, 300 000 new paediatric cancer are diagnosed every year. Only 20% are cured in low-income countries. Since 2000, the French African paediatric oncology group (GFAOP) provided drugs for five protocols in Africa: ALL, Nephroblastoma, Non Hodgkin Lymphoma, Hodgkin lymphoma and retinoblastoma. Many other pediatric cancers are also diagnosed and treated. However, inaccessibility of some drugs and lack of supportive care means that curative protocols are not available. Metronomic treatment is an alternative for many children.

The aim of this retrospective study was to assess the safety of metronomic chemotherapy in pediatric solid cancers.

Design/Methods: The study included children with a solid cancer. Metronomic treatment was proposed to children with partial response for whom no further curative treatments were available.

It consisted in cycles of 56 days (8 weeks) with weekly vinblastine 3 mg/m² (week 1-7), daily cyclophosphamide 30 mg/m² (days 1-42), and twice weekly methotrexate 15 mg/m² (days 21-42), and daily celecoxib 100 mg to 400 mg twice daily (days 1-42) followed by a 2-weeks chemotherapy break. Tolerance were evaluated by clinical examination and laboratory analysis.

Results: From July, 2011 to August, 2018 we included 30 children. Median age was 9 years old (range: 12 month- 16 years). 57% were female. Disease included osteosarcoma (14), neuroblastoma (9), sarcoma (3), hepatoblastoma (2), ovarian dysgerminoma (1) and chest relaps of nephroblastoma (1). Treatment was generally well tolerated; 4 episodes of moderate mucositis and 3 non febrile aplasia occurred. 8 patients completed 10 cycles of treatment without detectable disease including osteosarcoma (5), neuroblastoma (2) and sarcoma (1). 12 patients in treatment have stable disease. 6 patients in progressive disease died. 4 patients abandoned the treatment.

Conclusions: The metronomic regimen we report here was well tolerated and associated with disease stabilization. A multicenter study will be interesting in subsaharan Africa.

Keywords: Metronomic chemotherapy- Subsaharan Africa- Childhood cancer- GFAOP.

V755 SIOP19-0625 | Puberty Development and Testicular Growth after Cryoconservation in Prepubertal Boys Facing Gonatotoxic Therapy

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Background/Objectives: Advancements in oncologic therapies have improved long-term survival rates in childhood cancer, but increased the infertility rate among the survivors. Testicular cryopreservation is the current option in prepubertal boys at high risk of infertility. As the efficacy of fertility restoration is still unproven and little data is available about the puberty development and testicular complications after biopsy, some clinicians are still sceptic to propose the cryopreservation in daily practice.

Our aim was to illustrate the feasibility of testicular cryopreservation in prepubertal patients that undergo gonadotoxic

therapy, to describe characteristics of testicular specimens and to provide information of testicular development after biopsy.

Design/Methods: Retrospective review of gonadal biopsies, biological and clinical records of prepubertal boys with high infertility risk consented into the Toulouse Children's Hospital between 2011-2017. Patients were follow-up by ultrasound to evaluate the testicular volume and abnormalities and by a systematic endocrine assessment.

Results: Bitesticular specimens in 16 males (9 ± 2.7 years) provided an average of 25 slices per patient. None of the patients had complications during the testicular biopsy. Two patients had postoperative hematomas and one experienced hypoesthesia of the scrotum. One patient had persistent fibrotic lesions 4 years after biopsy. The last evaluation in the study group (age 11 ± 1.3 years) showed a mean testicular volume of 1.85 ± 2 ml [CI95%: 0.6 – 3]. A total of 3/28 (10.7%) testes had an epididymal cyst and 4/28 (14.2%) had a hydrocele.

Conclusions: Testicular cryopreservation can be safely performed in young patients facing gonatotoxic treatment, is easily accepted by families with little side effects in long term and does not impede the pubertal development of the testis. Future technologies may allow the spermatogonial stem cell utilization to provide fertility restoration in cancer survivors.

V756 SIOP19-1403 | Treatment Outcome and Abandonment of Treatment of Cancer in Children: An Experience from Jammu and Kashmir (India)

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Background/Objectives: Cancer is the ninth common cause for the deaths in children in five to fourteen years of age group in India. A dedicated pediatric hematology oncology ward was established in department of pediatrics, Government Medical College Jammu in October 2014 to provide free of cost treatment to children with cancer belonging to socio-economically poor families. The objective of this study was to assess the impact of establishment of dedicated pediatric hematology oncology ward on treatment outcome and abandonment of treatment of cancer in children.

Design/Methods: In this retrospective study, data of pediatric patients with cancer was collected from the Hospital records with effect from 1st Jan 2011 to 31st December 2018 and analysed to assess the impact of establishment of dedicated pediatric hematology oncology ward on treatment outcome and abandonment of treatment.

Results: A total of 172 children with cancer got registered with department of pediatrics, Government Medical College

Jammu with effect from 1st January 2011 to 31st December 2018. Majority (126) of these children had Acute lymphoblastic leukemia followed by Wilms Tumor (18), Hodgkin Lymphoma (10), AML (8), and other tumours (10). Out of these 172 children, 33 were in shared care, 47 were referred to higher centres and 92 opted for treatment in our centre out of whom 32 died, 21 completed and 18 abandoned their treatment. Rest of 21 children were under treatment. A marked and progressive decline in deaths from 32% to 26% and abandonment of treatment from 37% to 5% was recorded after the establishment of a dedicated pediatric hematology oncology ward in 2014 with a consultant trained in pediatric hematology-oncology, nurses trained in administering chemotherapy and a counselor.

Conclusions: Establishment of dedicated ward for Pediatric patients with cancer helped in improving the treatment outcome and reducing the deaths and treatment abandonment in resource constrained settings.

V757 SIOP19-0005 | Prevention of Oral Mucositis in Pediatric Patients with Acute Lymphoblastic Leukemia: A Randomized Controlled, Cross-Over Trial Using 0.12% Chlorhexidine Gluconate and 1% Povidone Iodine Mouthwash

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Background/Objectives: **Background:** Oral stomatitis occurs in up to 52-80% of children undergoing chemotherapy. Standard oral hygiene includes several mouthwashes that may be chosen for prophylactic and therapeutic use, however, there are only a few studies which compare their efficacy in pediatric acute lymphoblastic leukemia (ALL). **Objective:** To compare the efficacy of 0.12% chlorhexidine gluconate and 1% povidone iodine mouthwash in the prevention of oral lesions in children with ALL receiving chemotherapy.

Design/Methods: **Design:** Prospective, randomized controlled, non-blinded, two period cross-over trial was conducted at the University of Santo Tomas Hospital-Benavides Cancer Institute.

Method: Twenty-one eligible children ages 6 to 18 years from August 2013 to December 2014, were divided into two groups. Group 1 was instructed to rinse with 10 mL of 0.12% chlorhexidine gluconate mouthwash twice daily, and Group 2 with 10 mL of 1% povidone iodine mouthwash twice daily, for 14 days or until lesions healed. Alkaline saline mouthrinse was used during the two week 'washout' time. The groups then switched mouthrinses during the second study period. Occurrence of ulcerative lesions and severity of mucositis

were measured at baseline and twice weekly. Descriptive statistics, generalized linear models, paired t-test, and McNemar's test were applied.

Results: Four subjects experienced mucositis while using 0.12% chlorhexidine mouthwash, while two developed mucositis while using 1% povidone iodine mouthwash. Chlorhexidine gluconate mouthwash has a higher mean score than 1% povidone iodine mouthwash on both dependent variables. Mean duration of mucositis while using chlorhexidine is 9.5 days (3-16 days) while for povidone iodine, 6 days (3-9 days). The differences are not statistically significant. No side effects or complications were observed with the use of either mouthwash.

Conclusions: Both mouthwashes have similar effects in the prophylaxis and treatment of oral mucositis for pediatric patients with ALL and may be recommended in a consensus protocol for oral care during chemotherapy.

V758 SIOP19-0312 | Evaluation of Ketamine as Adjudicative Therapy for the Treatment of Dinutuximab Induced Pain in Pediatric Patients with Neuroblastoma

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Background/Objectives: Dinutuximab, a chimeric antibody used in the treatment of high risk neuroblastoma, induces cell lysis by binding to the disialoganglioside GD2 receptor. These receptors are highly expressed on neuroblastoma cells as well as other tissues including nerves and peripheral sensory nerve fibers, resulting in significant neuropathic pain experienced during therapy. The standard pain control regimen at Boston Children's Hospital includes gabapentin and morphine or hydromorphone via patient or nurse controlled analgesia (PCA/NCA). If pain is not well controlled on these agents, ketamine is considered for additional neuropathic pain control. At low doses, ketamine, a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist, produces analgesia and modulates central sensitization, hyperalgesia, and opioid tolerance. The primary objective of this study was to determine if the addition of ketamine to the standard of care for pain management reduced opioid consumption in patients undergoing dinutuximab therapy.

Design/Methods: A single center, retrospective, cohort study was conducted looking at patients that received at least one course of dinutuximab between January 2004 and March 2019. Patients eligible for inclusion were less than or equal to 18 years of age, received dinutuximab for the treatment of neuroblastoma and received standard of care with gabapentin and a morphine or hydromorphone PCA/NCA. Total opioid use was recorded as morphine equivalents. For patients

receiving ketamine, ketamine infusion rate and duration of use were collected. Additional data including baseline and maximum pain scores, maximum dinutuximab infusion rate and vital signs were also recorded.

Results: Fifty four patients met inclusion criteria for analysis. Of the 54 patients, 8 patients received ketamine for pain management during dinutuximab therapy. Average daily opioid consumption and pain scores were lower in patients receiving ketamine.

Conclusions: The addition of ketamine to the standard pain control regimen decreased opioid consumption in patients receiving dinutuximab therapy.

V759 SIOP19-1238 | Minimising Methotrexate Mistakes

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Background/Objectives: High dose methotrexate (HD MTX), defined as a dose above 1g/m², is used in the treatment of many childhood cancers, including acute lymphoblastic leukaemia (ALL), osteosarcoma, non-Hodgkin's lymphoma (NHL) and some brain tumours. All of these protocols are distinct in the HD MTX dose, frequency, specified monitoring and management of toxicity.

In our principal treatment centre (PTC), we treat approximately 15 patients per year with HD MTX. With the increasing complexity of the protocols, we anecdotally noted a rise in the number of incidents related to HD MTX.

We aimed to improve patient safety and reduce the number of errors by introducing some simple changes to practice.

Design/Methods: We retrospectively reviewed the incident reporting system for errors relating to HD MTX in our paediatric oncology population.

We introduced changes to practice including creating a specific HD MTX guideline folder, specifying each protocol and highlighting the differences in management for each cancer-type; in addition a bespoke monitoring sheet was created. Patient wrist bands were introduced to improve identification of children receiving HD MTX. An 'alert' message was added to the electronic-prescribing system to prompt clinicians to check the relevant protocol. Furthermore we presented departmental teaching sessions enhancing education around HD MTX and raising awareness of the potential for error.

Results: There were 9 reported incidents over a period of 12 months. Since the introduction of the above changes to practice and the shared teaching, there have been no further reported incidents.

Conclusions: With the advances in treatment and increasing complexities of management protocols and toxicity monitoring, the potential for error is increasing. We have shown that simple changes to practice, which are easily adopted, coupled with enhanced education and training, have made a significant impact on the reduction of errors and consequently improved patient safety.

V760 SIOP19-0713 | Clinical Safety of Glucose-Free Balanced Fluids in Pediatric Hematology and Oncology

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Background/Objectives: Traditionally, hypotonic fluids containing glucose were commonly used in pediatrics. Based on growing knowledge that these fluids can lead to hospital-acquired hyponatremia, guidelines changed to suggesting isotonic fluids. Nevertheless, most pediatricians in oncologic units still use hypotonic fluids.

In 2015, the pediatric oncology unit of Tuebingen changed to the use of glucose-free balanced fluids for all patients in hyper-hydration under chemotherapy as well as in maintenance therapy for septic patients. In this retrospective analysis, the clinical safety of this change in infusion therapy is evaluated.

Design/Methods: 140 patients with 3,224 days in stationary care 6 months before and 6 months after the change to isotonic fluids were included into this retrospective analysis. Primary outcome was equivalence in terms of change in plasma sodium (pNa) and the prevalence of hyper- and hyponatremia. Secondary outcomes were changes in acid-base balance, changes in other electrolytes than sodium and prevalence of hypo-/hyperglycemia or acute kidney injury (AKI).

Results: The changes of pNa stayed well inside the pre-defined equivalence margins. There were zero hypernatremic events. The prevalence of hyponatremia was significantly lower using isotonic fluids.

Secondary outcomes: balanced fluids decrease the risk of acidosis significantly at the cost of higher rates of alkalosis. Electrolyte levels were more stable. The rate of hypoglycemic events was slightly higher using glucose-free solutions under chemotherapy without decreasing the prevalence of hyperglycemia. The prevalence of AKI was the same in both groups.

Conclusions: Balanced fluids lower the rate of hyponatremia without causing hypernatremia in hyper-hydration and maintenance therapy and can therefore be recommended to avoid hospital-acquired hyponatremia in pediatric oncology. There were fewer disturbances in acid-base balance and electrolyte

levels. Still, the risks of metabolic alkalosis and hypoglycemia need further evaluation.

V761 SIOP19-1489 | Long-Term Childhood Cancer Survivors at High-Risk of Cardiac Disease: To Come or Not to Come at Long-Term Follow-Up Clinic ?

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Background/Objectives: To evaluate the adherence rate of childhood cancer survivors (CCS) at high-risk of cardiac disease to the long-term follow-up (LTFU) clinic program, and to determine the reasons for non-attendance.

Design/Methods: Since the initiation of Gustave Roussy (GR) LTFU program in 2012, 431 adults (age $\geq$ 18yo) 5y-CCS treated for lymphoma (n=272) or bone sarcoma (n=159) before the age of 20 years in GR between 1946 and 2000 and at high-risk of cardiac disease (i.e. anthracyclines cumulative dose $\geq$ 300mg/m² or cardiac volume irradiated at dose $\geq$ 20Gy [V20Gy] $\geq$ 5%) were contacted to propose them a LTFU visit. Two contact letters were successively used, without and with specific information regarding their cardiac risk.

Results: After first contact without specific information regarding their cardiac risk, 160 patients (91/272 treated for lymphoma, 33%, and 69/159 for bone sarcoma, 43%) had LTFU visit (sex ratio M/F=1.2, median age at diagnosis=11.1 years, median age at LTFU visit=38.3 years, range=20-63). After second contact with specific information regarding their cardiac risk, 52 other patients took an appointment (38/181 treated for lymphoma, 21%, and 14/90 for bone sarcoma, 16%). The overall adherence rate was 49%. The reasons for non-attendance were unknown for 87%; reasons reported were: having a medical follow-up elsewhere (n =11), living abroad (n = 3) or too far away from LTFU clinic (n = 3) and refusal to participate (n= 11). Female gender (OR=1.5, 95%CI=1.0-2.3, p=0.06), living address in Paris area (OR=2.6, 95%CI=1.7-4.0, p<0.0001), and response to FCCSS self-administered questionnaire (OR=4.3, 95%CI=2.7-6.9, p<0.0001) were independently associated with attendance to LTFU visit.

Conclusions: Despite the efforts of clinicians to convene high-risk patients and offer them participation to a LTFU

program, various individual factors, especially geographic remoteness, inhibit attendance. Moreover, patients who previously answered epidemiological questionnaires were more likely to come.

Fundings: Gustave Roussy foundation and “Ligue contre le cancer”.

V762 SIOP19-0817 | Evaluation of Thyroid Functions in Survivors of Childhood Head and Neck Cancers Treated with Irradiation

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Background/Objectives: To evaluate thyroid functions in survivors of childhood cancers treated with head-neck irradiation.

Design/Methods: Between 2003-2018, clinical characteristics of patients, RT and chemotherapy (CT) details, if any, side effects related to treatment were examined retrospectively. Patients were evaluated with thyroid examination, thyroid function tests (TFT), ultrasonography (USG).

Results: Of the 777 patients diagnosed with lymphoma and solid tumors, 104 patients were evaluated. The median age of diagnosis was 10years (5months-16years); M/F: 1.3. The diagnostic distribution is in table 1.93% of the patients had received CT-RT treatment, there were 7% patients receiving only RT treatment. 63%, 6%, 31% of the patients who received RT to the head-neck region received radiation to the thyroid area, partial thyroid area, non-thyroid area, respectively. TFT was abnormal in 28%(n:29) of the patients; twentythree patients had subclinical hypothyroidism, three patients overt hypothyroidism, three patient had central hypothyroidism. TFT was abnormal in twenty-six patients who received RT to the thyroid area, one patient to the partial thyroid area, two patients to the non-thyroid area. 32% of the patients (n:33) had abnormal USG; 12% nodule, 3% parenchyma heterogeneity, 13% decrease in parenchymal echogenicity, 3% thyroiditis, 1% cystic area. Hypothyroidism was present in 14/33 patients. Thyroid usg was abnormal in twenty five patients who received RT to the thyroid area, two patient receiving RT to the partial thyroid area, six patients who received RT to the non-thyroid area. 21% of the patients were receiving drug treatment due to thyroid dysfunction. Side effects associated with treatment were 6% ototoxicity and 1% cataract; no patients with secondary malignancy. Median follow-up time

was 5.8 years (10months-15years), the event-free survival rate was 97% at 1 year, 91% at 5 years, 89% at 10 and 15 years. Overall survival rate was 98% at 5 years, 96% at 10 and 15 years.

Conclusions: TFT was abnormal in 28% patients, an anomaly was detected with thyroid usg in 33% of the patients. None of the patients in this group had any secondary malignancy. Multidisciplinary follow-up with thyroid physical examination, TFT and thyroid USG is required in terms of possible thyroid dysfunction and thyroid malignancies for patients who received RT to head-neck region.

V763 SIOP19-1155 | The Effect of Early Warning Systems on Communication Surrounding Clinically Deteriorating Pediatric Oncology Patients Hospitalized in High-Resource and Resource-Limited Settings

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Background/Objectives: Pediatric Early Warning Systems (PEWS) are widely used in pediatric oncology, where implementation reduces mortality and clinical deterioration outside critical care settings. Previous qualitative work in a high-resource setting demonstrated additional benefits, including PEWS potential to empower providers to overcome barriers to care escalation. Little is known, however, about PEWS effects on communication in resource-limited settings, where mortality is high and hierarchical structures differ. This study sought to compare effects of PEWS on interdisciplinary communication in high-resource and resource-limited settings.

Design/Methods: This qualitative study included semi-structured interviews with 83 nurses, pediatricians, oncologists, and critical care providers at St. Jude Children's Research Hospital (SJCRH; N=42 participants) in Memphis, Tennessee, and at Unidad Nacional de Oncologia Pediatrica (UNOP; N=41 participants) in Guatemala City, Guatemala. Interviews were conducted in the participants' native language (English or Spanish), transcribed, and translated into English. Each transcript was coded by two members of the team and analyzed for thematic content using MAXQDA software.

Results: Themes related to communication hierarchy emerged, including “empowerment”, “reinforcement of hierarchy”, and “clinical judgment.” These themes were

explored by participants at both institutions and across all disciplines. Participants at UNOP described PEWS as principally empowering, while those at SJCRH had concerns that it diminished nurses' and floor-providers' clinical judgment, reinforcing traditional roles and hierarchy. Participants in both settings endorsed PEWS as increasing interdisciplinary communication. Methods of communication were grouped into "in-person" and "non-in person" communication. Participants at UNOP frequently described "in-person" communication, while technological advances and automatic notifications at SJCRH contributed to "non-in person communication".

Conclusions: In addition to known patient care benefits, PEWS may enhance interdisciplinary communication around patient deterioration events in high-resource and resource-limited settings. The communication advantages associated with PEWS may be particularly important in resource-limited settings, where PEWS can empower nurses and floor providers and increase face-to-face communication.

V764 SIOP19-0205 | Children with Cancer Vary Greatly in Their Resting Adrenaline Concentrations and Only Moderately Increase Adrenaline after High Intensity Exercise

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Background/Objectives: Exercise is generally recommended as an adjunct therapy for cancer patients as it counteracts the adverse effects of cancer and its treatment. Recent studies demonstrate anti-cancer effects of exercise-induced adrenaline through natural killer cell mobilization and Hippo signalling. The aim of this study was to measure the changes of the adrenaline (American English: epinephrine) concentration in children with cancer.

Design/Methods: We measured the adrenaline concentrations with a commercial ELISA kit in children aged 6-18 years between the first and third course of cancer treatment. The children performed a single bout of high intensity interval training (HIIT) on a bicycle ergometer (10x15 s at level 14-16 on a RPE scale). Blood for adrenaline analysis was taken prior to and within 3 min after exercise.

Results: Patients were 14.7 ± 4.0 years old and had the following diagnoses: Hodgkin Lymphoma (3 pts), rhabdomyosarcoma (1pt), synovial sarcoma (1pt), neuroblastoma (1pt). Finishing exercise, the blood lactate concentration increased to 4.9 ± 2.2 mmol/l and the maximal heart rate to 177 ± 11 bpm.

The average resting adrenaline concentration was 78.3 ± 82.6 pg/ml and increased to 94.0 ± 95.4 pg/ml post exercise. Two children had greatly elevated baseline adrenaline, one patient with 241.5 pg/ml (rhabdomyosarcoma) and one patient with 83.5 pg/ml (neuroblastoma). These patients showed an increase of adrenaline to 278.1 pg/ml and 118.1 pg/ml after exercise, respectively.

Conclusions: Children with cancer had greatly varying baseline adrenaline concentrations but only moderately increased adrenaline levels after exercise by 23%. High baseline concentrations of adrenaline could potentially be explained by adrenaline synthesis of the tumour, as reported in the literature. Our data may suggest that catecholamines may not contribute to potential anti-cancer effects of exercise in children, as the baseline concentrations seem variable and the increase of adrenaline during exercise is minor, even during high intensity exercise. The observation however needs to be confirmed in a larger patient cohort.

V765 SIOP19-1742 | Serious Clinical Deterioration Events of Children with Cancer at an Inpatient Area in a Referral Unit in a Middle-Income Country

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Background/Objectives: Patients admitted in pediatric hematology and oncology services are especially susceptible to develop life-threatening clinical deterioration. The aim of this study was to evaluate the incidence of serious medical complications defined as need for vasopressors, intubation, CPR, unplanned PICU transfer, or non-palliative death during their hospitalization.

Design/Methods: In 2018, we began a prospective quality improvement registry of clinical deterioration events occurring in patients hospitalized in the pediatric hematology-oncology unit of a general hospital in Mexico; the current study describes events identified from January 2018 to March 2019. Clinical data were extracted from the medical record and documented on case report forms. Data were analyzed using descriptive statistics. For qualitative variables frequency and proportion were calculated.

Results: During the 15 month study period, there were 38.33 events per 1,000 inpatient days. Analyzing the administration of critical care interventions outside the ICU, twenty events (52%) required treatment with vasopressors, eight (22%) mechanical ventilation, and 10 (26%) required

transfer to the PICU. No patients required CPR outside the PICU. Ultimately 29 (76%) of events resulted in PICU transfer, of which 12 died prior to hospital discharge, resulting in mortality of 41% and an average of staying in PICU of 5.3 days.

Conclusions: Treatment toxicity is a major cause of death in children with cancer in low-and-middle income countries, due to limited access to intensive care resources and late identification of deterioration. To address this issue, our unit plans to implement a Pediatric Early Warning System (PEWS) to reduce treatment-related complications and increasing the overall survival of our oncology patients

V766 SIOP19-0584 | Time to Antibiotics in a Cancer Center in a Low-Resource Cancer Center Setting

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Background/Objectives: In low- and middle-income countries (LMICs) like ours, delay in management of fever in the setting of neutropenia (F/N) can contribute to poor outcomes among pediatric cancer patients. Our hypothesis was that having fever incorporated into pediatric early warning score (PEWS) for triage in the emergency room (ER) would improve time to antibiotics (TTA) in F/N patients and decrease direct transfers from ER to the Intensive Care Unit (ICU). Therefore, we developed a modified PEWS score for triage in a cancer center in Lahore, Pakistan.

Design/Methods: This was a prospective cohort study of a modified PEWS scoring system that incorporated fever into the algorithm. We looked at TTA, direct ICU admissions and mortality related to F/N. All pediatric oncology patients who presented with a fever (defined as temperature of $\geq 38^{\circ}\text{C}$) to the ER were included. Univariate and simple statistical analyses were used to analyze data.

Results: We studied 93 patients who had 109 febrile neutropenia episodes before the implementation of the algorithm. There were 67 boys and 26 girls. Average TTA was 112 minutes and average stay in the hospital was 5.3-days. Mean absolute neutrophil count (ANC) was 0.24. Two children needed direct ICU admission from the ER. The modification in PEWS was done to aid early identification of sick F/N patients in our combined pediatric and adult ER. After implementation and multiple teaching sessions we conducted a post-analysis with 93 patients having 98 episodes of F/N. There were 58 boys and 35 girls. Average TTA improved by about 19.6% to 90-minutes. Average hospital stay was 4-days. Mean ANC was 0.13. None of the children needed direct ICU transfer from the ER.

Conclusions: Modified PEWS can help healthcare staff in resource-limited settings identify sick children with F/N in the ER and aid in shorter TTA, which can help reduce morbidity.

V767 SIOP19-1590 | Risk of Blood Culture Positivity During Pediatric Acute Lymphoblastic Leukemia Induction Therapy

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Background/Objectives: Pediatric patients with acute lymphoblastic leukemia (ALL) have an impaired immune system at diagnosis and are at increased risk of infection during the first 28 days of therapy. However, the rate of bloodstream infection (BSI) during induction remains unclear.

Design/Methods: All patients diagnosed between January 2005- April 2018 with ALL who were treated at the Monroe Carell Jr. Children's Hospital at Vanderbilt during induction therapy were included and their infectious complications were collected and analyzed using multivariable logistic regression.

Results: In 337 patients who received ALL induction therapy, the BSI rate from disease diagnosis through induction was 11.9% (40/337). A BSI was more common in those receiving 4-drug high-risk induction therapy (vincristine, corticosteroids, asparaginase, daunorubicin) (16.8%) versus 3-drug induction (no daunorubicin) (7.3%), $P=0.007$. A positive blood culture occurred after Day 8 in 6.5% of patients. Nearly three-fourths (73.6%, 248/337) of patients developed a fever prior to or during induction therapy and 8.5% (21/248) developed a BSI with the initial culture. On multivariable analysis, significant factors for positive initial culture included hypotension (Odds Ratio [(OR) 14.2, 95% confidence interval (CI) [2.3, 88.9], $p=0.005$) and the presence of a central venous catheter (OR 3.6, 95% CI [1.3, 10.1], $p=0.017$). Factors not found to be independently associated with a positive blood culture included fever at time of blood culture, presence of chills, and absolute neutrophil count $<500/\mu\text{L}$. Of the 99 patients discharged without antibiotics before Day 9, 21.2% (21/99) were readmitted for concern for infection during induction (fever, chills without fever, abdominal pain, cellulitis), and 8 (38.1%) developed a positive blood culture at readmission.

Conclusions: Patients in ALL induction have a moderate risk of BSIs, but the majority who are discharged do not require readmission. ALL patients undergoing a high-risk induction

and those who are readmitted for infection concerns have an increased risk of BSI.

V768 SIOP19-0839 | Outpatient Step-Down Management of Low-Risk Pediatric Patients with Fever and Neutropenia

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Background/Objectives: At Memorial Sloan Kettering Cancer Center, approximately 365 pediatric fever and neutropenia (FN) admissions occur yearly. Traditionally, these patients have been managed solely on our inpatient unit until absolute neutrophil count (ANC) recovery to $3500/\text{mm}^3$. Previous studies have demonstrated that FN patients who meet low risk criteria can be safely discharged with subsequent outpatient management prior to ANC recovery. The aim of this quality improvement initiative was to decrease inpatient hospital census, decrease healthcare costs for pediatric FN, and improve patient and caregiver QOL.

Design/Methods: We developed an algorithm for outpatient step-down management of low-risk pediatric patients with FN based on the International Pediatric Fever and Neutropenia Guideline. All patients with FN received initial inpatient treatment with intravenous antibiotics for a minimum of 48 hours. Patients who met low-risk eligibility and outpatient management criteria were discharged home on oral antibiotics until ANC increased to $>100/\text{mm}^3$. Readmission was required for recurrence of FN or for any clinical worsening prior to ANC recovery $>500/\text{mm}^3$.

Results: From September – December 2018, 58 (72.5%) of 80 pediatric admissions for FN met low-risk eligibility, and 27 (46.5%) of these patients met outpatient management criteria. Twenty (74%) of these 27 patients were discharged early according to our algorithm. In this group, median time from admission to ANC recovery $>500/\text{mm}^3$ was 5.6 days and median length of hospital stay was 2.5 days, saving an average of 3.1 hospital days per patient or a total of 50 inpatient hospital days. Two patients who were discharged early (10%) required readmission (one for fever recurrence; one for cellulitis). There were no deaths or serious invasive infections among early discharged patients.

Conclusions: Step-down management of FN in appropriately selected low-risk pediatric oncology patients is safe and efficacious. Further PDSA cycles are required to ensure continued safety, improved QOL, and to perform cost analysis.

V769 SIOP19-0504 | Optimising Nutrition Screening to Improve Nutritional Status in Paediatric Oncology Patients

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Background/Objectives: Malnutrition in children with cancer is related to increased risk of infections, decreased treatment tolerance and survival. The use of generic nutritional screening tools can result in poor sensitivity, leading to delayed dietetics interventions. We aim to reduce malnutrition by using an oncology-specific screening tool (SCAN) and facilitating timely dietetic intervention.

Design/Methods: SCAN was implemented 1st May 2018 after establishing inter-rater reliability among nurses, along with an auto-referral system from nurses to dietitians. Weight (1 month before, on admission, 1 and 3 months after) and timeliness of dietitian intervention (days from admission to dietitian's referral) were collected 6 months pre- and post-implementation. On each admission, children were defined as malnourished if they experienced 5% or more weight loss for age 2 to 20 years or any weight loss for less than 2 years. Comparison between groups was conducted using chi-square, Mann-Whitney and Student's T-tests.

Results: There were no significant differences in age ($p=0.42$) and gender ($p=0.11$) between pre- and post-implementation groups ($n=274$ pre, $n=267$ post). For children identified as high malnutrition risk, dietitian's referral rate improved significantly (pre: 4/11 (36.4%) vs. post: 42/49 (85.7%), $p<0.001$). Timeliness of dietitian referral improved from a median of 3 (Interquartile range (IQR): 1 to 14) to 1 (IQR: 1 to 1) day from admission ($p=0.010$). Early dietitian intervention (within 48 hours) in the malnourished patients was associated with reduced percentage of weight change at 3 months (early: $3.84 \pm 7.10\%$ vs late: $-2.21 \pm 6.75\%$, $p=0.012$) and reduction in malnutrition rate at 3 months post-admission (early: 17/55 (30.9%) vs late: 9/15 (60.0%), $p=0.039$).

Conclusions: A systematic nutrition screening and referral workflow facilitated prompt dietetic intervention, which helped to reduce weight loss in malnourished children. This project has demonstrated the importance of an interdisciplinary collaboration involving nurses, dietitians and physicians to identify malnutrition and provide timely dietetic intervention.

V770 SIOP19-1658 | Physical Activity During Hospitalization in Department of Pediatric Oncology and Hematology

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Background/Objectives: Oncological diseases are connected with diminished physical activity in patients. Prolonged hospitalization, immobilization, disease itself, coexisting eating and metabolic disorders, depression and many others are the reasons for low activity rate in oncological patients.

Design/Methods: We analyzed physical activity (PA) by 3-day observation of walked steps in 61 patients (49 boys) during antineoplastic treatment for leukemias and lymphomas (n=50), solid tumors (n=11). Control group composed of 30 children (15 boys) hospitalized from reasons others than oncological. We used TANITA – Model AM-120E to count steps, distance (km) and time (min) of activity. High PA was defined as more 10000 steps a day. In every patient we analyzed body mass index (BMI, kg/m²), percent of body fat (PBF,%), fat mass (FM, kg) and skeletal muscle mass (SMM, kg)

Results: Children treated for neoplastic diseases demonstrate lower level of PA comparing to the control group in every day of observation (p<0,05). In examined group median of number of steps was 1073 in day 1, 1160 in day 2 and 1890 in day 3. In controls – 4303, 4733, 4556 respectively. Distance in km and time of activity every day of observation was statistically higher in controls than in oncological patients (day 1: 2.29 vs 0.6 km, 31 vs 11 min; day 2: 2,88 0.65, 33 vs 15 min; day 3: 2.77 vs 0.92 km, 32 vs 13 min; p<0,01). In control group the highest PA was observed in 2nd day, in children with neoplasm PA was similar in 3 days. We didn't find differences in PA in cancer group taking under consideration diagnosis and gender.

Conclusions: Low level of physical activity of children during antineoplastic treatment is very concerning. Interventional programs based on physical activity adjusted to the disease, treatment and age should be introduced to pediatric oncology as a part of the therapy.

V771 SIOP19-0288 | Significantly Lower Requirement of Tissue Plasminogen Activator for Episodes of Central Venous Catheter Dysfunction in Patients with CNS Tumors Compared with Other Pediatric Oncology Patients

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Background/Objectives: Central venous catheters (CVCs) are important for delivery of care in pediatric oncology patients. However, CVC dysfunction (inability to draw blood and/or flush) is common. Tissue plasminogen activator (tPA) is often administered to re-establish function. However specific experience in pediatric central nervous system (CNS) tumors is lacking. The goal of this study was to investigate the CVC experience and use of tPA for episodes of CVC dysfunction in pediatric patients with CNS tumors in comparison to other patients.

Design/Methods: Records from January 2001 to December 2015 of all pediatric oncology patients from the Canadian Atlantic provinces (Nova Scotia, New Brunswick, Prince Edward Island, and Newfoundland & Labrador) were reviewed. Data collected included demographics, diagnosis and treatment, CVC type, CVC dysfunction and tPA use. Research ethics approval was obtained. SPSS version 24 was used for statistical analysis.

Results: 1152 patients were included, of which 222 (19.3%) had CNS tumors. The gender ratio of males to females was 1:1.18, and the mean age at diagnosis was 8.3±4.8 years. One or more CVCs were required in 127 (57.2%) patients with CNS tumors. CVC dysfunction requiring tPA occurred in 12 (5.4%) patients with CNS tumors compared with 182 (19.6%) patients with non-CNS tumors (p=0.0001). In patients with and without CNS tumors who received 1 or more CVC, multivariate logistic regression analysis (adjusted for age, sex, and separate treatment modalities [radiation, chemotherapy and surgery]) showed that administration of tPA for CVC dysfunction had an odds ratio of 2.5 (95% CI: 1.3-4.9) in patients with non-CNS tumors than those with CNS tumors (P=0.012).

Conclusions: Our study showed that children with CNS tumors require significantly less frequent administration of tPA for episodes of CVC dysfunction than other patients. Reasons may include: biologic differences between tumors, the role of the blood brain barrier, or systematic differences in treatment related inflammatory response.

V772 SIOP19-0291 | Does Intravenous Immunoglobulin (IVIG) Therapy in Children with Acute Lymphocytic Leukemia Reduce Infectious Complications?

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Background/Objectives: Children with acute lymphocytic leukemia (ALL) often develop a state of acquired immunodeficiency and low immunoglobulin (IgG) levels also known

as secondary hypogammaglobulinemia (IgG level <5 g/L). This study aimed to determine frequency of secondary hypogammaglobulinemia and incidence of serious infections (bacteremia or fungemia) before and after IVIG administration.

Design/Methods: This descriptive retrospective cohort study approved by IWK REB involved ALL patients aged 2 months to 19 years treated at the IWK from 2001-2016. Group 1 consisted on patients who received IVIG and Group 2 of those who did not. Children's Oncology Group protocols were followed. For each patient, IgG levels, date of IVIG doses, positive cultures and dates, hospital admission dates related to infection and adverse drug reactions were collected from IWK medical records. SPSS version 24 was used for statistical analysis.

Results: Data for 118 patients were analyzed (58 Group 1, 60 Group 2) with no significant differences between the two groups. The incidence of patients with IgG level <5 g/L was 52.5% (62/118) and 85.4% (53/62) of those patients received IVIG. Serious infections and hospital admissions were significantly lower after IVIG was administered ($p=0.050$ and $p<0.05$). The mean IgG level before IVIG administration in Group 1 was significantly lower than the mean IgG level of Group 2 ($p<0.05$). Number of infections, serious infections, and mean number of hospitalizations were significantly lower in Group 2 ($p<0.05$). However, overall duration of hospital admissions was not different ($p=0.536$). IVIG was well tolerated.

Conclusions: This study showed that children with ALL with secondary hypogammaglobulinemia benefit from the administration of IVIG. The authors of this study recommend monitoring of IgG levels in children with ALL and IVIG administration in those with levels less than 5 g/L and consideration in those with recurrent infections.

V773 SIOP19-1519 | Evaluating Clinical Outcomes, Resource Use and Economic Impact of Pediatric Cancer Patients with Solid Tumors Receiving Amphotericin-B Empirical Therapy at Children's Cancer Hospital 57357-Egypt-CCHE

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Background/Objectives: Empirical antifungal therapy is the standard treatment for persistent neutropenic fever. However, over-treatment resulting in increased toxicity and treatment-related cost is a major shortcoming.

Aim of work is to study the antifungal use, clinical outcomes and economic impact of managing antifungal infections for children with solid tumors treated with empirical therapy 'Ambisome®' over 3 months at CCHE.

Design/Methods: A retrospective observational study was conducted (December 2015 - February 2016) for children with solid cancers treated at CCHE and received Liposomal Amphotericin B as empirical therapy over three-month duration. Primary end-point included assessing the probability of fungal infection within six weeks from starting antifungal, based on EORTC/MSG Revised Definition. Survival status was evaluated by the end of week 6. Antifungal utilization and Economic assessment included expenses spent on antifungal agents, and cost of resource use (laboratory and radiologic investigations, and costs of hospital stay).

Results: Analysis of 119 pediatric patients with solid malignancies addressing empirical antifungal strategy was done using clinical, radiological and microbiological assessment. 94% of patients were fungal free, 3% had possible and 3% had proven fungal infection. Overall mortality was 1% and no fungal related mortality. Only 10 patients died after 6 weeks; 4 died free of fungal infection; 6 patients died showing possible fungal infection. The economic impact of managing fungal infections using empirical therapy 'Ambisome®' was calculated using direct medical costs with total expenses 4,135,233 EGP over 3 months; Ambisome® 1,005,379 EGP; microbiology 24,345 EGP; pathology 7,635 EGP; radiology: 4,100 EGP; hospital stay 3,105,450 EGP.

Conclusions: Pediatric cancer patients with solid tumor are low risk for fungal infection based on real-world evidence from CCHE. Antifungal stewardship program targeting shift from empirical to preemptive antifungal strategy may be of clinical and economic benefits among those patients in resource-limited countries. There is potential cost saving with optimization of antifungal use.

V774 SIOP19-0387 | Influence of Methylenetetrahydrofolate Reductase Gene Polymorphisms on the High-Dose Methotrexate Related Toxicity in Childhood Lymphoma and Leukemia Patients

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Background/Objectives: To analyze the influence of C677T and A1298C genetic variants of methylenetetrahydrofolate

reductase (MTHFR) on the clinical toxicity of high-dose methotrexate (HD-MTX) in childhood lymphoma and leukemia patients.

Design/Methods: We reviewed the medical records of patients who were treated with HD-MTX younger than 18 years old at Sun Yat-sen University Cancer Center (SYSUCC) from March 2014 to April 2017. The C677T and A1298C polymorphisms were genotyped by Sanger sequencing. Chi-squared test was used to compare the incidence of toxicities between different genotype groups.

Results: One hundred and ten patients were included. The cancer types included burkitt lymphoma (n = 42), lymphoblastic lymphoma (n = 32), acute lymphoblastic leukemia (n = 16), anaplastic large cell lymphoma (n = 13), diffuse large B-cell lymphoma (n = 7). HD-MTX was given 5,000mg/m² for 24 hours in 91 patients, and 1,000mg/m² for 6 hours in 19 patients. All patients were rescued with calcium folinate at 12 hours after the infusion of MTX. The 48-hours MTX plasma concentration was higher than 4×10⁻⁷mol/L in 23 patients. Among all of the patients, oral ulcer occurred in twelve patients, vomit in nine patients, dizziness in four patients, rash in three patients, diarrhea in two patients, and liver damage in one patient. The MTHFR 677 genotypes included C677C (n = 55), C677T (n = 44), T677T (n = 11). Except for two patients failed to genotype, the MTHFR 1298 genotypes included: A1298A (n = 62), A1298C (n = 43), C1298C (n = 3). When comparing with C677C genotype, patients with C677T and T677T genotypes had no significant correlation with the toxicities of HD-MTX. Besides, compared with the A1298A allele, the A1298C and C1298C alleles were also not associated with an increased risk of toxicities of HD-MTX.

Conclusions: We found the MTHFR C677T and A1298C alleles were not associated with increased toxicities of HD-MTX.

V775 SIOP19-0574 | Impaired Bone Health at Cancer Diagnosis in Paediatric Patients

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Background/Objectives: To evaluate the skeletal profile of paediatric patients with cancer at diagnosis

Design/Methods: Children diagnosed with cancer in our Oncology Centre were recruited during a two-year period and underwent metabolic bone profile and dual-energy X-ray absorptiometry (DXA) at the time of diagnosis.

Results: 88 children were evaluated (51 boys, 53 prepubertal), aged 7.6±4.6 years. Of those, 50 were diagnosed with haematological malignancies and 37 with solid tumours. 21 out of 69 patients had bone pain, (15 had a limp pain) and one sustained a femoral fracture. 43.2% (38/88) of the patients were vitamin D insufficient (25-OH-D: 12-20 ng/ml) and 5.7% (5/88) were deficient (25-OH-D <12 ng/ml). Hyperparathyroidism was present in 11.4% and hypercalciuria in 30% of all patients. One patient with hepatoblastoma had rickets. Bone turnover was also affected, particularly bone formation, because the patients had lower levels of osteocalcin (OC, p<0.001) and procollagen type I propeptide (PICP, p=0.001), compared to controls. Subgroup analysis revealed lower bone formation markers in the haematological subgroup i.e. OC and PICP (p=0.001 for both markers), whereas the solid tumour subgroup had higher bone resorption markers: tartrate-resistant acid phosphatase and urine deoxypyridinoline/urine creatinine (p=0.002 for both markers). DXA scan was performed in 47 patients; 21.2% (10/47) of them had low-normal bone mineral density (BMD) of the lumbar spine (LS BMD Z-score between -1 and -2) and only one patient had low BMD Z-score <-2 at the same site. Two patients had low/normal BMD of total body less head scans.

Conclusions: Skeletal health is already affected at the time of diagnosis in paediatric cancer patients. Low vitamin D levels are common. Bone turnover is disturbed and follows different patterns, depending on the type of cancer. These observations support bone health surveillance and early intervention at the time of diagnosis.

V776 SIOP19-1459 | Blood Culture Collection Volumes and Pathogen Yield at British Columbia Children's Hospital (BCCH) Before and After Implementation of an Evidence-based Blood Culture Guide

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Background/Objectives: Blood stream infections (BSI) are a leading cause of morbidity and mortality in pediatric oncology patients. We sought to establish the impact of the introduction of a weight-based pediatric blood culture collection guide at BCCH on the mean volume of blood collected, the BSI pathogen yield of blood culture collections during

septic episodes, and the blood culture contamination rates. The new guide also recommended use of central venous catheter “discard” blood for blood culture collection.

Design/Methods: Numerous information sessions were run with oncology nursing and phlebotomy staff and laminated lanyard cards were developed that summarized the new collection guides. Mean blood volume collected was determined by weighing blood culture bottles before and after collection. For the BSI pathogen yield and contamination analysis, the first 12 weeks following the introduction of the new blood culture guide was compared to the same 12 week period in the prior three years. Duplicate positive blood culture bottles with the same pathogenic organism during the same septic episode were not included in the pathogen yield analysis. Contamination was defined as growth of a generally non-pathogenic skin organism from a single blood culture bottle.

Results: Patients in the post-implementation period had on average more blood volume collected per collection (1.5ml vs. 4.0ml, $p < 0.001$) and this was the case across patient weight categories. In the 12 week period following the blood culture guide introduction (July to October 2018) the BSI pathogen yield was significantly higher than in the same July to October periods in 2015, 2016 and 2017 (3.7% vs. 2.5%, $p = 0.018$, 95% CI 1.04 to 2.26). Contamination rates remained similar in the post-implementation vs pre-implementation periods (2.7% vs. 2.3%).

Conclusions: Implementation of a weight-based institutional blood culture collection protocol was associated with increased blood volume collection, improved BSI pathogen yield and similar rates of blood culture contamination.

V777 SIOP19-0405 | Compliance with Referrals at the Paediatric Oncology Unit in a Teaching Hospital, Ghana

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Background/Objectives: Caretakers may be faced with a number of barriers before they comply with a referral advice. Such barriers can be financial, geographical and cultural. The most complex aspect of referral care is often the caretakers acceptance of and compliance with a referral recommendation. This is determined by factors such as perceived need of a referral (disease severity), caretaker or community experience with and impressions of the referral facility (quality) and cost (time and resources). The objective of this study was to determine caretaker barriers to compliance with referral in order to improve diagnosis, treatment outcomes and guidelines for the Integrated Management of Childhood Illness (IMCI).

Design/Methods: The study was cross sectional conducted at the Paediatric Oncology Unit (POU) at the Komfo Anokye Teaching Hospital (KATH), Ghana from October to December 2018. The POU receives about 28 referrals per month. Seven caretakers were recruited weekly for a period of 12 weeks. A sample size of 84 was used for the study. Data on time of arrival at the referral facility and the barriers to compliance with referral were obtained after informed consent. Ethical approval was sought before the commencement of the study.

Results: The barriers to compliance with referral from caretakers perspective were lack of financial resources 38 (45.2%), time wasting at the referral facility 30 (35.7%), seeking alternative treatment 23 (27.4%), experience and impression of the referral facility 18 (21.4%) and lack of knowledge on the disease severity 16 (19.0%).

Conclusions: Lack of financial resources, time wasting, seeking alternative treatment, experience and impression, and lack of knowledge on the disease severity were the barriers to compliance with referral. A further study on these barriers to compliance with referral will inform outcome improvement interventions.

V778 SIOP19-1247 | Surgical Tracheostomy in Children with Malignancy Receiving Intensive Chemotherapy- A Retrospective Review

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Background/Objectives: Surgical tracheostomy is very infrequently performed in children on active chemotherapy due to concerns about complications.

Design/Methods: We conducted a retrospective study to assess safety and outcomes of children (0-16 years) who underwent surgical tracheostomy for prolonged ventilation, during intensive induction chemotherapies. PICU database was reviewed to identify children who underwent tracheostomy between January 2007- January 2017 and had an underlying diagnosis of malignancy. Patients receiving chemotherapy were identified and indications, timing and duration of tracheostomy and complications associated with it were documented. Outcome of tracheostomy and patient outcome (patient comfort, sedative use and survival) were noted.

Results: During the study period 677 children were admitted to PICU with an oncological diagnosis. One hundred and forty-two were admitted during initial diagnosis and commenced on induction chemotherapy. Six of these underwent tracheostomy – two patients had intracranial tumour and required airway protection for bulbar palsy (excluded from this report). Four patients (age range 1.3-6 years) underwent

tracheostomy for prolonged invasive ventilatory support due to massive abdominal distension (1), intrathoracic tumours (2), septicaemia and All-transretinoic acid (ATRA) syndrome (1). Three patients had solid tumours (2 rhabdomyosarcoma, 1 pleuropulmonary blastoma) and 1 had Acute Promyelocytic leukaemia. Duration of ventilation prior to tracheostomy ranged from 12-31 days. All children had at least 1 episode (range 1-7) of neutropenia with tracheostomy in situ. Two patients had minor complications (infective tracheostomy granuloma, transcutaneous fistula). Duration of tracheostomy ranged from 7-128 days. Tracheostomy improved patient comfort and reduced use of sedatives in all. All patients were successfully decannulated and are alive with survival ranging from 4 years to 10 years.

Conclusions: Tracheostomies may be safely performed in children receiving intensive chemotherapies without increased risk of serious tracheostomy related complications and should be considered early in selected children requiring prolonged mechanical ventilation to aid patient comfort.

V779 SIOP19-0046 | Traditional Herbal Medicine Rikkunshito Prevents Intestinal Mucosal Injury Induced by Cisplatin in Rats

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Background/Objectives: High doses of anticancer drugs often damage the intestinal mucosa, which can cause severe diarrhea, malnutrition and sepsis due to bacterial translocation. The traditional herbal medicine, Rikkunshito, is reported to improve gastrointestinal function in various conditions. The purpose of the present study was to examine the effect of Rikkunshito on mucosal damage induced by cisplatin in a rat model, and to elucidate the mechanisms responsible for its protective effects.

Design/Methods: Twenty-eight rats were randomly assigned to one of four experimental groups. Group A (control): intraperitoneal injection of saline; Group B: intraperitoneal injection of cisplatin, Groups C and D: oral administration of low and high dose Rikkunshito (C: 1.0 g/kg, D: 2.0 g/kg, respectively) before injection of cisplatin. Daily oral administration of Rikkunshito was commenced 3 days before cisplatin injection. The rats' body weight and fecal condition were assessed, and the intestinal segments were removed for morphological analyses. Proliferation rate of enterocytes were analyzed by assessing the immunostaining of Ki-67.

Results: Weight loss was significantly lower in Group C than in Group B (-1.0 g vs. -11.0 g, respectively) ($p < 0.05$). Diarrhea was significantly more severe in Group B than in Groups C and D ($p < 0.05$). Ileal mucosal villous height was significantly higher in group C and D than in group B (235 and 220

vs. 156 μm , respectively) ($p < 0.05$). Ki67 positive cells per jejunal crypt were significantly increased in Group C and D compared with Group B (33.2 and 34.2 vs. 18.8, respectively) ($p < 0.05$).

Conclusions: The traditional herbal medicine Rikkunshito prevented intestinal mucosal injury induced by cisplatin and improved gastrointestinal function via increased proliferation of intestinal epithelial cells.

V780 SIOP19-1456 | Temporal Trends in Late Mortality in 5-Year Survivors of Childhood Malignancy: The Experience of the French Childhood Cancer Survivor Study

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Background/Objectives: Late mortality of childhood cancer survivors have improved during more recent eras of treatment. The aim of this study was to evaluate the overall mortality and mortality by cause and to investigate changes in patterns across time among 5-year childhood cancer survivors (CCS).

Design/Methods: The FCCSS (French Childhood Cancer Survivor Study) cohort includes 7670 5-year CCS diagnosed between 1946 and 2000 before age 21 in France. The vital statuses of all patients were obtained from the National Identification Repertory. The causes of death were obtained from the Center for Epidemiology on Medical Causes of Death. Medical and treatment data were collected. All cancer deaths were attributed to either primary or subsequent neoplasm and causes of death were classified by "European shortlist" of causes of death. Treatment era was segmented into four time periods based on date of diagnosis: before 1975, 1975-1987, 1988-1994 and 1995-2000. The cumulative incidence of mortality were computed using Gray's method.

Results: Among the 7670 CCS, a total of 1042 patients were deceased. The median follow-up was 27.0 years (IQR 19.6-35.33). The median year of diagnosis of childhood malignancy was 1986 (IQR 1978-1994). The cumulative incidence of death after 20 years of the occurrence of childhood malignancy was 9.3% (8.7%-10.0%) and reached 15.3% at 30 years. The 20-year all-cause mortality improved during more recent treatment eras dropping from 10.9% (95% CI 9.2%- 12.7%) among children diagnosed before 1975 to 7.1% (95% CI 5.9%-

8.6%) among children diagnosed during 1995-2000 (P-value <0.001).

Conclusions: Analysis are ongoing to determine the patterns of cause-specific late mortality and the association between exposure to different treatment modalities. Improved knowledge about the morbidity and mortality after childhood cancer will help improve treatment strategies for patients as well as follow-up guidelines for long-term survivors.

V781 SIOP19-0177 | Health Habits of Childhood Cancer Survivors of a Pediatric Oncology Unit

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Background/Objectives: To describe childhood cancer survivors health habits and compare them with healthy controls from the same population. As a secondary objective, to establish whether there are differences in the BMI percentile (pBMI) between both groups.

Design/Methods: Prospective case-control study of surviving patients of childhood cancer (≥ 1 year after the end of treatment [surgery, and/or radiotherapy, and/or chemotherapy and/or autologous hematopoietic stem cell transplant]) followed in aby Pediatric Oncology Unitunit from 10/01/2018 to 02/28/2019. Each case was sex and age-matched with three healthy controls.

Variables studied were pBMI, physical activity, sedentary lifestyle, eating and toxic habits, according to WHO recommendations on healthy lifestyle.

Results: One hundred and one survivors were included. The tTumor distribution was 25.8% leukaemias, 21.8% lymphomas, 11.8% CNS tumors, 32.7% solid tumors and 7.9% other tumors. Among survivors, 71.3% perform physical activity ≥ 3 times/week (65.4% ≥ 3 hours/week). 24.8% of survivors spend ≥ 7 h/week in electronic devices (TV/PC/tablet). Regarding eating habits, 40.6% eat fruit ≥ 5 times/week, (17.8% consuming ≥ 3 servings/day (vs controls 19.5%, $p=0.008$)). 18.8% eat vegetables ≥ 5 times/week with 3% consuming ≥ 3 servings/day, vs controls 21.1% ($p=0.007$) and 7.1%, $p=0.02$ respectively). Fast food was consumed less than once a week by 27.7% of survivors. 46.5% consume soft drinks (vs 39.9% controls, $p = 0.002$) and 36.6% packaged juices ≤ 1 time/week respectively. Tobacco use was 5% (vs 9.2% controls). Mean pBMI was 55.4% among survivors vs 45.3% among controls ($p=0.002$). Obesity ($pIMC \geq 95\%$)

and overweight ($pIMC \geq 85\%$) percentage were 15.6% vs 5.6% ($p=0.002$) and 28.9 vs 8.8% ($p<0.001$) respectively.

Conclusions: In our sample, most survivors comply with WHO recommendations regarding physical exercise, but spend too much time with electronic devices. Regarding eating habits, less than half of survivors follow recommendations about consumption of vegetables and fruit, being slightly lower than healthy controls. In general, survivors showed higher rates of overweight/obesity than healthy controls, reaching three times the overweight rates compared to them. Childhood cancer survivors represent a population at risk for late side effects which can have negative impact on their quality of life. Specific health promotion programs may achieve key improvements in their health habits.

V782 SIOP19-1184 | Addressing Barriers to Successful Implementation of a Pediatric Early Warning System (PEWS) at a Pediatric Oncology Unit in a General Hospital in Mexico

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Background/Objectives: Children with cancer in limited-resource settings have higher mortality compared to high-resource settings. Contributing factors include high toxicity and limited supportive care. At Hospital General-Tijuana, the largest general and public hospital in northwestern Mexico, treatment-related mortality in hospitalized pediatric cancer patients was very high. In 2018, we aimed to implement Pediatric Early Warning System (PEWS) to improve outcomes.

Design/Methods: PEWS was implemented as part of an international multicenter quality improvement initiative. During implementation, we faced several barriers: a) Buy-in from hospital leadership as pediatric oncology is not top-priority at general hospitals; b) Conduct training with overworked staff; c) Staff resistance to new interventions; d) Lack of equipment; and e) Limited intensivists support. To overcome these barriers, we utilized a variety of strategies: 1) Meetings with hospital leadership to discuss the potential impact of PEWS on patient, staff and the institution; 2) Engagement of hospital's quality director as member of the PEWS team; 3) Scheduling PEWS training around staff's schedule; 4) Early staff engagement and using feedback to inform implementation processes; 5) Adaptation of PEWS tool, algorithm, and documentation for easier adoption; 6)

Rewarding early adopters; and 7) Application for federal funding in collaboration with hospital leadership.

Results: PEWS was successfully implemented in our hospital between January and May 2018, resulting in high staff satisfaction (100%) and low error rates (<10%). We successfully obtained hospital funding for pediatric intensivist support and federal funding for equipment. Deterioration events/1000-inpatient-days and event-associated mortality/1000-inpatient-days were reduced from 5.7 to 2.4 ($p=0.10$) and from 2.9 to 0.5 ($p=0.08$), respectively. Mechanical ventilation days/1000-inpatient-days and vasopressor days/1000-inpatient-days were reduced from 45.0 to 19.6 ($p<0.001$) and 46.7 to 32.1 ($p=0.02$), respectively.

Conclusions: PEWS was successfully implemented in our general hospital resulting in improved clinical outcomes. Leadership/staff engagement, demonstrating potential impact beyond pediatric oncology, and incorporation of feedback were pivotal to successful implementation. Future directions include focus on long-term sustainability of PEWS implementation and impact.

V783 SIOP19-0146 | Bloodstream Infections in Immunocompromised Children and Emergence of Multi-Resistant Bacteria, Lyon, France, from 2014 to 2017

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Background/Objectives: Bloodstream infections (BSI) remain a major cause of morbidity and mortality in immunocompromised children. Documenting bacteremia at the onset of fever in immunocompromised patients is problematic: this leads to an early administration of broad-spectrum antibiotics. This study was performed to investigate the epidemiology of BSI: the bacterial spectrum and antibiotic resistance profiles.

Design/Methods: A retrospective, descriptive study was conducted from January 2014 to December 2017, in a tertiary care center in France, Lyon. Our cohort included a large scale of immunocompromised children: hematological malignancies, oncology patients, children undergoing hematopoietic stem cell transplantation, as well as patients with severe combined immunodeficiency syndromes. A BSI was defined by a positive blood culture sample, associated with fever. Empirical antibacterial therapy was adjusted to the immunosuppression risk group, and prior bacterial colonisation. All patients received vancomycin, amikacin and a broad-spectrum penicillin.

Results: We identified 310 (4.2%) BSI episodes among 186 patients, for a total of 7301 hospitalisations. Gram-positive cocci were the most common isolates, 226/310 (72.9%).

Coagulase negative staphylococci were identified in 49.7% (154/310) BSI and *Staphylococcus aureus* caused 6.5% (20/310) infections. None of the latter were methicillin resistant. Gram-negative bacilli accounted for 21.6% (67/310) isolated bacteria and *Pseudomonas* for 4.8% (15/310). The incidence of BSI annually decreased of 0.75% ($p=0.002$). Only 11/310 (3.5%) BSIs were caused by multidrug-resistant bacteria (MDRB), none were vancomycin resistant.

Conclusions: BSI in our immunocompromised patients was mainly caused by Gram-positive bacteria. The controlled use of broad-spectrum antibiotics was not associated with the emergence of MDRB.

V784 SIOP19-1300 | Stringent Infection Control Policies Help to Decrease the Morbidity in Oncology Wards: Results from a Multi Speciality Hospital in Mumbai, India

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Background/Objectives: Infections are a major cause for morbidity and mortality in the pediatric oncology unit especially in presence of central venous access devices (CVAD). Implementation of good infection control policies is essential to reduce multi drug resistant (MDR) infection related events & improve outcomes. We report our efforts towards this goal at our newly commissioned multi-speciality children's hospital in Mumbai, India.

Design/Methods: All blood cultures sent from the Oncology department from 1st Jan 2018 to 31st Jan 2019 were retrospectively analyzed. 62 children who took treatment with us during this period were included in this study. Of these, 48 (77%) had CVAD. "Scrub the hub", strict hand hygiene, aseptic handling of the CVAD & antibiotic stewardship policy were followed as part of infection control policies since the inception of the unit. These were strictly monitored by the infection control nurse.

Results: 40/62 children (64.5%) had febrile episodes which warranted blood culture sampling. Of the 227 blood cultures, 29 (13%) cultures from 12 children came positive. The organisms grown were *Klebsiella pneumoniae* (59%); *Escherichia coli* (15%), *Klebsiella oxytoca* (10%), Coagulase negative *Staphylococcus* (10%), *Enterobacter cloacae* (3%), *Streptococcus pyogenes* (3%). 2 children had MDR infection at presentation, while 1 changed from Carbapenem sensitive *Klebsiella* strain to MDR strain during the 3rd admission. Only 1 child succumbed to MDR infection.

Conclusions: Infections in pediatric oncology are known to be a cause for morbidity & mortality. Our incidence of

culture positive Blood Stream Infection (BSI) is 13%. The incidence of MDR sepsis is 4.8% (3/62 children). Studies from other centres in India have quoted infection rates of 20-25% and MDR infection rates of 30%. Adoption of good infection control policies from inception of unit has helped to keep the incidence of MDR sepsis in abeyance.

Reference: Trehan A. et al. Invasive bacterial infections in a pediatric oncology unit in a tertiary care center. Indian Journal of Cancer.2014;51 (4):428-431.

V785 SIOP19-0946 | Novel Germline GOLPH3 Mutation Confers Hypersensitivity to Ionizing Radiation in Fibroblasts Derived from Patient with High Risk Leukemia

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Background/Objectives: We report a case of a 16-year-old male with Philadelphia chromosome-like acute lymphoblastic leukemia who experienced significant toxicities from chemotherapy including prolonged myelosuppression, methotrexate neurotoxicity, liver cirrhosis, plastic bronchitis and optic neuritis. Peripheral blood whole exome sequencing revealed a previously undescribed *de novo* heterozygous germline Golgi Phosphoprotein 3 (GOLPH3) mutation (*GOLPH3*^{+/-}, p. Thr21le). GOLPH3 is a trans-Golgi membrane protein that mediates Golgi trafficking and is essential for cell survival following DNA damage. We hypothesize that GOLPH3 haploinsufficiency in this patient contributed to his hypersensitivity to DNA-damaging agents.

Design/Methods: Patient skin fibroblasts were used to generate *GOLPH3*-corrected and uncorrected cell lines via retroviral transduction with HA-tagged *GOLPH3* or HA control expression vectors, respectively. These cells were assayed for colony forming potential following exposure to increasing doses of ionizing radiation (IR). Endogenous GOLPH3 expression was assessed from lysates of corrected and uncorrected cells before and after IR, using normal human dermal fibroblasts (NHDF) for comparison. Statistical significance was examined using a 2-way ANOVA.

Results: *GOLPH3*^{+/-} fibroblasts formed significantly fewer colonies than *GOLPH3*-corrected fibroblasts following 1 (mean difference 17%; 95% confidence interval [CI] 9-25; $p < 0.0001$) and 2 Gray radiation (mean difference 8%; 95% CI 0.2-16; $p = 0.04$). Western blot analysis revealed a significant increase in GOLPH3 levels four hours after irradiation

in NHDF lysates (mean difference 48%, 95% CI 15-80, $p = 0.0016$), but not in *GOLPH3*^{+/-} lysates.

Conclusions: The *GOLPH3*^{+/-} mutation confers hypersensitivity to ionizing radiation in patient derived fibroblasts. IR-induced accumulation of GOLPH3 in normal fibroblasts is consistent with a role for GOLPH3 in the DNA damage response. Lack of IR-induced accumulation of GOLPH3 protein in *GOLPH3*^{+/-} cells suggests that threonine to isoleucine at position 2 may decrease protein stability following radiation. These findings may explain this patient's increased toxicity. Further studies are required to determine the mechanisms of impaired DNA damage response in *GOLPH3*^{+/-} cells.

V786 SIOP19-0050 | Prevalence of Vitamin D Deficiency in Children with a Diagnosis of Malignancy

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Background/Objectives: Vitamin D is essential for calcium homeostasis, adequate growth and skeletal development. Evidence supports wider roles for vitamin D focusing on anti-inflammatory and immunomodulatory effects. Children with malignancies risk vitamin D deficiency due to; lengthy hospital admissions leading to decreased sun exposure; poor nutrition; radiotherapy treatment affecting bone density; chemotherapy potentially causing hepatotoxicity and nephrotoxicity, interfering with activation of vitamin D; glucocorticosteroids stimulating vitamin D catabolism; mucositis reducing absorption of nutrients; cytotoxic drugs, radiotherapy and antifungals potentially causing phototoxicity leading to avoidance of sun exposure.

To determine prevalence of vitamin D deficiency in children with malignancy.

Design/Methods: Children admitted with a malignancy, known to a dietitian, had blood results reviewed. As per UK national guidelines, serum vitamin D of 25-50nmol/L classified as insufficient and <25nmol/L classified as deficient.

Results: Of 478 patients aged 0-13 years, 57% had vitamin D levels checked. Vitamin D <50nmol/L in 34% ($n = 92$); 24% ($n = 67$) insufficient, 9% ($n = 25$) deficient. This appears to be in line with national average of ~11% deficiency in children. Children with haematological malignancies ($n = 147$) were twice as likely to have vitamin D deficiency as children with solid tumours ($n = 127$), 12% ($n = 18$) vs 6% ($n = 7$). Insufficient vitamin D levels, 25-50nmol/L, were found in 32% ($n = 47$) of children with haematological malignancies compared with children with solid tumours who had 16% ($n = 20$).

Conclusions: Vitamin D deficiency is prevalent in children with malignancy, with particular concern for haematological malignancies. As these children had been reviewed by a

dietitian and may have been on supplementation, either from oral supplements, tube feeds or parenteral nutrition, it is likely that levels of vitamin D deficiency are actually higher. It is therefore proposed that all children should be screened for vitamin D deficiency at diagnosis and regular intervals throughout treatment. Supplementation should be given per national guidance.

V787 SIOP19-1405 | Comparative Approaches to Fever Management in Pediatric Oncology Patients: A Multicenter Perspective

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Background/Objectives: Fever is one of the most common reasons for hospitalization in pediatric oncology patients, however its etiology and management is not well understood in many regions of the world. We tested the feasibility of a strategy to develop fever management algorithms (FMA) in sites in the Philippines, Zimbabwe, Honduras, and Guatemala, and compared initial output.

Design/Methods: A multidisciplinary approach was used to construct locally adapted FMAs for the first seven days of fever. First, we reviewed current local antimicrobial and diagnostic practices. Next, we conducted a systematic literature review and compared practices to published guidelines. Third, we gathered microbiology data through clinician interviews and laboratory results. Finally, we identified data elements which would be required to revise local FMAs. We then compared the algorithms and data elements.

Results: Differences were identified in four domains: definitions, risk stratification, empiric therapy, and antifungal management. Fever definitions differed at every site, with a maximal difference of 0.6°C between the highest and lowest temperature ranges. Neutropenia was defined as equal or less than 500 cells/mm³ in 3/4 sites; one used equal or less than 1000 cells/mm³. Risk stratification criteria prioritized identification of high complication risk but differed for each site. Only one site offered outpatient management for low risk patients. Antipseudomonal monotherapy was available in 2/4 sites; the other sites used aminoglycosides with ceftriaxone for high risk patients. As antifungal therapy, 3/4 sites offered an option of fluconazole versus amphotericin B deoxycholate, and only one site required imaging and fungal biomarkers at initiation of antifungal therapy.

Conclusions: We demonstrated that FMAs tailored to institutional resources will vary based on cost, access, institutional practices, and epidemiology. Standardizing definitions and data elements for predictors and outcomes of febrile episodes across global sites will enable us to measure the effects of variations and test components that can be used universally.

V788 SIOP19-0554 | Improvement of Clinical Indicators in Hospitalized Pediatric Oncology Patients Following Implementation of a Pediatric Early Warning Score System

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Background/Objectives: Introduction: The implementation of an early warning score system facilitates the timely identification of patients at risk of deterioration; its use has been shown to decrease deterioration indicators in hospitalized patients.

Objective: To compare the deterioration indicators of the period before and after the implementation of a modified pediatric early warning score system (PEWS) in a pediatric oncology hospital. To describe the changes in deterioration indicators including but not limited to transfers to PICU (Pediatric Intensive Care Unit), length of stay in days in PICU, morbidity and mortality of the deterioration events registered in 2015 and 2017.

Design/Methods: Methodology: A retrospective cohort was conducted to assess the indicators of clinical deterioration in the year prior to the use of the scale (2015) and the year after implementation during which it was used systematically for patient assessment (2017).

Results: Ninety nine (99) cases were reviewed from 2015 and 86 cases from 2017 of patients who required assessment by PICU. A reduction was found in the number of transfers to PICU, from 49 events in 2015 (49.5%) to 32 events in 2017 (37.29%) ($X^2=2.307$, $p=0.129$). Patients who required transfer to the PICU, 96.8% had critical EVAT score ≥ 5 . Reduction of the length of stay in PICU was registered ($t=0.03956$, $p=0.9685$), ($F=3.65$, $p=0.002$) as well as a significant decrease in mortality during 2017 ($p=0.052$).

Conclusions: Conclusions: The implementation of PEWS showed decreased mortality and improves the selection of patients who need admission to the PICU. The successful implementation of the PEWS score shows an improved timely

identification of patients with clinical deterioration during inpatient hospitalization.

V789 SIOP19-0555 | Enhancement of the Clinical Outcome in Patients with Neutropenia and Fever Related to the Correct Adherence to the Golden Hour Protocol for the Antibiotic Administration

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Background/Objectives: Introduction: Neutropenia is one of the most frequent toxicities related to chemotherapy. Neutropenia and fever pose an urgency that unattended promptly leads to rapid deterioration, sepsis, shock or death. The early administration of antibiotics has shown to reduce the morbidity and mortality associated with disseminated infection.

Objective: Describe the reduction of indicators such as transfers to the pediatric intensive care unit (PICU), length of hospital stay for patients admitted to the emergency department with neutropenia and fever who had adherence to antibiotic administration within one hour compared with those who were delayed in the administration of antibiotic over an hour during the period from 2016 to 2018.

Design/Methods: Methodology: An analytical, retrospective, descriptive and transversal study was conducted. We analyzed the files of patients who were admitted for neutropenia and fever between the months of January 2016 and May 2018, recording the variables in an Excel worksheet.

Results: A total of 182 cases of patients admitted to the emergency department diagnosed with neutropenia and fever were analyzed, dividing the cases in those who received antibiotics within the first hour after admission to the emergency department (n = 130) and those who had a delay in administration of the antibiotic (n = 52). A reduction in admissions to PICU at diagnosis was found from 11.5% to 1.5% (p = 0.002); a decreased need for antibiotic progression during their hospital stay (59% vs 20%, p < 0.05); fewer intravenous antibiotic days on average 8.9 days vs 6.5 days; as well as lower progression to septic shock during evolution (34.6% vs. 2.3%, p < 0.001).

Conclusions: The timely administration of antibiotic, less than an hour, in the emergency department admitted febrile neutropenic patient has a positive impact on the clinical evolution improving clinical outcomes with fewer complications during hospital stay.

V790 SIOP19-1173 | Impact of Infection Control Education to Nurses and Patient's Family in Reduction of Infection Rates in Paediatric Oncology Unit Indus Hospital Karachi

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Background/Objectives: Patients with cancer are on high risk of infection because of the suppression of immune system. The awareness of infection control among paramedical staff play vital role in the reduction of hazardous infections. Practices of Hand hygiene, line care bundle and family education about personal, food and water hygiene are very effective in controlling the infections among patients. The objective of the study is to determine the impact of education in reduction of infection at oncology department Indus Hospital.

Design/Methods: Observational study was conducted from September 2017 – June 2018. Data was collected from daily surveillance and medical record. Total 500 Patient's and family were covered and 290 nurses were enrolled in the study. Education was provided to nurses regarding practices of hand hygiene and use aseptic technique during invasive procedure and apply bundle care, also provided the education to patient's family about personal, food and water hygiene. Education provided through videos, booklets, demo and face to face sessions.

Results: A total number of 11,589 patients were observed during daily patient care in pre and post intervention. There were 6,008 patients and infections result was 41 (0.68%) in the pre intervention and there were 5,581 patients and infections results was 21 (0.37%) in the post intervention.

Conclusions: An intervention focused on the education of health care provider on the prevention of blood stream infections may lead to a decrease in the incidence of blood stream infections. Education programs may lead to a considerable decrease in medical care costs and patient morbidity and mortality.

V791 SIOP19-1067 | Optimizing Outcomes with the Implementation of a Center of Excellence for the Care of Pediatric Patients with Cancer in Mexico

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Background/Objectives: Telethon Children's Hospital of Oncology (HITO) is a free-standing pediatric oncology hospital in Mexico, whose sole mission is to provide the highest

quality in diagnosis, treatment, and monitoring of the pediatric population diagnosed with cancer. The objective of this study is to analyze the challenges, success, and profitability of this pediatric cancer hospital to help develop us an optimal model to be implemented in the context of a low- and middle-income country.

Design/Methods: HITO delivers childhood cancer treatment that is partially subsidized by state/donors. We developed a pediatric oncology program that provides comprehensive care in children and adolescents with cancer, with a subspecialized ward in transplant. We provided housing for patients' families near hospital. The supportive care team developed an infection prevention program from the facility to a dedicated staff. The antibiotic use program was implemented in the first hour of the presentation of fever. As part of a quality care improvement, a pediatric early warning system scale has been implemented to reduce the unplanned PICU transfers.

Results: We have treated 318 patients from December 2013 to December 2018. The frequency of the diseases treated is 28% for leukemias, 17.3% CNS tumors, 8.1% for lymphomas, 7.8% osteosarcomas, 7.3% retinoblastoma, 11.3% soft tissue sarcomas, 3% neuroblastoma, 2.5% renal tumors, 3.7% germinal, and 6.2% for others tumors. The abandonment of therapy was 0.3%. There were 52% of patients with advanced disease. The overall survival (OS) at 5 years is 89% and the event-free survival (EFS) of 76.8%.

Conclusions: Despite advances in therapy and supportive care in HITO, 52.2% of patients have a high risk of recurrence of the disease. However, the EFS and OS are similar to what is reported in the international literature, due to a combination of adequate infrastructure and well-trained specialists with the support of government, the private sector, and philanthropic organizations.

V792 SIOP19-0684 | Prevalence of Acute Kidney Injury in Pediatric Cancer Patients

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Background/Objectives: The incidence of pediatric acute kidney injury (AKI) is recognized as a cause of increased morbidity in critically ill cancer patients. Therefore it is essential to assess baseline renal functions before and during therapy, adjusting drug dosages accordingly, avoiding nephrotoxic drug combinations. This study was done to assess prevalence of acute renal impairment in pediatric cancer patients during the first year of diagnosis.

Design/Methods: A retrospective epidemiologic study included 220 pediatric cancer patients who presented to the

Children's Cancer Hospital Egypt during the period from January to December 2013. These patients were subjected to Pediatric RIFLE criteria during their first year of diagnosis.

Results: A total of 220 patients were identified as having acute kidney injury. Initial serum creatinine of the patients ranged between 0.3 and 4, with the mean of 0.97 ± 0.418 , and median 1. Final serum creatinine ranged between 0 and 9, with mean of 1.88 ± 1.261 and median of 2. The peak of serum creatinine was reached over a range between 2 and 86 days, with the mean of 24.33 ± 18.18 and median of 20 days. It was found that the majority of causes of AKI was due to intrinsic renal failure with a variety of underlying causes (32.9% Tumor lysis syndrome, 23% nephrotoxicity from methotrexate and Cisplatin, 2.7% acute tubular necrosis, 0.5% atrophic kidney, 0.5% bilateral renal infiltrates, 2.3% heart failure). 70% of the patients admitted with AKI during that year had been recovered while 12% have been suffering from chronic renal impairment and the rest had died.

Conclusions: Chemotherapy-induced nephrotoxicity is a common finding among children and adolescent patients treated for cancer. It can be indicative of a significant renal disease. Pediatric nephrologist referral is recommended when renal dysfunction persists beyond 2-3 months after completion of anticancer therapy.

V793 SIOP19-1463 | Experience of Using Blood Methotrexate Monitoring in Childhood Acute Lymphoblastic Leukemia in Limited Resource Setting: Preliminary Study

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Background/Objectives: Administration of high dose methotrexate (HDMTX) needs meticulous monitoring. The blood MTX concentration is used to determine the regimen of leucovorin rescue. Pediatric oncologists in the developing world are reluctant to use HD MTX, since it is technically and logistically difficult to routinely screen the patients and due to its severe toxicity. **This study aims** were to evaluate level of HD-MTX at 24, 48 hour using ELISA methods and describe clinical HDMTX toxicity in childhood ALL.

Design/Methods: a prospective cohort was done of 20 consecutive children with confirms confirmed diagnosis of ALL who had received at least one cycle of 1g/m^2 HDMTX as part of their consolidation treatment. Leucovorin rescue was given to all patient within three times dosage 15mg/m^2 . Clinical toxicity including: hematologic disorder, platelet reduction, leucocyte reduction, liver toxicity, nephrotoxicity, and mucositis based on CTCAE version 4.3. Serum MTX concentrations

were measured at 24 and 48 hr after beginning the infusion and were analyzed retrospectively.

Results: The median MTX level at 24, 48 hour in the first cycle was 7.75 (4.87-65.5) ng/mL and 6.43 (2.84-45.61) ng/mL respectively, meanwhile median in second and third cycle were as followed: 2nd cycle 24 hr 5.87 (3.46-66.89) ng/mL, 48 hr was 5.77 (3.24-56.13) ng/mL; 3rd cycle 24 hr 6.67 (2.93-78.12) ng/mL; 48 hr was 5.43 (2.79-50.46) ng/mL. The most common toxicities clinically observed were neutropenia 4/20 (1st cycle), 5/20 (2nd cycle) and 6/20 (3rd cycle). Creatinin clearance <100 mL/min/1.73m² were observed in 8/20, 4/20, and 4/20 patients 1st, 2nd, and 3rd cycle respectively. Nephrotoxicity grade 1 was found 4/20 patients. There were no serious mucositis recorded in this study

Conclusions: The level of MTX in 48 hr considered to be safe as it belows recommended value with neutropenia as the common toxicity. Further study need to conduct to confirm this results

V794 SIOP19-0499 | Oral Nutritional Supplement for Children with Cancer: 7 Different High-Energy Drinks Compared to Cacao, a Double-Blinded Feeding Trial

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Background/Objectives: In order to increase energy intake in children with cancer under chemotherapy who cannot meet the required energy intake many different high-energy commercially available drinks are offered. However children often don't like them and refuse them. This prospective study aimed to examine the taste preference of commercially available oral nutritional supplements in Germany.

Design/Methods: In this double-blinded trial, 26 children and adolescents with a median age of 14 years (range 6-20 years) were asked during chemotherapy to try 7 different commercially available high-energy drinks and hypo-caloric cacao as a control. The patients were given the same small amount for each drink and had to answer questions about the drinks e.g. rating the taste, colour and temperature by a scale of 1-6.

Results: We found that cacao was the best accepted drink. Frebini® Energy Drink Strawberry was rated lower than cacao, although not statistically significantly. All other drinks were rated significantly lower than cacao. The third- and fourth best rated drinks, Nutrini® Drink Smoothie Summer Fruits and Energea P enriched with cacao did not differ significantly from Frebini® Energy Drink Strawberry. Commercially available HIPPI Drinking Food Milk/Banana, Energea P, HIPPI Drinking Food Pumpkin & Carrot, HIPPI Drinking

Food Chicken Tomatoes & Fennel were not accepted. Cacao, Frebini® Energy Drink Strawberry and Energea P/cacao were tasted as sweet and Nutrini® Drink Smoothie Summer Fruits as sour.

Conclusions: Cacao and Frebini® Energy Drink Strawberry were best accepted by the children perhaps because they are familiar with this flavour. Cacao could be offered as a cheap first choice. To achieve a high energy drink the cacao could be enriched with the unflavoured supplement Energea P.

V795 SIOP19-1432 | Central Venous Line Salvage after Gram Negative Bacteraemia

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Background/Objectives: Central venous line are prone for infection which can be life threatening. Antibiotic treatment is initiated to treat such infections and clear the CVLs. Gram negative bacteria are difficult to clear, often leading to removal of line. This audit was done to look at whether CVLs can be successfully saved with antibiotic treatment.

Design/Methods: This audit looked at the cases of bacteraemia in our haematology and oncology patients caused by gram negative bacteria. The aims of this audit were to identify gram negative bacteria from blood cultures, note sensitivities, and to identify whether central venous lines were successfully saved after an episode of bacteraemia. It was a retrospective audit over an 18 month period from January 2017 to August 2018. Patients were identified from the microbiology data base and clinical details were obtained from patient records. A proforma was used to collect information and analyse the results.

Results: A total of 1795 blood cultures were taken from the patient population during this period. 132 (7.4%) were positive for gram negative bacteria during 54 episodes of fever from 46 patients. 5 patients were excluded. 121 positive cultures during 50 episodes from 41 patients were included. Age ranged from 1 month to 18 years (15 male). The bacteria most commonly found were *Klebsiella pneumonia* (16), *Enterobacter cloacae* (28), *Stenotrophomonas maltophilia* (14), *Acinetobacter ursingi* (6), *Escherichia coli* (9), *Klebsiella oxytoca* (9), and *Pseudomonas aeruginosa* (8). Meropenem was the most sensitive antibiotic (73%) and Augmentin had the highest resistance (40%). Ceftazidime, amikacin, gentamicin and ciprofloxacin had similar sensitivities at around 60%. Tazocin was sensitive in about 50%. Lines were only saved in 32% of patients during the episode. In further 6% of cases line had to be removed within 2 months due to recurrence of infection.

Conclusions: Gram negative bacterima resulted in removal of CVLs in 68% of cases.

V796 SIOP19-0227 | The Prevalence of Household Food Insecurity Affecting Children Diagnosed with Cancer in Two Paediatric Oncology Units in South Africa

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Background/Objectives: Food insecurity is defined as the lack of nutritionally adequate, safe and sufficient amounts of food for all household members, which is a major cause of malnutrition in developing countries. Families cope with food insecurity by decreasing the variety of foods they buy for the household, as well as portion sizes. In 2015 UNICEF reported that 70% of households in informal settlements in South Africa (SA) suffered food insecurity. The prevalence of food insecurity of children diagnosed and treated for cancer in SA is unknown

Design/Methods: The Household Hunger Scale (HHS) consists of eight "Yes/No" questions and is used to determine food security or child hunger. Five or more "yes" responses indicate food insecurity. The family of each newly diagnosed child with cancer family was interviewed with the HHS questionnaire within 72h after diagnosis from 1 Oct 2018. The study is ongoing until December 2020.

Results: The interim analysis includes the responses of parents of 51 patients, but as the study is ongoing, will include more in future. The majority of families (74.5%; 38/51) rely on limited number of food types to feed their children. A further 62.7% (32/51) run out of money to buy food during the month, while 58.8% (30/51) of the caregivers eat less than they should and 52.9% (27/51) cut the size of their meals due to inadequate money to buy food. The final score indicated that 52.9% (27/51) have a risk for hunger, while 25.5% (13/51) of patients have food shortage and only 21.6% (11/51) had food security at home.

Conclusions: The high percentage of newly diagnosed children with cancer that are at risk for food insecurity at home is of great concern. Interventions are needed to ensure adequate nutrition for children during cancer treatment.

V797 SIOP19-1471 | Correlation Between Measured GFR (MGFR) and Estimated GFR (EGFR) for Monitoring Renal Function During Chemotherapy in Paediatric Patients

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Background/Objectives: Despite the advances in the supportive treatment of childhood cancer, nephrotoxicity remains major concern. Nephrotoxicity not only impacts on the intensity of treatment administration which can compromise the outcome, but also contributes significant mortality and morbidity. This reflects the importance of accuracy of measuring the renal function and monitoring. This audit was undertaken to compare the measured GFR (using ⁵¹Chromium-EDTA) against estimated GFR (using serum creatinine)

Design/Methods: This is a retrospective study comprising data from 117 solid tumour patients over a 5 year period from 2012 to 2017. The patients were identified using the departmental data base, electronic records of patients and biochemistry department records. Clinical and biochemical information were collected using a proforma. SPSS was used to analyse the correlation of ⁵¹Cr-EDTA and eGFR by using a scatter graph and correlation coefficient was measured using Pearson's coefficient. The pre and post- chemotherapy value was analysed by constructing a box plot.

Results: A total of 117 patients were identified. 240 values of mGFR and eGFR from 61 patients were included for the analysis, as other patients either did not have eGFR or mGFR. The measurements and estimations were done pre chemotherapy, during chemotherapy and at the end of treatment. There was positive linear correlation between the two methods when the mGFR was over 90 (p<0.001). However the correlation was poor when mGFR was less than 60 (p <0.1).

Conclusions: mGFR and e GFR correlated highly when the measured GFR value was more than 90mmol/min/1.73m². There was poor correlation when the measured GFR was less than 60 mmol/min/1.73m².

V798 SIOP19-0847 | Identifying the Critically Ill Pediatric Cancer Patient – A Pilot Study

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Background/Objectives: Pediatric cancer patients are at risk of acute clinical deterioration as a result of the severity of illness and toxicity of treatment regimens. Timely detection is imperative to prevent further deterioration and promptly initiate treatment. Currently, the Bedside Pediatric Early Warning Score (BedsidePEWS) is the only validated tool to identify critically ill pediatric patients. However, its predictive value in this specific oncologic population is uncertain. Our prospective cohort study aims to evaluate the predictive value of the BedsidePEWS for Pediatric Intensive Care Unit

(PICU) admission and/or cardiopulmonary arrest in pediatric oncology patients and, if necessary, optimize this score. In this pilot study the feasibility of the study was assessed.

Design/Methods: During a 2-month pilot study (19/02/2018 to 20/04/2018) all patients, aged 0-18 years, admitted to the inpatient oncology ward were eligible for inclusion. Patients with a restriction in care (palliative patients, do not resuscitate orders, no PICU admission) were excluded. During these admissions BedsidePEWS were documented according to the existing algorithm.

Results: Seventy-seven hospitalized patients were eligible for inclusion. Two patients were excluded (due to palliative care and no consent), resulting in 75 included patients with 167 admissions. Of these 167 admissions, 10 (6%) resulted in an unplanned PICU admission. During 24 hours before PICU admission, median BedsidePEWS was 6 [range 3-15]. A score of ≥ 6 should be repeated every hour, the median time between score registration for BedsidePEWS was 3 hours [IQR 1-8]. Thus, in the higher range of BedsidePEWS scores 25% of the nurses showed adherence to the protocol. Continuous monitoring and storage of vital parameters was implemented in order to facilitate calculation of BedsidePEWS more frequently if necessary to improve predictive value of the score.

Conclusions: This pilot study endorses the feasibility of our prospective cohort study. Ongoing implementation of the BedsidePEWS is currently performed to improve algorithm adherence.

V799 SIOP19-0045 | Treatment-Related Mortality in Children with Acute Lymphoblastic Leukemia in a Low-Middle Income Country

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Background/Objectives: To determine the frequency of treatment-related mortality (TRM) among all mortalities in children being treated for acute lymphoblastic leukemia (ALL) in a low-middle income country (LMIC) along with determination of etiological and contributing factors to TRM.

Design/Methods: Analytic, observational; retrospective, cohort study, conducted in the department of Pediatric Hematology-Oncology, The Children's Hospital Lahore, Pakistan. Patients under 16 years of age, diagnosed as ALL, admitted either for remission induction chemotherapy or any treatment related complication and expired during the course of treatment, were included in the study.

Results: Total 247 patients of ALL expired during study period. Among all mortalities, the incidence of TRM was found to be 58.3% (n=144), death due to relapsed disease

was found in 88 patients (35.6%) while 15 patients (6.1%) had early death due to disease. We enrolled 144 patients who had TRM. The median age was 5 years with male-to-female ratio of 1.3:1. The most common cause of TRM was sepsis (n=126, 87.5%), followed by hemorrhagic complications (n=11, 7.6%), drug toxicity (n=4, 2.8%), tumor lysis syndrome (n=2, 1.4%) and thromboembolism (n=1, 0.7%). Significant factors associated with TRM were weight-for-age (WFA), primary diagnosis, reason for admission and absolute neutrophil count. WFA less than/equal to 25th percentile was found in 112 patients (77.8%), commonest diagnosis was B-cell ALL (n=129, 89.6%), majority of patients (n=98, 68.1%) had been admitted for remission induction chemotherapy and profound neutropenia was present in 118 (82%) patients.

Conclusions: The incidence of mortality is quite high in patients with ALL in LMIC. TRM though potentially avoidable is still a significant cause of treatment failure. Infections are a major challenge in managing TRM and infection control is imperative in improving the outcome. Maximum supportive care must be provided to the patients on remission induction chemotherapy with malnutrition, high-risk immunophenotype and profound neutropenia.

V800 SIOP19-1177 | Bacteremia in Pediatric Oncology Patients-A Tertiary Care Center Experience

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Background/Objectives: Bloodstream infections account for approximately 25-30% of febrile episodes in patients with febrile neutropenia (FN). If not treated promptly with antibiotics, they can lead to significant morbidity & mortality in children with cancer. We aimed to study different organisms causing bacteremia and their outcome in children with cancer admitted to Shaukat Khanum Cancer Hospital Lahore.

Design/Methods: This was a retrospective study. Data fields included age, diagnosis, culture, antibiotics and outcome. All pediatric oncology patients with FN from January 2017 to December 2017 were included. Data analysis involved quantitative analysis and mean calculations.

Results: About 391 episodes of FN were documented among 86 patients. Mean age was 4.7 ± 2.7 years. Fourteen percent (n=12) had ICU admission and 10.5% (n=9) died. Sixty three percent (n=54) had primary diagnosis of ALL and NHL. Sixty five percent had risk factors as mucositis, central catheter or both. About 1523 blood cultures were drawn. Of these, 39 isolates were cultured. Escherichia coli was commonest

isolate found in 41% (n=16) followed by *Pseudomonas* and *Streptococcus pneumoniae* in 10.3% (n=4) each. Polymicrobial isolates were 10.3% (n=4). Multi-drug resistance was found in 28.2% (n=11). Eighty seven percent patients (n=34) with positive cultures received appropriate antibiotic. Most organisms were sensitive to piperacillin/tazobactam (35.9%, n=14) followed by meropenem (25.6%, n=10) and colistin (15.4%, n=6).

Conclusions: Bacteremia is an important issue in FN patients occurring in 9.97% of the patient visits in this study. The overall sensitivity of high-risk bacteremia to Piperacillin-tazobactam provides justification for its empiric use in FN pediatric oncology patients.

V801 SIOP19-0856 | Nutritional Prevention of Accelerated Ageing and Chemotherapy-Induced Side-Effects

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Background/Objectives: Nowadays most paediatric cancer patients -fortunately- survive thanks to improved therapy strategies. Therefore, long-term consequences of the treatment have become one of the most prominent problems. Chemo- and radiotherapy mainly target DNA and our previous work has revealed that DNA damage is a main cause of ageing and ageing-related diseases. As a result of their life-saving chemo- or radiotherapy paediatric patients as well as long-term cancer survivors experience many features of premature ageing-like disorders, including neuro-, nefro-, hepato- and cardiological decline, type 2 diabetes, osteoporosis, fatigue, secondary tumours and other traits. We previously showed that nutritional interventions like dietary restriction (DR, 30% reduced food intake) and short-term fasting (STF) trigger a 'survival response', delaying ageing and diminishing several ageing-related pathologies. Here we investigated in a preclinical setting whether implementation of nutritional interventions prior to DNA-damaging treatments could result in reduced side effects and improved quality of life in paediatric cancer patients.

Design/Methods: Young mice were subjected to either an *ad libitum* diet or a period of STF (2 days) followed by 2 Gy whole body irradiation or cisplatin treatment (10 mg/kg i.p.). Body weight, food intake and activity were monitored until moment of sacrifice. Subsequently, blood and a range of organs were collected for further analysis.

Results: Mice receiving *ad libitum* food before administering radiotherapy or cisplatin showed a reduced appetite after treatment. The effects observed were significantly larger with cisplatin as these mice also lost body weight remaining for multiple days after treatment. Strikingly, all signs of direct toxicity were diminished simply by two days of fasting.

Conclusions: By translating current findings with simple nutritional interventions into treatment regimens for paediatric oncology patients we believe we can, similarly to what is shown in mice, prevent or strongly reduce many short- and long-term health conditions thereby improving overall quality of life.

V802 SIOP19-1662 | A Study of Mortality in Childhood Cancer Patients in Tertiary Referral Hospitals in the Private Sector in India

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Background/Objectives: Mortality rates are an essential statistic to measure outcomes of children with cancer including efficacy and toxicity of treatment. We aimed to find mortality rates in our patients and examine factors associated with mortality.

Design/Methods: All children ≤ 18 years of age newly diagnosed with cancer at Max Super Speciality Hospital, Saket and Patparganj in New Delhi (tertiary referral hospitals in the private sector) are registered onto the online hospital based cancer registry. Those registered between March 2013 to Aug 2018 were included in this study. Outcome of interest was mortality (any cause) as well as treatment-related mortality (TRM) and disease-related mortality (DRM). Associations of mortality were investigated with demographic variables and cancer type.

Results: There were 399 children registered (66% Indian, 65% male). Most common cancers were leukaemias (28%), CNS tumours (23%), bone tumours (12%), lymphomas (11%) and soft tissue sarcomas (7%). There were 91 deaths (mortality rate 22.8%). No significant difference in mortality rate was noted by gender, age group, hospital location, nationality and cancer type. Of these deaths, 51 were DRM and 29 treatment related mortality giving an overall TRM of 7.3%. The distribution by age, gender, hospital location and nationality did not vary significantly in DRM and TRM. However, there was significant difference by cancer type ($p=0.008$). CNS tumours, sarcomas and leukaemias were the largest contributors to DRM while leukaemias, lymphomas and neuroblastomas were the largest contributors to TRM. Median time to TRM was 103 days while DRM was 317 days.

Conclusions: 22.8% of children with cancer having a relatively modest follow up die in our setting. TRM for all

cancers combined is 7.3%. DRM and TRM vary significantly by cancer type.

V803 SIOP19-0156 | Creation of a Sustainable Voluntary Platelet Donor Source Fulfilling Massive Requirement of a Tertiary Cancer Center - A Model Worth Replication, for Saving Lives

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Background/Objectives: More than 60,000 new cancer patients register in our Institute every year. Treatment of cancer necessitates a sustainable source of voluntary platelet donors.

Design/Methods: In 2009 societal education and innovative awareness initiative named 'SAVE A LIFE'(SAL) was initiated for encouraging voluntary platelet donations. People in large numbers from varied demographics were motivated through lectures, discussions, videos and pamphlets. A platelet donor registry was created for those who volunteered. Non-incentivised approaches like half-day leave, appreciation tokens, birthday-anniversary wishes, hospital rounds, a mobile app (to increase the outreach and facilitate the processes) were introduced for donors to stay motivated & become regular voluntary donors. Board members from Departments of Transfusion Medicine, Medical Oncology, NGOs, Volunteers and Good Samaritans from the society increased the scope and participation of SAL initiative.

Results: Through 65 educational drives over 2009 - 2018, a voluntary platelet donor registry of 5023 individuals was created. In 2009, of the 2018 Single Donor Platelets (SDPs) collected in our institute, 228 (11%) were by voluntary donors. With the SAL initiative, the voluntary SDPs pool has consistently increased YOY – in 2010 (491/2651-18.5%), 2011 (424/2349-18%), 2012 (630/2393-26.3%), 2013 (813/2675-30%), 2014 (1306/3105-42%), 2015 (2368/3747-63.7%), 2016 (2900/3800-76.3%), 2017 (3001/3806-78.8%) and in 2018, of the 3864 SDPs collected, voluntary pool was 3349/3864-86.6%. Dedication to the cause is evident by the regular voluntary donors - Ten donors have donated SDPs more than 100 times, 28 between 50-99 times, and 304 individuals have donated between 10-49 times. A multi-pronged approach targeting finances, accommodation, hygiene and transfusion support (through SAL) has significantly reduced

our pediatric Treatment Refusal and Abandonment rates from 25% in 2009 to consistently less than 5% from 2014 till date.

Conclusions: The SAL initiative has demonstrated a successful and sustainable model for fulfilling huge requirement of SDPs through dedicated team efforts mobilizing societal participation and the model can be replicated in other cancer centers throughout the world.

V804 SIOP19-1667 | Abstract Title: Factors Related to ICU Admissions of Childhood Cancer Patients in Tertiary Referral Hospital in the Private Sector in India

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Background/Objectives: Modern day treatment of childhood cancer is punctuated by necessary need for intensive care. This adds to morbidity, cost and anxiety. There is no published data on ICU admission patterns of childhood cancer patients in India and we aimed to address this gap.

Design/Methods: All children ≤ 18 years of age newly diagnosed with cancer at Max hospital, Saket, Delhi (tertiary referral hospital in the private sector) are registered onto a registry. Those registered between March 2013 to May 2018 were included. ICU admissions were recorded and demographic and disease-related factors associated with ICU admission were investigated.

Results: There were 258 children registered (61% Indian, 66% male, median age 7 years). 149 (58%) patients had 204 episodes of ICU admission (of these 74% needed only one ICU admission). Median duration of ICU stay was 3 days (range 1-38). There were 17 ICU deaths (11% of patients admitted to ICU and 8% of ICU episodes).

Age group, gender and nationality were not significantly associated with ICU admission but cancer type was ($p=0.008$). ICU admission rates were highest for CNS tumours (33%), leukemias (22%) and neuroblastomas (12%).

There were two broad reasons for ICU admission – 53% operative/procedural, while 47% sick/supportive. On multivariate analysis, the distribution by age and gender did not vary significantly in these two categories. However, there was significant difference by nationality (higher ICU admission rates for international patients with $p=0.007$) and by cancer type ($p=0.008$). Cancer types associated with operative/procedural reason were CNS tumours (61%), neuroblastomas (16%), soft tissue sarcomas (12%) while those with sick/supportive reason were leukaemias (40%), lymphomas (15%), and CNS tumours (14%).

Conclusions: Our admission rates for children with cancer to ICU are higher and the mortality rates lower than those reported in the literature. An absence of a high dependency unit in our hospital leading to a greater use of ICU may be a possible explanation.

V805 SIOP19-0777 | Does Routine Surveillance Imaging after Completing Treatment for Childhood Solid Tumours Cause More Harm Than Good? A Systematic Review and Meta-Analysis

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Background/Objectives: Whether surveillance imaging is associated with survival benefit and what burden surveillance places on patients, families or healthcare services, is unknown. This systematic review examines the survival benefits and harms, including radiation dose and psychological impact of routine off-treatment surveillance imaging in pediatric patients after childhood cancer treatment.

Design/Methods: Literature reporting a programme of surveillance imaging used to detect relapse in pediatric patients in first remission from a malignant extra-cranial solid tumours, published from 1990 onward, were systematically identified and reviewed. Informed by Patient and Public Involvement, data on survival benefit, harms associated with imaging, cost-effectiveness and the quantity, frequency and type of scanning were extracted and synthesised from 55 studies, all of which were assessed for risk of bias. Registration: PROSPERO (CRD42018103764).

Results: Studies were observational and reported on 10,207 patients across 48 cohorts. Literature was judged as moderate, serious or critical risk of bias for all except one study. In no case, did data allow for meaningful meta-analysis. Data for patients with Wilm's tumor accounted for 49.5% of all data and indicated possible survival benefit. For patient with all other cancers, data were inconsistent and did not support the detection of relapse by scans prior to clinical symptoms. Surveillance programmes comprised large numbers of scans (range: 3.5-55 per patient) and were associated with false positive imaging and substantial radiation dose. No data regarding the psychological impact of surveillance or the experience of patients were available and cost-effectiveness data were lacking.

Conclusions: At present, no conclusive statement regarding the survival benefit of surveillance imaging within this patient population can be made. The identified evidence gaps, suggest that both high quality, randomised evidence and qualitative research are required to determine the true impact of surveillance imaging and to provide the data

on patient experience that is needed to inform policy and practice.

V806 SIOP19-1294 | Body Composition Phenotypes in Young Adult Survivors of Childhood Acute Lymphoblastic Leukemia

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Background/Objectives: Survivors of childhood acute lymphoblastic leukemia (ALL) are predisposed to treatment induced excess fat and sarcopenia. The combination of high adiposity (HA) and low muscle (LM) mass entail important health consequences. A new classification system using cut-offs for HA and LM defines 4 body composition phenotypes (after Prado et al., 2014): low adiposity with high muscle mass (LA-HM), high adiposity with high muscle mass (HA-HM), low adiposity with low muscle mass (LA-LM) and high adiposity with low muscle mass (HA-LM).

This study compares the body composition phenotypes of 27 survivors of childhood ALL (mean age 24.8±4.2 y, range 18 – 32 y) and 25 age- and sex-matched controls.

Design/Methods: Participants' body composition was assessed using Dual-energy X-ray absorptiometry. We used the published age-, sex- and BMI-specific decile reference values for appendicular muscle mass index (AMMI) and fat mass index (FMI) developed by the 1999-2004 National Health and Nutrition Examination Survey cohort, and classified all survivors and controls into the 4 aforementioned body composition phenotypes.

Results: HA-LM and LA-LM were the common phenotypes among ALL survivors (37.04% and 29.63%, respectively). The prevalence of the HA-LM phenotype was higher among male survivors compared to male controls (38.46% vs 7.69%, p=0.06). The LA-HM phenotype was significantly less frequent in survivors than in controls (7.41% vs 32%, p=0.02) and in male survivors compared to male controls (7.39% vs 46.15%, p=0.03). Body composition phenotypes were similar in female survivors compared to female controls.

Conclusions: Survivors of childhood ALL, especially men, present with abnormal body composition phenotype consistent with sarcopenic obesity in their early adulthood. The applied body composition measure is relevant and may help to

identify individuals at risk of metabolic conditions and functional muscle deficits.

V807 SIOP19-0837 | Rehabilitation for Children with Childhood Cancer: A Pilot Study

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Background/Objectives: Children diagnosed with cancer can experience cancer-related or treatment-related problems, which can impact on their physical, cognitive, and psychosocial functioning. A comprehensive programme conducted by physiotherapists, occupational therapists, speech and language therapists, and music therapists aims to minimise the secondary effects of cancer through functional rehabilitation.

Design/Methods: Children diagnosed with cancer in KK Women's and Children's Hospital between March 2017 and February 2018 were screened to be part of the pilot rehabilitation programme. WeeFIM (Functional Independence Measure for Children) raw and age-normative scores were collected at baseline and six months post-rehabilitation. Descriptive analysis, paired *t*-test and McNemar Test were used for analysis.

Results: Eighteen of the 36 children diagnosed with cancer were eligible for the rehabilitation programme. Eight children were diagnosed with blood cancer, four with a solid tumour and six with a brain tumour. The mean age at baseline was 88 months, with a median age of 79 months, ranging from 27 to 174 months. At baseline, four children scored within the average range and the remaining 14 children were placed at below average range in the Total WeeFim scores. At six months, six children scored within the average range and the other 12 children scored below average. There was no statistical significance in age normative scores at baseline and six months. Four children maintained their scores within the average range, whereas two children demonstrated improvements and fell within average scores for their age at evaluation at six month. Overall, significant improvements were found in the domains of self-care ($p=0.009$) and mobility ($p=0.018$) at baseline and 6 months post rehabilitation.

Conclusions: Early rehabilitation was effective in improving the functioning status of children with cancer. However, these children continue to present with below average functioning compared to their peers. Results suggested the need for children to receive ongoing rehabilitation to improve their physical functioning.

V808 SIOP19-1237 | Communication about Traditional Complementary Alternative Medicine in Childhood Cancer: A Comparison Between Dutch and Indonesian Health-Care Providers at Academic Hospitals

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Background/Objectives: Communication about traditional complementary and alternative medicine (TCAM) use is important in both Western and Eastern countries to prevent interference with conventional cancer treatment. This study compares communication about TCAM of health-care providers (HCP) involved in childhood cancer care in Netherlands and Indonesia.

Design/Methods: Cross-sectional study at Dutch and Indonesian academic hospital using semi-structured questionnaires.

Results: Overall 342 HCP participated: 119 Dutch and 223 Indonesian HCP (response rate 80% and 87%). HCP have negative perspectives about TCAM according to more Dutch (80%) than Indonesian (42%) HCP ($p < 0.001$). More Dutch (97%) HCP think cancer patients use TCAM than Indonesian (75%) HCP ($p = 0.001$). Less Dutch (36%) than Indonesian (65%) HCP ask parents, during routine history taking, if they use TCAM in their child ($p < 0.001$). In both settings, most HCP (98%, 90% respectively) consider it important that parents inform them if their child uses TCAM ($p = 0.004$). Parents do not disclose their TCAM use to doctors according to 75% of Dutch and 84% of Indonesian HCP ($p = \text{ns}$). Parents are afraid of receiving less care from doctors if they disclose their interest in or use of TCAM according to more Indonesian (74%) than Dutch (42%) HCP ($p < 0.001$). Parents actually receive less care from doctors if they disclose their interest in or use of TCAM according to more Indonesian (40%) than Dutch (2%) HCP ($p < 0.001$). More Dutch (46%) than Indonesian (30%) HCP never openly discuss TCAM with parents ($p = 0.002$).

Conclusions: Dutch HCP have more negative perspectives and communicate less openly about TCAM with parents than Indonesian HCP. In both settings HCP realize that their patients use TCAM and do not disclose this. Doctors need to initiate and facilitate open discussions about TCAM with parents, without retributing families after TCAM disclosure.

V809 SIOP19-1210 | Efficacy of Inflammatory Cytokines in Detection of Bacteremia in Children with Febrile Neutropenia

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Background/Objectives: In the current literature, multiple inflammatory markers have been proposed for detecting bacteremia, but no consensus has yet been established. We aimed to evaluate the success of inflammatory cytokines to detect bacteremia in febrile neutropenic patients.

Design/Methods: This prospective study included patients who were followed-up 9 months due to febrile neutropenia. Blood samples from patients who met the determined criteria were studied separately at 0-24-48 and 72th hours starting from the day when neutropenic fever started. From blood samples; lactate, blood sugar, CRP) procalcitonin, D-dimer, blood culture, respiratory virus panel, cell membrane markers: CD-64, CD-48, Cytokines:IL-6, IL-8, MCP, STREM were studied. At the 0th hour of the fever, the markers were expressed as [Variable-1], at the 24th hour [Variable-2], at the 48th hour [Variable-3] and at the 72th hour as [Variable-4]. According to the data obtained, patients with bacteremia were determined as group 1 and others as group 2. Both groups were compared in terms of all variables.

Results: There was no significant difference between the two groups in terms of gender ($p=0.61$), age ($p=0.24$), duration of neutropenia ($p=0.70$), neutrophil count ($p=0.66$), number of monocytes ($p=0.45$), pH ($p=0.73$). In group 1 patients, there was a significant increase in hypotension ($p=0.01$), tachycardia ($p=0.01$), fever ($p=0.01$), presence of sepsis ($p=0.001$). There was no significant difference between the CRP levels in the blood samples taken on the 1st and 2nd days ($p=0.87$, $p=0.25$) and there was a significant difference in CRP levels on the 3rd and 4th days ($p=0.03$, $p=0.01$). Despite this, all of the procalcitonin levels were significant in group 1 ($p=0.03$, $p=0.01$, $p=0.005$). Other cytokines evaluated were CD64-1, CD64-2, CD64-3, CD64-4, CD48-3, CD48-4, IL6-1, IL6-2, IL6-3, IL6-4, IL8-1, IL8-2, IL8-3, IL8-4, MCP-1, MCP-2, MCP-3, MCP-4, STREM-1, STREM-2, STREM-3, STREM-4, MASC-C were not significantly different. Only CD48-1 and 2 ($p=0.01$ and $p=0.02$) were significantly different between the groups.

Conclusions: Procalcitonin and CD 48 can be used as an effective marker for the detection of bacteremia in febrile neutropenic patients and in determining the efficacy of treatment. In addition, CRP values are another marker that can be used safely to assess antibiotic response from the 48th hour of neutropenic fever.

V810 SIOP19-1476 | Consequences of Treatments of a Brain Tumour on the Learning of Written Language: Prospective Studies on 12 Paediatrics Patients

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Background/Objectives: The tumours of fossa posterior represent 50% of paediatric brain tumour. The treatment is very aggressive and combines complete excision surgery, radiotherapy and chemotherapy. In the last decade, the overall survival rate of these children increased dramatically and the management the side effects like neurocognitive sequelae are mandatory. Children treated for a tumour of fossa posterior have deficits in speed processing, attention, memory and academic performances. The learning of written language is complex and appeals to executive functions like memory working or attention.

Design/Methods: We tested information processing, aspects of attention and planning in 12 paediatric posterior fossa tumour survivors. We evaluated oral language (BILO 3C), constraints (E2C), reading, attention (TEA-ch), memory and cognitive efficiency (WISC-V).

Results: Among the 12 patients, 7 had medulloblastoma, 3 astrocytoma, 1 ependymoma and 1 PNET. 100% of patients had a surgery, 75% a radiotherapy including the cranio-spinal axis for 7/12 patients, 75% a chemotherapy and 50% an intensive chemotherapy. We compared patient's results to the results of all coming population of the different tests. 50% of patients are below the 10th percentile with a 95% confidence interval for the anarchist attention. All these patients received chemotherapy. Likewise, 41.7% of patients are below the 10th percentile with a 95% confidence interval for auditory-verbal memory. All these patients received radiotherapy by photon therapy. 33.3% of patients are below the 10th percentile with a 95% confidence interval for reading speed.

Conclusions: In comparison with an all coming population, these patients have deficits in auditory-verbal memory, anarchist attention and reading speed. These deficits have impact on speed processing. These functions are essentials for learning of written language, academic performances and social integration. It is necessary to include speech therapists earlier in the management of paediatric brain tumours sequelae, because of their important role in the learning of written language.

V811 SIOP19-1404 | Population Pharmacokinetics of Vincristine Administered Through Push-Injections and One-Hour Infusions in Pediatric Oncology Patients

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Background/Objectives: Vincristine (VCR) is frequently used for treating pediatric cancer. It can be administered through push injections or one-hour infusions intravenously. However, differences in the pharmacokinetics (PK) of these administration methods are unknown. The aim of this study was to describe the PK differences due to the type of administration of VCR.

Design/Methods: The study is part of the VINCA trial, a randomized controlled trial studying effect of administration method on the development of VIPN in pediatric oncology patients. PK was assessed one to five times throughout treatment. Each PK assessment included up to eight samples over 24 hours. Samples were analyzed using high-performance liquid chromatography/tandem mass spectrometry. The population PK of VCR along with the effects of type of administration on the PK was determined using non-linear mixed effects modeling via Monolix. A linear two-compartment model, with first-order elimination, was used to model the data. Individual post-hoc parameter values were used to estimate the area under the concentration time curve (AUC) and the maximum concentration (Cmax).

Results: Overall, 70 PK assessments in 35 children were evaluated. The population estimated clearance was significantly higher in the push vs 1-hour infusion group (26.9 vs. 10.7 L/hr/m², $p < 10^{-3}$). This translated to a significant lower AUC (131.1 vs 211.0 ng hr/mL, $p < 10^{-9}$) in the push group. Additionally, Cmax was significantly higher in the push group compared to the 1-hour group (75.8 vs 29.6 ng/mL, $p < 0.03$). Other PK parameters (volume of the central/peripheral compartment and intercompartmental clearance) were not significantly associated with administration method.

Conclusions: Push injections of VCR are associated with a significant higher Cmax and clearance, yielding lower AUC than one-hour infusions. Further clinical studies are needed to determine whether achieving higher systemic exposure to VCR while avoiding high peak concentrations with one-hour infusions translates into improved anticancer effects and/or lower toxicity to VCR.

V812 SIOP19-1165 | Improving Outcomes on Induction Therapy of Standard-Risk Acute Lymphoblastic Leukemias in Children with Supportive Care and Adapted Risk Stratification in a Middle-Income Country

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Background/Objectives: Acute lymphoblastic leukemia (ALL), the most common cancer of childhood is characterized by high cure rates and good treatment outcomes in high-income countries. In developing countries results are significantly lower because they face unique problems such as lack of resources and non-integrated scheme of medical attention.

Design/Methods: This study was conducted at Teleton Children's Oncology Hospital (HITO) in Queretaro, Mexico, and aimed to estimate the induction phase response rate and mortality in induction of newly diagnosed standard-risk (SR) ALL in children.

Patients were treated according to Dana-Farber Cancer Institute ALL Protocol 05-001. Patients were assigned to an initial risk group based on characteristics of age, leukocyte count, SNC status, immunophenotype and underwent 32 days of induction therapy. Those who achieved complete remission after induction were assigned to a final risk group according to the measurement of minimal residual disease (MRD). A multidisciplinary team was available for early detection of complications and adequate treatment.

Results: From December 2013 to March 2019, 84 patients were treated. Patients with SR at diagnosis were 38 (45%). At the end of induction therapy 100% of patients achieved remission. Only one patient was re-classified at very high risk by MRD. With a median follow-up of 26 months of complete remission (CR) induction death rate was 0%. There was one death in a patient with CR associated with infectious toxicity.

Conclusions: Infection and treatment related toxicity are the main causes of death during induction phase for children suffering ALL, specially in low and middle income countries. Better results can be achieved with an integrated medical model to overcome disadvantages. Accuracy in diagnosis, evidence based treatment protocols, and better management of complications improve outcomes. HITO is a pediatric oncologic hospital, a comprehensive family centered hospital with hospital & house model to reduced mortality rate.

V813 SIOP19-1186 | Preventing DNA Damage Induced Accelerated Ageing and Chemotherapy Side-Effects by Dietary Changes

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Background/Objectives: Although most children with cancer are cured, they are increasingly confronted with the negative effects of the treatment later in life. Chemo- and radiotherapy mainly target DNA and our previous work has revealed that DNA damage is a main cause of ageing and ageing-related diseases. This is apparent from DNA repair-deficiency syndromes and corresponding mouse models, in which endogenous DNA damage builds up quickly and thereby accelerates ageing, but also from paediatric long-term cancer survivors with many late-life effects.

Restricting diet in progeroid DNA repair mouse mutants triggers a temporary redesign of metabolism, which attenuates growth and prioritizes protection and maintenance systems, tripling lifespan and dramatically reducing accelerated ageing.

Design/Methods: We next applied such nutritional interventions to young wt mice prior to chemo- or radiotherapy treatment, monitored changes in behaviour, food intake and body weight and examined multiple tissues for treatment toxicity. Also, a pilot investigation was started restricting diet in a progeria child due to DNA repair deficiency.

Results: Administering cisplatin (10 mg/kg IP), and radiotherapy (2 Gy whole body irradiation), to young mice lowered appetite and decreased body weight for multiple days after treatment. Triggering a protective response by short-term fasting before administering exogenous DNA damage in mice (e.g. by cisplatin and radiotherapy) diminished all signs of direct toxicity and protected against many ageing-related side-effects.

Interestingly, mildly reducing food intake in a first progeria child has recently also yielded spectacular improvement of overall performance and health, even surpassing results obtained in mice.

Conclusions: Nutritional interventions can trigger a protective response preventing the negative side-effects and accelerated ageing induced by DNA damage in both mice and human. Thus, nutritional preconditioning holds a very promising potential for paediatric oncology patients preventing short-

and long-term health conditions thereby improving overall quality of life.

V814 SIOP19-1555 | Single Nucleotide Polymorphisms Associated with Methotrexate Toxicity are Unequally Prevalent in Acute Lymphoblastic Leukemia Patients of Different Races and Ethnicities

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Background/Objectives: Patients from different ethnic and racial groups experience different methotrexate toxicity rates. To clarify this disparity, we described the prevalence by race and ethnicity of single nucleotide polymorphisms (SNPs) associated with methotrexate toxicity in pediatric acute lymphoblastic leukemia (ALL) patients at Texas Children's Hospital (TCH).

Design/Methods: SNPs that have been identified as associated with methotrexate toxicity were identified from a database (www.PharmGKB.org). Whole genome sequencing information was obtained from a cohort of 565 pediatric patients with ALL. Prevalence of all risk alleles were calculated by for each subject. Minor allele frequencies (MAF) were calculated for the SNPs with the highest level of evidential support (LoE) and compared by race using Pearson's Chi-squared test.

Results: Forty-one SNPs were identified from the database. There were 234 Caucasian, 222 Hispanic, and 29 black patients with mean (standard deviation) risk allele prevalence of 38.7% (0.047), 38.7% (0.045), and 37.0% (0.045) respectively. Of the SNPs with the greatest LoE, the MAF for rs11045879 (SLCO1B1) was 17% for Caucasian patients, 15% for Hispanics (p=0.53, with Caucasians as reference comparator), and 6% for blacks (p=0.08), for rs1801394 (MTRR) the MAF was 52% for Caucasians, 9.0% for Hispanics (p=1.0x10⁻¹¹), and 32% for blacks (p=0.01), for rs1045642 (ABCB1), 50% for Caucasians, 15.8% for Hispanics (p=0.02), and 34% for blacks (p=0.5), and for rs1801133 (MTHFR), 12.0% for Caucasians, 23.4% for Hispanics (p=1.2x10⁻⁰⁶), and 14% for blacks (p=0.02).

Conclusions: SNPs associated with methotrexate toxicity are highly prevalent in the population of pediatric ALL patients at TCH. The SNPs with the highest LoE were not only highly prevalent, but significantly differently prevalent for Caucasian, Hispanic, and black patients. These summary statistics suggest that genomic factors may help explain the different rates of methotrexate toxicity for patients of different races and ethnicities.

PUBLICATION ONLY

Brain Tumours

PO001 SIOP19-0935 | Refractory Brain Tumors in Pediatric Patients. Therapy Based on Exome Study. A Case Report

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Background/Objectives: Brain tumors are de second more frequent solid tumors in children, but they continue to be the fist cause of death so we are looking for new strategies to improve survival and quality of life.

Design/Methods: A 17-year-old male patient was diagnosed with a brain tumor on June, 2016 so it was partially resected. The patient presented postoperative complications that required placement of a tracheostomy, gastrostomy and a prolonged hospital stay. Histopathological diagnosis of **ANAPLASTIC EPENDIMOMA** was confirmed, hence he was sent to receive 60 Gy focal radiotherapy.

After that, he was sent for evaluation to our hospital. The patient was found prostrate, with a Karnofsky functional scale of 50 points. Extension studies were performed documenting residual tumor (38x39x38mm). Magnetic resonance of spinal cord was negative but lumbar puncture was with presence of neoplastic elements. He was not a candidate for a new surgical resection.

He started treatment with chemotherapy. As result, a significant reduction of the residual tumor was obtained, so radiosurgery was performed on December 2017 and continued with chemotherapy treatment. The patient recovered mobility, language and improved his quality of life. However, in September 2018 a tumor progression was documented. A second line of chemotherapy was offered but he rejected so we began with palliative care.

We performed **WHOLE EXOME SEQUENCING** in tumor tissue embedded in blocks of paraffin documenting genetic variants in the MTOR gene, so we started treatment with metronomic chemotherapy based on **temozolamide and molecular target therapy with MTOR inhibitor**.

Results: Follow-up studies were carried out documenting a remarkable improvement. The patient has five months of sur-

vival with target therapy and with a good quality of life. Actually he is independent for daily life activities.

Conclusions: Personalized therapy should be given in all patients, so we should invest in molecular biology in order to perform a better oncology medicine.

PO002 SIOP19-1751 | Whole Exoma Sequencing to Identify Molecular Signature of Brain Tumors in Pediatric Mexican Patients. Multicenter Study

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Background/Objectives: At Centro Medico Nacional (CMN) 20 de Noviembre, in Mexico City, we are developing research in the area of precision medicine focused on pediatric oncology for the molecular characterization of brain tumors in Mexican children.

Childhood brain tumors constitute approximately 20 to 25% of all malignancies in children and remain the leading cause of death associated with cancer.

There is a high probability that the genesis of the brain tumor is a consequence of inherited, acquired and epigenetic phenomena. We believe that individualized diagnosis and treatment can improve the prognosis, reduces duration and treatment costs and decreases the quantity and severity of the sequelae, which translates into an improvement in the quality of life of patients, their families and society.

Design/Methods: This is a multi-center study with the participation of 3 Medical Centers and a Genomics Institute.

In this study, clinical data were collected from pediatric patients with brain tumors such as gender, age, diagnosis, histology, stage of the disease, treatment received, current status of the disease and survival. Each of these variables was correlated with the data obtained from the complete exome sequencing (WES).

Results: Twelve patient samples have been characterized, four medulloblastomas, four astrocytomas, two craniopharyngiomas and four ependymomas. We observed there are 10 genes that contain the largest number of variables among

which are MUC16, MUC3A, ZNF717, TTN, OBSCN, CCDC168, AHNK2, FSIP2, DNAH14 and GPRIN2.

Conclusions: Despite the new advances in diagnosis and treatment in Mexico, there have been no studies associated with the molecular characterization of tumors in the central nervous system in pediatric patients. Therefore, continuing with this study will give us the necessary tools to determine the molecular signature in Mexican pediatric patients, not only will it contribute to a better diagnosis and treatment, but it will also have an impact on the quality of life of patients.

PO003 SIOP19-1484 | Clinical and Radiological Response to Dabrafenib in Diffuse Midline Glioma Harboring H3.3K27M and BRAF-V600E Mutations

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Background/Objectives: Diffuse midline H3.3K27M-mutant gliomas are rare tumours first described in the WHO 2016 classification, with aggressive clinical behavior and dismal prognosis, sharing the same outcome as DIPG. Rarer cases harbour both H3-K27M and BRAF-V600E mutations. We report the case of a 16-year-old girl with such disease treated at progression with dabrafenib and trametinib, obtaining a clinical-radiological, but short-lasting, astonishing response.

Design/Methods: The girl underwent subtotal surgical removal and VP shunt. Histology confirmed diffuse midline glioma H3.3K27M mutated. She received systemic nimotuzumab and vinorelbine, radiotherapy (54 Gy/1.8 Gy per fraction) and local re-irradiation at progression (19.8 Gy after 7 months). Eleven months after diagnosis she had severe neurological deterioration with incoming epileptic seizures leading to coma. We then acknowledged that the tumour had BRAFV600E gene mutation. Dabrafenib on a compassionate basis was obtained, being a selective inhibitor of BRAF kinase suppressing ERK -a downstream of BRAF in the MAPK pathway- with known anti-proliferative activity against BRAF V600 mutated tumours in vitro and in vivo.

Results: After 6 days of dabrafenib, neurological amelioration with awakening and progressive neurological recovery were observed and MRI documented PR at day 14. Trametinib (anti-MEK compound) was obtained on a compassionate basis as well, but after one month the patient died for tumour progression.

Conclusions: Even if infrequently described, BRAF mutations can be found in patients with diffuse H3.3K27M-mutated gliomas. BRAF status should be known from the diagnosis to allow targeted inhibitors at progression (or at

diagnosis). The short-lasting response we observed warrants further investigations about mechanism of action and resistance to these new drugs.

PO004 SIOP19-0596 | High Grade Gliomas in Children Under 5 Years of Age Treated with Bbsfop Chemotherapy: A South Thames Neuro-Oncology Unit Study

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Background/Objectives: High grade gliomas (HGG) represent 8-12% of paediatric brain tumours. The mainstay of treatment comprises maximal safe surgical resection, focal radiotherapy and chemotherapy. The BBSFOP protocol was a chemotherapy-based approach devised in the 90's to avoid/delay radiotherapy in young children with HGG. It comprises seven cycles of three drug-pairs (carboplatin/procarbazine, cisplatin/etoposide and vincristine/cyclophosphamide) administered over a 16 month period. Our objective was to assess the efficacy of BBSFOP chemotherapy in patients treated off-trial at our institution.

Design/Methods: Children aged <5 years with non-brainstem HGG treated at first line with surgery and BBSFOP chemotherapy between 1995 and 2018 were eligible. Patients who received radiotherapy at first line were excluded. Descriptive statistics and survival outcomes were analysed.

Results: Overall 19 children with HGG aged <5 years were identified over the study period, 5 of which fulfilled eligibility criteria for this study. Median age 1.6 years (range, 1.3-4.0). Tumour location: 2 hemispheric, 1 cerebellar, 1 spinal and 1 multifocal supra-infratentorial. Complete resection was achieved in 2 cases, sub-total resection in 2 and biopsy only in 1. Two children died of tumour progression: a 1.2 year-old girl with subtotal resection who progressed at 33 months from diagnosis; and a 4 year-old boy who had biopsy only, due to multifocal disease, who progressed on treatment at 2.3 months from diagnosis. Three children are still alive without radiotherapy at 18, 20 and 91 months from diagnosis. The median progression-free and overall survival were 32.5 and 52 months, respectively.

Conclusions: These outcomes are comparable to those previously reported and support BBSFOP chemotherapy to avoid/delay radiotherapy in young children with newly diagnosed HGG.

PO005 SIOP19-0667 | Meningiomas in the Pediatric Age: A Case Series in a Center in Mexico

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Background/Objectives: The presence of Pediatric Meningiomas (PM) is extremely rare. PM constitute neoplasms of the central nervous system derived from the arachnoid cell layer and it is estimated that their incidence in childhood ranges from 0.4 to 4.1% of all pediatric tumors. The aim of this study is to present the findings about PM at a reference institution in western Mexico during the last 12 years.

Design/Methods: This is a retrospective and descriptive study. All files of patients diagnosed with PM between 2006 and 2018 were revised. Clinical profiles, radiological characteristics, histology and treatment were analyzed.

Results: The age distribution of the patients ranged between 1 and 15 years of age the average age was 7 years. Three patients were female and 2 were male. The main symptom for consultation was headache, but one patient presented tremors in upper limbs. The most frequent location of the lesions was the left parietal intra-axial region (n = 3). In 1 of the 5 patients, the location was extra-axial in the right petroclival region. Total resection was performed in 4 of the 5 patients. Pathology varied between Meningoepithelial meningioma, fibrillary meningioma and 1 case had a rhabdoid focal component classified as WHO grade III. None of the patients received radiotherapy. The 5-year overall survival and event free survival was 100% for this series, in a period between 3 and 11 years in surveillance.

Conclusions: The diagnosis of Pediatric meningiomas is exceptionally rare and prognosis is very good in a long recovery follow-up. Treatment requires complete surgery. Radiotherapy is not necessary according this experience. The Clinical presentation may appear in the intra-axial localization, as occurred more frequently in our series

PO006 SIOP19-1734 | Incidence and Clinical Characteristics of Pediatric Patients with Craniopharyngioma in the Low Medium Income Country an Experience of Eleven Years

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Background/Objectives: Diagnosis of Craniopharyngioma (CP) is rare in pediatric age and its treatment is complex due to

its location and infiltration, making gross total resection challenging. Adjuvant treatments include radiation, chemotherapy, and intratumoral injection.

Design/Methods: This is a retrospective, observational study. All clinical files of children under 18 years diagnosed with CP between 2007 and 2018 in the Civil Hospital of Guadalajara were analyzed

Results: Thirteen patients were identified. Cumulative incidence of presentation was 1 cases/year. Median age of presentation was 9 years (range 6 to 13). Male/female ratio was 1. 1:1. The main symptom was visual problems (69%), including loss of visual acuity (23%), amaurosis (15%), squint (15%), diplopia (7%) and blurred vision (7%). Treatment only surgery in 38% of cases and surgery plus radiotherapy in 46%, 2 patients received surgery plus intratumoral bleomycin (15%). Regarding sequelae the most common was endocrine dysfunction included hyperlipidemia and hypopituitarism (16%) and hypothyroidism (50%). Seven children abandoned surveillance after treatment. Those who continued surveillance are alive, with a median follow-up of 3 to 10 years.

Conclusions: In our experience diagnosis of CP is rare, survival is good but it was affected by sequelae and a high rate of abandonment.

PO007 SIOP19-1178 | Five-Year Experience with Brain Tumors Diagnosed and Treated in Hospital Infantil Teleton de Oncologia (HITO), the First Pediatric Oncologic-Devoted Hospital in Mexico

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Background/Objectives: Background: Brain tumors constitute the most common pediatric solid tumor; in Mexico these is the third most frequent diagnosis (9.4%) after leukemia and lymphoma. Hospital Infantil Teleton de Oncologia (HITO) started its operation at December 2013 and is the first pediatric oncology devoted hospital in Mexico. **OBJETIVE:** To know the epidemiology and characteristics of patients admitted to HITO with brain tumor diagnosis.

Design/Methods: Patients and Methods: These is a transversal, descriptive and observational study. Medical records of children admitted in HITO with brain tumor diagnosis between December 2013-January 2019 were revised.

Variables: Ages, gender, histopathology diagnosis, tumor grade, topography, treatment schema, follow-up status and time of free progression survival.

Results: We found 55 cases of brain tumor. Average age at diagnosis was 8 years; 55% correspond to female gender; about histologic diagnosis, most frequent was astrocytic tumors (38%), low grade gliomas (20%), followed by embryonic tumors (27%), ependymoma (9%). 54.5% of operated patients had gross-total or near total resection. Average follow-up time is 27 months (range 4–60 months); Currently, 63.6% of patients are in treatment and follow-up; 3% showed progressive disease. Mortality is 36%.

Conclusions: The findings and characteristics of children with brain tumors in HITO are similar to published in international reports. HITO is following the protocols of treatment sponsored by COG, unlike other national institutions. Currently, we are doing cytogenetic and molecular analysis of tumor tissue, and cellular-proliferation index, that allow is to get relevant information for treatment.

PO008 SIOP19-0791 | Treatment of Children with Malignant Brain Tumours Using Adapted International Guidelines: Survival and Quality of Life Analysis

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Background/Objectives: Risk stratification has the known impact on survivorship as pediatric brain tumours require multimodal treatment to achieve remission. International guidelines were adapted locally for the treatment of brain tumours. The aim of the study was to analyze what was the impact on survival and quality of life.

Design/Methods: A retrospective chart and National cancer registry data review of 117 children with brain tumours treated and observed from 2007 to 2018 was performed. Demographics, presentation, treatment and survival follow up were described. Quality of life was assessed due to late effects and treatment toxicity.

Results: The largest cohorts were patients with low grade glioma (LGG) and medulloblastoma. The main symptoms that led to diagnosis were headache, nausea and vomiting, cerebellar dysfunction, visual impairment, peripheral neuropathy and cognitive decline. The median interval to diagnosis was 4.5 months. Only 20% of patients had preliminary diagnosis of brain tumor established by primary physician. HIT-MED guidelines were used for risk stratifica-

tion and treatment in patients with medulloblastoma: surgery, distant beam radiotherapy and adjuvant chemotherapy with 3-year OS overall survival 53%. SIOP guidelines were used for patients with WHO grade I-II glioma (LGG). Such patients received adjuvant distant beam radiotherapy after surgery in the case of residual tumour and age over 8 years or chemotherapy in the cases of progressive unresectable symptomatic disease. The 3-year OS in patients with WHO grade I-II glioma was 81%. The most common adverse events that worsened the quality of life of long term survivors were associated with neurosensory and movement disorders.

Conclusions: Factors that influenced the overall survival were gross total resection of the primary tumour, time to final diagnosis, radiotherapy after subtotal resection and risk based chemotherapy. The prognosis for children with medulloblastoma improved after implementing risk stratification in low income countries comparing to historical control.

PO009 SIOP19-0864 | Management of Pediatric Neuro-Oncology from 2015 to 2017: An Institutional Review

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Background/Objectives: Pediatric Neuro-Oncology is undergoing a rapid transformation within all of its key disciplines in developed country, but in resource limited countries, we are still faced with great challenges. In order to better understand management of central nerve system tumor in children, we analyze the diagnosis, treatment, multi-disciplinary team (MDT) work in our hospital.

Design/Methods: The study recruited 124 cases in Shenzhen Children's Hospital from January 2015 to December 2017. The distributions of patients, pathology, comprehensive care, causes of death were studied.

Results: The pediatric brain tumor number was increased steadily from 2015 to 2017, 31, 38 and 55 cases, respectively. Among the 124 patients, 105 cases were conducted operations, accounting for 85%, while 19 patients could not get the pathology and most of them were brainstem tumors, occupying for 74% (14/19). The most common pathology types of the patients were glioma, medulloblastoma and ependymoma, accounting for 31% (33/124), 26% (27/105) and 14% (15/124). The treatment for brain tumor included operation, radiation, chemotherapy and autologous transplantation. There were totally 49 patients needed radiations, patients were sent to radiation department outside Shenzhen Children's Hospital leading to 12 patients lost follow up.

Fifty-nine patients were given chemotherapy, only 2 patients in Hematology and Oncology department. One patient diagnosed pinealoma was performed autologous transplantation. There were 19 deaths and the causes were due to progress, relapsed and severe complications, showing 7, 7 and 5 cases, respectively. We lacked of resource for intensive follow up of the quality of life in the clinic.

Conclusions: Our study shows that pediatric neuro-oncology patients' numbers are rising in latest three years. Radiation and chemotherapy are important in the management for these patients. Adjuvant treatment options have to be implemented by MDT discussion closely. The issue of long-term sequelae has to be clearly recognized.

PO010 SIOP19-1722 | Awake Craniotomy for Brain Tumor in A 9-Year-Old Child

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Background/Objectives: A 9-year-old girl presented with seizures due to tumor in left temporo-parietal region. In order to identify language and motor-controlling areas during resection an awake craniotomy was proposed. Because of her age, she was prepared by a multidisciplinary team. The child's cooperation during the mapping procedure and tumor resection was exceptional. There was no impairment in the patient's speech, but she exhibited involuntary movements of right arm and leg. Postoperative cranial MRI confirmed partial resection of the lesion, whose remanent was located at left motor area. She had no seizures during the postoperative period and was discharged without neurological disability on the fifth day after the surgery. Histology revealed a dysembryoplastic neuroepithelial tumor (WHO grade I).

Design/Methods: Case presentation: Results: Discussion: The challenge of surgery in neurooncology is to maximize extent of resection while preserving eloquent functions. Intraoperative cortical mapping during resection of a brain tumor allows direct stimulation in eloquent areas with reduction in post-operative deficits. This procedure has been performed in adults and children down to the age of 11 years. There is only one case reported in the literature of a 9-year-old child submitted to an awake craniotomy for brain tumor resection. Patients may feel pain related to skin incision, dissection of periosteum, dural incision and manipulation of vascular structures. Pediatric patients are prone to more risks than adults because they become easily agitated after pain sensation. Extensive prepa-

ration for the procedure is important for pediatric patients in order to avoid lack of cooperation. The anesthetist has an important role in ensuring minimal discomfort to the patient without using drugs which may hinder brain mapping. Continuously communication with the patient must be ensured.

Conclusions: Brain mapping during resection of a tumor in an awake pediatric patient is feasible and can be safely performed even in patients under 11-year-old.

PO011 SIOP19-1168 | Case Report: Medulloblastoma in a Child with Wiedemann-Steiner Syndrome

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Background/Objectives: Wiedemann-Steiner Syndrome (WSS, MIM 605130) is rare Autosomal dominant inherited syndrome is typically characterized by hypertrichosis cubiti, growth retardation, developmental delay and facial dysmorphism but was not reported before to be associated with malignancy.

Design/Methods: We present a case of 5 years old girl with mild developmental delay came to medical attention when she was diagnosed with Medulloblastoma Desmoplastic-Nodular WHO IV Group # 4 subtype on 2014, she was diagnosed as Wiedemann-Steiner Syndrome WDSTS based on identification of pathogenic variant splice site mutation MLL/KMT2A gene (OMIM: 159555) by Whole Exome Sequencing and supported by characteristic phenotypic features she was treated with multi modal chemotherapy consisting of subtotal resection followed by postoperative craniospinal radiation and adjuvant chemotherapy as high Risk Medulloblastoma protocol, immediately after the first cycle of chemotherapy (cyclophosphamide vincristine VCR) she had stormy treatment course and severe vincristine (VCR) induced neurotoxicity with progressive neurological impairment in the form of quadriparesis, cranial nerve palsy, bilateral vocal cord paralysis with progressive respiratory failure that need permanent tracheostomy and prolonged pediatric intensive care unit admission with speech and swallowing difficulty after stabilization of her clinical condition she continued her chemotherapy with omitting all doses of VCR without any added toxicity.

Results: after end of therapy she need intensive rehabilitation program to partially retrieve her motor abilities and now

5 years after diagnosis she is in remission with no symptoms or signs of tumor recurrence but still hypotonic and unable to walk independently

Conclusions: To the best of our knowledge, this is the first report of Medulloblastoma in a child with Wiedemann-Steiner Syndrome and due to her underlying inherited genetic defect had extreme VCR neurotoxicity and may need modification or omitting Vinca alkaloids for treating malignancy in this rare syndrome.

PO012 SIOP19-1367 | Management of Refractory Extensive Intracranial Juvenile Xanthogranuloma (JXG) in a Child

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Background/Objectives: Juvenile xanthogranuloma (JXG), is rare form of the non- Langerhans Cell Histiocytosis LCH, involves primarily the skin, but may be localized to a single extra cutaneous site without any skin disease, or may be disseminated and life-threatening

Design/Methods: We present a case of 11 years old Saudi boy, not known to have any medical problem presented with RT ear pain and erythema with progressive hearing loss and RT side facial nerve weakness with headache and recurrent generalized tonic clonic convulsions MRI imaging showed bilateral extensive leptomeningeal based multiple brain and spine lesions including Bilateral vestibular lesions surgical biopsy was done Pathology confirmed Juvenile Xanthogranuloma with numerous histiocytic cells and large tuft cells S100, GFAP & CD1a negative CD68 positive, BRAF mutation was negative skin examination and CT CAP images was Unremarkable no other organ involvement he started treatment Langerhans Cell Histiocytosis (LCH) with CNS disease protocol with vinblastine and prednisone with moderate improvement of his general condition he started tapering of steroid as per protocol post induction phase he developed progressive severe headache and 7th cranial nerve palsy repeated MRI showed Progressive disease with interval increase in the size of multiple necrotic brain lesions and new intramedullary spinal lesions he was STARTED ON Salvage treatment for refractory (LCH) chemotherapy protocol (Cladribine (2CdA) /Cytarabine) AFTER 2 cycles MRI response evaluation showed Improvement of the intracranial lesions

Results: he continued on chemotherapy followed by maintenance therapy Vinblastine with oral 6-MP and methotrexate, currently he is in remission with gradual improvement of MRI imaging and neurological statues

Conclusions: we present rare presentation of refractory intracranial Juvenile xanthogranuloma (JXG), that was challenging in management and may need future potential target therapy especially in recurrent disease.

PO013 SIOP19-0539 | Efficacy of Bevacizumab Alone or in Combination with Temozolomide and Irinotecan in the Treatment of Recurrent and Refractory Brain Tumors in Children in Lebanon

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Background/Objectives: Introduction: Bevacizumab, an anti-angiogenic monoclonal antibody, has shown efficacy in the treatment of recurrent and refractory brain tumor in adults. However, evidence is still lacking in children.

Design/Methods: Between 2016 and 2019, 12 patients (age 5-18 y) in 3 pediatric oncology centers in Lebanon (St George Hospital UMC, Lebanese Hospital Geitaoui UMC and ND de Secours UMC), with recurrent or refractory brain tumor were treated on second or third line regimen. Among them 4 had high risk medulloblastoma, 2 optic glioma, 1 high grade glioma, 2 glioblastoma, 1 grade III glioma with high risk mutation, 1 nonoperable glioma, and 1 had choroid plexus papilloma. The regimen consisted of bevacizumab (10 mg/kg) every 2 weeks alone or in combination with Irinotecan (125 mg/m²) and temozolamide (200 mg/m² for 5 days every 4 weeks). Treatment response was evaluated by MRI done at 3, 6, 12, 24, and 36 months of treatment. Quality of life including physical, cognitive, social, and emotional aspects of patients was also studied.

Results: Six patients (50%) showed radiological regression, 3 patients (25%) showed stabilization, and 3 patients (25%) showed progression of the tumor size. Bevacizumab was well tolerated with minimal side effects (epistaxis in 3 patients). All 12 patients are still alive regardless the aggressive tumors they have. Quality of life has been significantly improved in all patients.

Conclusions: Bevacizumab in children alone or in combination with irinotecan and/or temozolomide as a second line or third line therapy is effective in improving survival and tumor

stabilization with good quality of life and minimal side effects. Further prospective trials in children are needed to confirm these results.

PO014 SIOP19-0867 | Treatment Outcome of Children with Choroid Plexus Carcinoma: Retrospective Analysis - A Single Institution Experience

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Background/Objectives: Choroid plexus carcinoma (CPC) is a rare intraventricular tumor, which usually presents in infancy. There is limited literature reporting outcomes of CPC in children.

Design/Methods: A retrospective analysis of pediatric patients with primary diagnosis of CPC treated at Nicklaus Children's Hospital was conducted using descriptive measures to outline clinical findings, treatment, and outcomes.

Results: A chart review of pediatric patients diagnosed with brain tumors from 1999 to 2019 revealed that nine patients (median age 7 months, range 6-10 months) were diagnosed CPC. Six patients (66%) were male. Initial clinical presentation included vomiting (n=4), cranial nerve palsies (n=3), increased head circumference (n=1), and irritability (n=1). Diagnostic imaging showed tumor located in the lateral ventricle (n=4) and posterior fossa (n=5). Two patients had spinal metastasis at presentation. Obstructive hydrocephalus was present in all patients; three of them underwent ventriculo-peritoneal shunt placement. Surgical intervention was in the form of gross total resection (n=5), subtotal resection (n=1), and biopsy (n=3). One patient died after biopsy from bleeding complications. Another patient never started on therapy as per parents' wishes. Seven patients (77%) were treated with chemotherapy per Head Start II regimen (n=5) and Baby POG-1 (n=2). Four patients (44%) had Li-Fraumeni Syndrome, and all of them received therapy as per Head Start II regimen. One patient underwent a second look surgery prior to treatment with high dose chemotherapy and autologous stem cell transplant. One patient received craniospinal irradiation due to spinal metastasis. At a median follow up of 6 years (range 0.2 to 18 years), six patients completed therapy, and one patient was still undergoing chemotherapy. Long-term toxicities varied as follows: hearing loss (n=5), cranial nerve palsies (n=3), and developmental delay (n=2).

Conclusions: Complete surgical resection remains the mainstay of treatment. Intensive marrow-ablative chemotherapy regimens improved the prognosis of choroid plexus carcinoma including those with Li-Fraumeni Syndrome.

PO015 SIOP19-0844 | The Result of High-Dose Chemotherapy with Autologous Stem Cells Transplantation of the Central Nervous System Tumor in Children

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Background/Objectives: Children under 3 years of age with central nervous system tumors have a lower overall survival rate of 5 years of 12-28% compared with the older age group of 55-73%. In order to increase the MI of this group of patients, the use of high-dose chemotherapy (HDCT) with autologous transplantation of hematopoietic stem cells has been introduced, which allows achieving high concentrations of chemotherapy in the central nervous system and contributes to the improvement of treatment efficacy. The high efficiency of auto-THSC is established in the treatment of supraentorial PNEP in the first line of therapy or in combination with radiotherapy - 40%, survival without progression - 24%, which may be a method of choice in a group Patients with primary disseminated and recurrent hemorrhagic CNS tumors, which are characterized by an unfavorable prognosis, range from 5-30%.

Design/Methods: In the department of children's oncology of the National Cancer Institute 13 patients with CNS tumors have been conducted HDCT in the period from 2011

Results: At present, 7 patients are in remission, 3 patients continue treatment (1 patient for the early relapse of the disease, 2 - the second element of the HDCT with auto-THSC), 2 patients died from the progression of the disease, 1 patient died of complications that arose during the second element of the HDCT. The overall survival rate of patients is 76.9%.

Conclusions: Thus, as can be seen from the data presented, conduction of HDCT with auto-THSC is an important stage in the complex treatment in a certain category of patients with CNS tumors and needs further study, which will allow them to significantly increase their OS.

PO016 SIOP19-0562 | Choroid Plexus Carcinoma-The South Thames Neuro-Oncology Unit Experience

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Background/Objectives: Choroid Plexus Carcinomas (CPCs) are rare paediatric brain tumours and generally have a poor prognosis. Our aim was to describe the treatment

and outcome of CPC treated within The South Thames Neuro-Oncology Unit.

Design/Methods: We conducted a retrospective review of children with CPC aged 1-18 years, diagnosed and treated within The South Thames Neuro-Oncology Unit from 1990 to 2019. Clinical, radiological and outcome data were analysed.

Results: Three patients were identified (two females, one male). Median age at diagnosis was 1.7 years (range 1.3-1.8 years). At diagnosis, two patients had localised tumours (one supratentorial, one posterior fossa). One patient had leptomeningeal involvement. All patients were offered testing for *TP53* mutation, two consented and tested negative. Paediatric tumour profiling was done in two patients. There were no molecular findings. All patients underwent upfront subtotal resection followed by adjuvant chemotherapy either as per SIOP choroid plexus tumour guidelines (n=1) or ifosfamide, etoposide and carboplatin (ICE) (n=2). Only one patient with primary tumour in the posterior fossa received focal radiotherapy. All three patients had recurrences. One patient had intracranial relapse at multiple sites at 35 months, another had metastatic relapse at 77 months and the other had metastatic relapse at 17 months from primary diagnosis. At recurrence, all patients received at least two further lines of chemotherapy and one received craniospinal radiotherapy. One patient had a second malignancy (supratentorial primitive neuroectodermal tumour) outside the radiotherapy field seven years after primary diagnosis. The two patients with metastatic recurrence died of disease progression 0.9 and 11.8 years from initial diagnosis, respectively. The other patient is alive and free of disease, 3.5 years after primary diagnosis.

Conclusions: CPCs are extremely rare paediatric brain tumours and the prognosis remains poor. There is no consensus on best standard of care for these patients and worldwide collaboration is needed to improve survival outcomes.

PO017 SIOP19-1312 | Outcome of Pediatric Glioblastoma in Serbia – A Series of 23 Cases

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Background/Objectives: To evaluate characteristics of childhood glioblastoma, effectiveness of treatment modalities, and detect factors related to outcome.

Design/Methods: A detailed analysis was performed on a series of 23 patients younger than 18 years at the time of

diagnosis of glioblastoma, treated between 2000 and 2018, based on their clinical, radiological, pathological, treatment, and follow-up data. All patients were diagnosed and operated on at the Clinic of Neurosurgery, Clinical Center of Serbia, Belgrade and underwent postoperative radiotherapy and chemotherapy at Institute of Oncology and Radiology of Serbia, Belgrade, national referral centers for the treatment of childhood brain tumors.

Results: Median survival time of children with glioblastoma was 15 months. One- and two-year overall survival probabilities were 65.2 and 21.7%, respectively. There were no significant differences in survival based on patients' gender, age, disease presentation with or without epileptic seizures, signs/symptoms of increased intracranial pressure, or tumor location. The presence of neurological deficit initially, as well as prior to radiotherapy, which was quantified by neurologic function score (NFS), had an impact on overall survival. Children with NFS 0 lived longer compared to others (p=0.01). Survival of children that underwent gross total resection was longer than that of children that underwent subtotal resection (p=0.03). Mean survival time of children with gross total resection was 33.1 months, compared to 12.4 months in children with subtotal resection. There was no significant correlation between outcome and type of radiotherapy. In five patients with giantocellular glioblastoma, we found no evidence of a better prognosis. Two long-term survivors were recorded. Both of them underwent gross total resection and were assigned a NFS 0.

Conclusions: Gross total resection is essential for longer overall survival among pediatric patients with glioblastoma and offers a possibility for long-term survival. Severity of neurologic symptoms quantified by NFS can be considered as a potential predictor of outcome.

Childhood Cancer International (CCI)

PO018 SIOP19-1740 | Unmanipulated Related Haploidentical Stem Cell Transplantation for Children with High Risk Leukemia: Is It a Feasible Option for Cure in Developing Countries?

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Background/Objectives: More than 65% of Mexican children that need stem cell transplantation (SCT) lack a suitable matched family donor (MFD), access to unrelated donor

(URD) registries is limited because of high costs, protracted time to find a donor, and difficulty identifying donors due to underrepresentation of patients of Mexican ethnicity in the registries.

Design/Methods: We assessed the feasibility, costs and outcomes of unmanipulated haploidentical related bone marrow transplantation (UHRT) using myeloablative conditioning: Total Body Irradiation plus Cy for patients with high-risk ALL lacking a suitable MFD. Graft versus host disease (GVHD) prophylaxis was Post transplant Cy, Mophetilmicophenolate and Tacrolimus.

Results: From May 2018 to December 2018, 6 patients with mean age of 9, (5-13y), received UHRT grafts in Hospital Infantil Teletón de Oncología. Donors were father (n=3), brother (n=2) and half sister (n=1). All patients in remission and MRD negative at time of SCT. Median Cell CD34+ doses were $7.2 \times 10^6/\text{kg}$. All patients achieved engraftment, 5/6 are alive and in complete remission at a median follow up of 6 months (range 3-11 months). One patient died of marrow relapse 4 months after transplant. There were no deaths from transplant-related toxicity (TRM). Viral infections were the main post transplant complication: 4/6 developed positive Cytomegalovirus (CMV) viral load, 1 developed CMV disease. One patient developed acute GVHD GIII, then chronic skin GVHD. Average cost of each transplant was around 100,010 USD. Median time from pre SCT workup to SCT was 45 days.

Conclusions: UHRT using unmanipulated stem cells a cost effective approach in developing countries where access is limited to international URD registries. Donors can be rapidly mobilized avoiding the medically and economically costly delays during protracted searches for an URD. Our early data suggests acceptable outcomes, low TRM. CMV reactivation was common so patients must be closely monitored.

PO019 SIOP19-0831 | All Together for ICCD in Rennes France

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Background/Objectives: In November 2017, the pediatric oncology department of the Rennes University Hospital has organized a special event named "day for associations". 30 associations were asked to promote either scientific research or patient and family assistance, in order to hold a special event in Rennes for the International Childhood Cancer Day. The idea was to federate the health care actors focused on children affected by a cancer. Around this project, associations were motivated and demonstrated team working abilities.

Design/Methods: After a year of preparation and with the partnership of Rennes City Hall and Rennes University Hospital, International Childhood Cancer Day took place on the main square of the city, in front of Rennes city hall, on February 15th. This strategic location allowed us to reach many people, including medical students and enabled us to raise awareness about child cancer. The event was advertised through the city means of communication (billboards, digital displays), newspapers as well as local radios.

Results: We were able to welcome visitors in 3 different areas A hospital room scenery with activities proposed to sick children:

-care, adapted physical activity, music, magic, socio-aesthetic workshop.

-a welcome area to share a friendly moment around a coffee and give informations about associations, and their actions, in order to highlight their significance.

-a game with questions on childhood cancer, with the answers on posters or with help of health care professionals and volunteers. Game's themes were divided into 4 topics: children's daily life, supportive care, epidemiology, treatment and research.

Conclusions: Given the success of this day, that has managed to federate associations, professionals from the University Hospital and the Town Hall representatives, it has been decided to repeat ICCD in Rennes next year and to start working on preparation to make February 15, 2020 a new success.

PO020 SIOP19-1234 | International Variation in Childhood Cancer Mortality Rates from 2005 to 2015

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Background/Objectives: The International Cancer Benchmarking Partnership (ICBP) showed variation in cancer survival with poorer outcomes for four common adult cancers in the UK and Denmark compared to Australia, Canada, Norway and Sweden. It is unclear if similar variation in childhood cancer mortality exists. We report trends in childhood mortality between 2005 and 2015 in ICBP countries.

Design/Methods: Annual mortality data were extracted from the WHO mortality database for all cancers, leukaemia and CNS tumours from 2005-2015 in UK, Australia, Canada, Denmark, Norway and Sweden in children aged under 15 years. Age standardised mortality rates (ASR per million) were calculated using the world standard population. Average annual percentage change in mortality rates per country were estimated using joinpoint regression.

Results: For all cancers combined in 2005-2007 ASRs ranged from 18.4 (95%CI 13.3-23.5) in Norway to 27.7 (22.8-32.6) in Sweden. Significant temporal reductions in mortality were observed in the UK, Australia, Denmark and Sweden. In 2014-2015, ASRs ranged from 16.1 (10.4-21.9) in Denmark to 23.6 (18.3-28.8) in Sweden. Significant reductions in leukaemia mortality were observed in the UK, Canada, Denmark and Sweden. In 2014-2015, ASRs for leukaemia mortality ranged from 3.8 (1.0-6.7) in Denmark to 7.6 (3.6-11.6) in Norway. For CNS tumours, significant declines in mortality were observed in the UK and Australia. In 2014-2015 CNS mortality ranged from 5.9 (2.5-9.3) in Denmark to 11.2 (7.6-14.8) in Sweden.

Conclusions: Childhood cancer mortality rates have generally declined steadily over time reflecting continuing success in outcomes for childhood cancer. The UK and Denmark showed a clear fall in mortality and a higher relative position than previous ICBP studies concerning adults. This may reflect shorter time to diagnosis due to earlier patient presentation and referral, although could be confounded by differing incidence trends within countries. These findings may provide important intelligence to facilitate service improvements.

Epidemiology - Pathways of Care

PO021 SIOP19-1213 | Overview of Langerhans Cell Histiocytosis Among Children in Low Income Countries: Single Institutional Experience from Pakistan

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Background/Objectives: Langerhans Cell Histiocytosis is a relatively rare disease accounting for around 1% of new cases each year enrolled in The Children's Hospital Lahore. The purpose of this study was to analyze its clinical manifestations, course and outcome in resource limited settings lacking salvage therapy

Design/Methods: Retrospective review of 65 patients enrolled between January 2011 – December 2018 was done. Data regarding their age, sex, clinical classification, course of therapy, and outcome analyzed. The therapy mainly comprised of prednisolone and vinblastine or cytarabine pulses. SPSS 20 used to analyze the data

Results: Total 65 patients with age ranging from < 1 to 8 years (25% <2 yrs) were included. M: F Ratio was 1.3:1. 47/65(%) patients presented with Multisystem-LCH (MS-LCH) with 32/65 (49%) had Risk Organ involvement 42/65 (65%) of patients had bone lesions with 42% with multifocal bone disease while 15/65 (23%) patients presented with central nervous system (CNS) involvement. Total 38/65 (59%) have completed treatment, 2/65 (3%) are on treatment, 11/65 (17%) left against medical advice (LAMA) and 12/65 (18%) expired due to progressive disease and worsening infection 2 cases were put on palliation with progressive brain parenchyma disease. 21 patients (32%) had reactivations of disease requiring therapy for more than one year (p-value=0.06). 23% (15/65) of cases received two cycles of initiation therapy before continuation therapy started. The treatment initiated >6 months after the onset of symptoms in 48/65 (74%) of cases

Conclusions: Early diagnosis with better awareness among health professionals, timely initiation of treatment and effective infection control measures are of utmost importance to improve long term overall survival (OS) with reduced morbidity. Strong and sustained social support is essential to minimize treatment abandonment in low income countries.

PO022 SIOP19-0488 | Primary Central Nervous System Tumors in Children and Adolescents: Descriptive Epidemiology in the National Neuroscience Institute (King Fahad Medical City, Saudi Arabia)

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Background/Objectives: Primary Central Nervous System (CNS) tumors are the most common solid tumors in children. The capacity of the National Neuroscience Center (NNI) at King Fahad Medical City (KFMC) had significantly increased over the past years to accommodate the number of patients with brain tumors. This study aims to describe the epidemiological trends of primary CNS tumors in children and adolescents at the NNI in Saudi Arabia.

Design/Methods: A retrospective epidemiological approach was used where data was obtained from the department of pathology registry files and pathology reports. The records of infants (0 - < 1), children (1-14 years) and adolescents (15-18 years) registered from January 2005 to December 2014 with a diagnosis of primary CNS tumor (brain and spinal cord) were selected. Data about sex, age, tumor location, and histologic type were collected. The classification was based on the International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3).

Results: Two hundred and seventy-eight (278) children and adolescents with primary CNS tumors were reviewed. Males (60.07%) outnumbered females (39.93%) by a ratio of (1.5:1). The mean age was 7.4 years, with a standard deviation of 4.90 years. The ratio of malignant to non-malignant tumors was 1.43 to 1. The majority of tumors (57.45%) were found in the infra-tentorial compartment including the cerebellum (47.21%) and brainstem (6.35%). Medulloblastomas were the most common histologic type (26.62%) followed by pilocytic astrocytomas (17.99%), ependymomas (11.51%) and high-grade gliomas (10.07%).

Conclusions: This is an institution-based, detailed and descriptive epidemiological study of children and adolescents with primary CNS tumors in Saudi Arabia. In contrast to other regional and international studies, the medulloblastomas in our institution are more frequent than pilocytic astrocytomas. The referral bias and the pathology-driven methodology of our study design could have contributed, in whole or part, to the relatively higher rates of medulloblastoma.

PO023 SIOP19-0783 | Impact of Executive Round on Healthcare Key Performance Indicators (KPIs) and Metrics - Experience from Pediatric Hematology / Oncology Setting

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Background/Objectives: Pediatric Hematology / Oncology (PHO) department at King Faisal Specialist Hospital & Research Centre, Riyadh is a tertiary care referral center. Benchmarks for Healthcare metrics are set by institutions to monitor performance measurements encouraging improvement in healthcare processes.

Design/Methods: Weekly interdisciplinary executive round entitled "Discharge Planning Meeting (DPM)" was introduced in 2016, a retrospective analysis of departmental operational KPIs and quality of documentation was performed for 2017 to 2018, whilst comparing the same.

Results: Discharge Before Noon rate (DBN) increased by 7% (59% in 2018 vs, 52% in 2017) with a slight increase (1%) in total discharges, while new patients increased by 10% in 2018. Inpatients and discharge documentation compliance increased by 1.5%, respectively; scoring more than the set institutional trigger (>90% compliance rate) on several occasions; however delinquent medical records rate reduced significantly by 8% (9% in 2018 vs. 17% in 2017). An increase of 15% in HSCT was observed against a set trigger of 5% increase, while a decrease in Day – 100 transplant mortality rate by 5% was observed reflecting the quality of care delivery. Overall Inpatient & outpatients satisfaction score of 88.6% & 87.5% was observed, which is above the regional (GCC) benchmark in both instances (Healthlinks Press Ganey Associates). Presence from attending physicians, pharmacists, social workers, case managers, clinical Nurse coordinators, nutritionists, charge nurses, clinical research specialist, and front-line staff resulted in early identification of sub-specialized medical issues, OP care evaluation and early pre-HSCT work-up.

Conclusions: In our experience, DPM enabled system of effective communication during patient handover, while maintaining most operational KPI's above operational triggers set forth by the institution; area (s) of improvement were identified that resulted in increased number of performance improvement (PI) projects (four in 2018 vs. two in 2017); however detailed cost-effectiveness analysis of PI initiatives is warranted.

PO024 SIOP19-1167 | Yogyakarta Pediatric Cancer Registry: Continuation Study of 10-Year-Profile of Childhood Malignancy (2009-2018)

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Background/Objectives: In 2001, Dr. Sardjito General Hospital (SGH), Yogyakarta, Indonesia did a collaboration project with Saskatchewan Cancer Agency, Canada to create

a computer-based pediatric cancer registry at SGH. A prior study was done during 2001-2009 to give basic profile of childhood malignancy in Yogyakarta Special Province (YSP). The aim of this study was to update the profile of childhood malignancy and to compare with the previous 10-year study of Yogyakarta Pediatric Cancer Registry (YPCR).

Design/Methods: Data from January 2009 to December 2018 were analyzed. All children below 18 years diagnosed with cancer were included in this study. The profile was focusing on the incidence of childhood cancer and categorized based on age, sex, disease group, and the regions of patient origin.

Results: There were 1,788 new patients registered in YPCR; 1,206 (68%) with hematologic malignancies (67% males) and 582 (33%) with solid tumors (54% males). Fifty percent were diagnosed at the age group of 0-5 years old. Seventy percent patients came from outside the YSP area. Average annual incidence rate (AAIR) of pediatric malignancy in YSP was 4.9 with the highest incidence came from Kulon Progo Regency (5.7). The AAIR of hematologic malignancy was 3.1, while solid tumor was 1.8. There was an increase of teenager age (15-18 years old) percentage compared to previous study (8% to 0.4%) with AAIR of 1.3 in YSP region.

Conclusions: This study provided more specific profile of childhood malignancy and mapping of incidence rate. There was an increase number of malignancy diagnosed in teenagers, thus adolescence and young adult (AYA) group need to be paid more attention.

PO025 SIOP19-0558 | Implementation of Multidisciplinary in French-African Group of Pediatric Oncology (GFAOP) sub-Saharan Teams: A Process Build by the Teams

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Background/Objectives: Created in 2000, GFAOP is now supporting fifteen sub-Saharan African units through training, clinical research and access to drugs. Over 400 people were trained, with a one year diploma for pediatricians, and short courses for pathologists, surgeons and nurses (*African school of pediatric oncology supported by My Child Matters, Sanofi Espoir Foundation*). In 2017, according to the 2025 GFAOP project, a program was built to develop training in multidisciplinary care in pediatric oncology, through the creation of Institut Jean Lemerle in Dakar (*seminars funded by a grant from the Bristol-Myers Squibb Foundation*).

The goal is to improve practically multidisciplinary at each step of care, in the context of each unit.

Design/Methods: Methods: - a three-day residential interactive seminar with precise objectives: to share general notions about childhood cancers, to understand why multidisciplinary care is mandatory, to better organize daily multidisciplinary: informative reports from each specialist, regular multidisciplinary team meetings (MDT) organized to optimize everyone's time, common referential of care adapted to each country

- followed by local workshops to elaborate care pathways for 6 pediatric cancers, according to medical protocols defined by GFAOP committees and to organize regular MDT meetings.

For the first seminar, 6 sub-Saharan pediatric oncology teams were invited to send 5 doctors participating to the care of children with cancers to participate.

Results: Thirty doctors from Abidjan, Antananarivo, Dakar, Lubumbashi, Nouakchott and Ouagadougou (7 pediatricians, 6 pathologists, 6 general surgeons, 6 ophthalmologists, 3 radiologists and 2 radiation oncologists) + two animators were attending the three-days course in June 2018, in Dakar, with fruitful interactive discussions opening to recommendations. Workshops, including also nurses, began in April 2019 in Madagascar and were then implemented in all the units during 2019.

Conclusions: This process will have concerned the fifteen pediatric oncology units in sub-Saharan Francophone Africa at the end of 2019.

PO026 SIOP19-1134 | Thoracic Tumors: One Pathology of Diverse Presentations. Our Experience in a Pediatrics Hospital

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Background/Objectives: Determine the incidence of thoracic tumors in children at a Pediatrics Hospital, in Quito Ecuador between 2007 to 2012

Thoracic tumors in childhood are classified into mediastinal, associated to chest wall, Neurogenic, and Germ cell tumors. Anterior mediastinal tumors are related to leukemia or lymphoma followed by germ cell tumors. Middle mediastinal tumors are secondary to anterior mediastinal pathology and Posterior are due to CNS tumors

Design/Methods: Retrospective, descriptive study. Thoracic Tumors were classified using 668 Histopathologic samples collected between January 2007-December 2012 in a Pediatric hospital of Quito.

Results: Only 3.7%(28) of the samples were identified as thoracic tumors by Histopathology. The group with highest incidence was between 1 to 5 years old. The youngest patient diagnosed was 1.4 months and the older 14 year old. Predominance in males (68%) was found.

Most of thoracic tumors were found in anterior mediastinum (44%), most commonly related to blood and Germ cell cancer. Teratomas (20%) and lymphangiomas (20%) followed by lymphomas (16%) were the most common types found. Seventy Five percent of thoracic tumors caused by Lymphomas, were due to Hodgkin type versus non Hodgkin (25%). Tumors caused posterior mediastinal mass in 12% of the patients, mostly Neuroblastomas. The least frequent thoracic tumor were associated to the chest wall, all arising from the ribs.

Conclusions: Lymphoma was the most common cause of mediastinal mass in our study. Most of them due to Hodgkin lymphoma (HL). According to literature, 75% of patients with HL present with anterior mediastinal mass versus NHL 50%. This explains why Hodgkin lymphoma is the most common cause although 60% of all lymphomas in this age group are due to NHL.

While the thoracic tumors incidence in childhood is low, continuous vigilance of patients should be done since they have diverse clinical presentation because localization or are secondary to pathologies of very high incidence as Lymphoma.

PO027 SIOP19-0612 | Brazilian Task Force on Pediatric Oncology: New Ways to Improve Access to Diagnosis and Treatment

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Background/Objectives: Brazil's socioeconomic inequalities result in a difference in the diagnosis and treatment of childhood and adolescence cancer in the various regions of the country. Our objectives were to identify regional difficulties and propose changes along with stakeholders.

Design/Methods: This project was idealized by the Brazilian Society of Pediatric Oncology (SOBOPE), with support from the Ronald McDonald Institute and CONIACC. We developed minimum criteria for diagnosis and treatment of different pediatric cancers. These criteria, along with epidemiological state data on pediatric cancer and the Ministry of Health requirements to be recognized as a pediatric specialized oncology service, were shown to the pediatric oncologists and information was collected on such difficulties. The

results were presented to the relevant social and political actors. Finally, a strategic planning was developed for each region

Results: Between August/2015 and December/2018, 14 Forums were held in 14 different states. We achieved greater engagement of decision makers and the community. As examples, there was the consolidation of the Pediatric Oncology Hospital in Pará (transfer from a hospital with several deficiencies to another exclusive for children and adolescents with cancer); inauguration of a Retinoblastoma Center in Pernambuco; creation of the Parliamentary Front and immediate transfer of patients to a hospital with better structure until the construction of another in Espírito Santo; a new unit of pediatric oncology in Sergipe; and an active movement to resolve the problems pointed out by the Forums in the various states.

Conclusions: This project resulted in greater union of the pediatric oncology services, increasing the integration among all the health professionals, managers, child and adolescent cancer support institutions and representatives of official child advocates, providing actions that culminated in the improvement of the pediatric cancer care in the different states of Brazil.

PO028 SIOP19-0651 | Pediatric Cancer Flyers: A Visual Instrument to Standardize Diagnosis and Treatment in Brazil

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Background/Objectives: The Brazilian Ministry of Health defines the minimum structural and professional criteria for the governmental registry of a pediatric oncology unit to treat children and adolescents with cancer. However, diagnosis and treatment are not standardized. Our goal is to address this gap through a visual aid containing colorful figures that contemplate suggested procedures for diagnosis and treatment.

Design/Methods: This project was conceived by the Brazilian Society of Pediatric Oncology (SOBOPE) and was elaborated by professionals from Brazilian Cooperative Groups looking at different types of childhood cancer. In each pathology flyer, health professionals, diagnosis, laboratory exams, tumor classification, treatment, medication and follow-up were classified as red (mandatory), yellow (highly recommended) or green (optional with referral possibility). These colorful flyers containing the minimum criteria for cancer diagnosis and treatment were designed so that the organized civil society could easily know the needs of the pediatric oncology population and guide the actions needed to improve the care

of children and adolescents with cancer in all regions of Brazil.

Results: Between August/2015 and December/2018 these flyers were shown to representatives of institutions that support children and adolescents with cancer from 16 Brazilian states; to public defenders and public ministries; to federal, state and municipal managers; to directors of hospitals that treat pediatric oncology; and to the legislative institution of each state. The flyers became a document that the organized civil society uses to seek a quality care for children and adolescents.

Conclusions: A guideline establishing the basis for diagnosis and treatment of each type of pediatric cancer was created using images with key words. It aims to improve the care of these conditions, allowing the identification of the most adequate diagnosis and therapeutic protocol. Our next step is to measure how this visual aid impacts the correct diagnosis and treatment.

PO029 SIOP19-0630 | The Treatment of Pain Related to Gestures in Pediatric Hematology and Oncology Unit of Marrakech

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Background/Objectives: Introduction: Pain is the most feared problem for children with cancer and deserves special attention. the pain of children with cancer is therefore mainly iatrogenic. Knowing the negative physiological and psychological effects of pain, its management plays an important role in the care of children with cancer.

Objective: evaluate the management of pain related to the gesture at the day hospital of the pediatric hemato-oncology unit of Marrakech

Design/Methods: prospective study conducted from November 2018 to February 2019 in the day hospital of the pediatric hematology and oncology department of Mohamed VI University Hospital.

Results: during this period 94 gestures have been recorded; intrathecal was the most frequently performed in 63%; bone marrow aspiration 28% and bone marrow biopsy in 8%. peripheral vein outlet was excluded since no prevention of pain was performed. treatments done to prevent pain was the lidocaine-prilocain cream (EMLA) application 60 minutes before the gesture in 53% association of xylocaine and EMLA application was done in 19%, association of EMLA and oral morphine in 11% and sedation by ketamine performed in 14%. The intrathecal was repeated on average three time for the same patient. the pain reaction measured on a visual analogue scale (VAS) or on an observer's verbal scale showed a median

of 6,5/10. The VAS was > to 7/10 in 20%. 63% of the Parents have judged that the means used were effective.

Conclusions: Due to limitations in the documentation of childrens pain related to gesture it was difficult to determine the effectiveness of pain management interventions. This result reflects that Pain management practices in our unit is insufficient and it was noted that Non-pharmacological methods of managing pain were absent.

PO030 SIOP19-1574 | GOCE: A Structured Interregional Hospital Organisation for Pediatric Oncology

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Background/Objectives: The western interregional hospital organization for pediatric oncology GOCE was identified by INCA (National Institute for Cancer) in 2010 and regroups 7 university hospitals and 3 centers against cancer diseases. Since that year, GOCE has been working on 4 lines: interdisciplinary meetings twice a week by videoconferences, the research, care streams, and training course. Since 2012, GOCE has decided to be involved in audit quality.

Design/Methods: The medical network organizes training days for new practitioners, videoconference courses for junior doctors twice a week, and searching meetings for doctors from different centers.

New interregional collaborations have been created in other fields: - Paramedics (teaching and research)

- Psychology (Human and social science plan: points of support and limiting factors, for patients or parents, in the medium and long term follow-up in pediatric oncology)

- Oncogeneticists (national project: EXOme, rare child cancer)

To improve the patient refunding, GOCE organize every 2 years an audit in each center (drawing among 140 files) to evaluate different actions and to assure that centers follow the INCA recommendations.

Results: Announcement device:

There was evidence of a diagnosis announcement for 81% of files. Nearly all of them (99%) had a medical consultation and 46% had a paramedical consultation.

Interdisciplinary meetings:

- 88% of the files are presented
- Therapy has been given through interdisciplinary meetings reports for 97% of the files.

Protocol inclusions:

- 39% of patients were included in a research protocol.

Conclusions: GOCE permitted the creation of a new network in which results have been proven with the agreement of several project requests. In addition, this organization is part of an audit quality to evaluate the efficiency of the process and eventually adjust it if necessary in order to assure the best support for patients.

PO031 SIOP19-1707 | Epidemiology of Pediatric Cancers in a Developing Country

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Background/Objectives: Information on the epidemiology of childhood cancer is mandatory for the planning of health-care policies. This study aims to establish a baseline of the epidemiologic features of pediatric cancers recorded in a Tunisian pediatric oncology unit included in the GFAOP (Franco-African Pediatric oncologic Group).

Design/Methods: All new cases of histological proven cancers in children under 15 years between 2013 and 2018 were collected and recorded on the Redcap baseline. This software allowed the collection of data through electronic questionnaires within the registry as part of observational studies conducted by the GFAOP.

Results: Between 2013 and 2018, a total of 351 new cases of cancers diagnosed in children aged under 15 years were reported. The most common morphological types were: Neuroblastoma (79/351, 22%), renal tumors (54/351, 15%), retinoblastoma (50/351, 14%), soft tissue tumors (30/351, 8.5%), Lymphoma (24/351, 6.8%), Leukemia (23/351, 6.5%). The average age of the patients was 44 months (range: 0-15 years). There is a predominance of patients 1-4 years (44.8%), compared to those under one year (31.9%), 5-9 years (17.3%) and those between 10 and 15 years (6%). We have noted a decrease of mortality incidence passing from 32% in 2013 and 2014, to 28% in 2015, 18% in 2016 and 2017, 9.8% in 2018. The average incidence of toxic death was 21% during the period 2013-2018.

Conclusions: Even survival is lower than what has been reported for developed countries, improving results remains a challenge for the health-care system in developing countries. Pediatric cancer registries are paramount for progress

to increase awareness and to improve the survival of children affected by cancers.

PO032 SIOP19-0162 | Challenge to Increase Cure of Children and Adolescent with Cancer in West of Paraná-Brazil

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Background/Objectives: Childhood and juvenile cancer is a rare disease, but it is the second leading cause of death in the age group of 5 to 19 years. On the other hand, the cure rate reaches more than 70% if diagnosed early. In Parana-Brazil we have developed the training program for health professionals to suspect childhood cancer since 2008.

Objective: To evaluate the time between the onset of symptoms and the diagnosis and cases number diagnosed with cancer during the 10-year period since the training program

Design/Methods: Two periods of 5 years, called period first of July 2008 to June 31, 2013 and period 2 of first July, 2013 to June 30, 2018 were evaluated. The following variables were analyzed between the 2 periods: number of cases attended, time elapsed between onset of symptoms at diagnosis and evolution. Fisher's exact test with a significance level of 5% was used for statistical analysis.

Results: 505 patients were enrolled, 220 in period 1 and 285 in period 2, with an increase in the number of cases between period 1 and 2 ($p < 0.004$). There was an increase in the number of cases referred in the first 15 days of onset of symptoms from 35 to 89 cases ($p < 0.0006$) in periods 1 to 2 respectively and a reduction in the number of cases referred over 60 days from 83 to 59 cases ($p < 0.0005$) in period 1 to 2 respectively. 136 (62%) cases from period 1 and 227 (80%) cases from period 2 are alive in follow-up at the institution ($p < 0.02$).

Conclusions: The analysis of the data allows us to infer that the 10-year period in the region of Paraná has increased the chance of the child and adolescent to access treatment more quickly and effectively and contributing to the improvement of the chance of survival.

PO033 SIOP19-0165 | Distribution of Cancer in Children and Adolescent in the West of the Parana State, Brazil

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Background/Objectives: In Brazil it is estimated that about 12,400 new cases of cancer per year in children and adolescents, and is the second cause of mortality in children under 19 years. It is important to know the epidemiological profile for the planning of health care and patient care.

Objective To analyze the distribution of cancer in patients under 19 years attended from January of 2001 and May 2018 proceeding from the West Region of the Parana State, Brazil.

Design/Methods: The data were obtained from the medical handbooks and analyzed according to International Classification of the Cancer in childhood

Results: 571 cases were registered, distributed in the following groups: Group I - leukemia in 199 (35%) cases; II lymphomas and other reticuloendothelial neoplasms 72 (13%) cases; III Central Nervous System Tumor 72 (13%) cases; IV Tumor Nervous System Sympathetic 24 (4.5%) cases; V. Retinoblastoma 3 (0.5%) cases; VI Renal tumors 39 (7%) cases; VII Liver tumors 7 (1%) cases; VIII Malignant bone tumors 24 (4%) cases; IX Soft-tissue sarcoma 55 (9%) cases; X Germ cell neoplasms 34 (6%) cases; XI Carcinoma and other malignant epithelial neoplasms 15 (3%) cases; XII Other and malignant tumors, unspecified 27 (4%) cases. There were 455 (79%) under 14 years of age and 116 (21%) between 15 and 19 years old, 331 (58%) males and 240 (42%) females. Of the 571 patients, 407 (71%) were living under follow-up.

Conclusions: There was a progressive increase in referrals of new cases from 2013, demonstrating an improvement in the conditions of care for children and adolescents with cancer, provided by the Reference Hospital in Paraná. We found the distribution of childhood cancer similar to data published in the national and international literature, with the exception of the increase in frequency in group XI, represented by the increase of cases of adrenal carcinoma.

PO034 SIOP19-0167 | Time Estimation Between the Beginning of the Symptoms of Young Child Cancer and the Medical Care in the West of Parana- Brazil

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Background/Objectives: Childhood and adolescent cancer (under 19 years) is a rare disease, accounting for 2% to 3% of all malignant tumors, being one of the main causes of death due to illness in childhood and adolescence. It affects children primarily in the first five years of life. Today 70-80% of children with cancer can be cured, provided the diagnosis is made early and the child can receive appropriate treatment in a specialized center. **Objective:** To estimate the average time between onset of symptoms in children and adolescents

with cancer, until the attendance and / or specialized medical treatment.

Design/Methods: The data has been collected retrospectively of the medical handbook, from the Cancer Hospital of Cascavel, Paraná, Brazil, taken care of the period between January 2001 and May 2018.

Results: There were 571 cases, 455 (79%) were younger than 14 years old and 116 (21%) were between 15 and 19 years old, 331 (58%) males and 240 (42%) females. The most frequent groups of diseases were leukemia (35%), followed by lymphomas (13%) and CNS tumors (13%). The mean time between onset of signs and symptoms until diagnosis ranged from 2 to 34 weeks, with an average of 8 weeks. The fever (24%), followed by lymphadenopathy (21%), skin pallor (19%), vomiting (10%) and headache (9%) had been the symptoms that had more precociously led to the precocious diagnosis of the neoplasm illnesses. Of the group studied, 406 (71%) cases are alive under follow-up by the institution.

Conclusions: There is a delay between the onset of symptoms until diagnosis and / or initiation of treatment, mainly related to solid tumors. Therefore we need to plan strategies of precocious detention of the Infantile-juvenile cancer in our region so that it has faster investigation of a suspicious case.

PO035 SIOP19-1686 | A Database of General and Pediatric-Specific Population-based Cancer Registries Globally

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Background/Objectives: Population-based cancer registries (PBCRs) are a crucial resource for national and global cancer control efforts but do not exist in all countries due to resource and capacity limitations. Information regarding the PBCRs that exist globally will be important in planning for the recently announced Global Initiative for Childhood Cancer. To create an open access database of PBCRs globally, we performed a systematic search for PBCRs that cover children 0-14 years.

Design/Methods: Data sources included networks of cancer registries (International Association of Cancer Registries; African Cancer Registry Network; European Network of Cancer Registries; Automated Childhood Cancer Information System; North American Association of Central Cancer Registries; SEER-18), studies of cancer burden (International Incidence of Childhood Cancer, Volume III; Cancer Incidence in Five Continents, Volume XI; Global Bur-

den of Disease 2017 Study; CONCORD-3; GLOBOCAN 2018), and a systematic literature review (Pubmed; Web of Science; SCOPUS; LILACS). Cancer group-specific PBCRs were excluded.

Results: A total of 1139 cancer registries were identified, of which 844 were PBCRs (801 general, 43 pediatric-specific). The PBCRs were located in 157 countries; four countries did not have a 2019 World Bank designation. The database is comprised of 53% (447/840) PBCRs in high-income countries, 32% (265/840) in upper middle-income countries, 12% (100/840) in lower middle-income countries, and 3% (28/840) in low-income countries. Of high-income countries 78% (63/81) had a PBCR, while 75% (42/56) of upper middle-income countries, 68% (32/47) of lower middle-income countries, and 59% (20/34) of low-income countries had a PBCR.

Conclusions: We created a global database of PBCRs collecting data on children with cancer. As expected, high-income countries had a greater number and proportion of PBCRs than low- and middle-income countries. Future work will aim to assess the quality, activity, and population coverage of PBCRs in our database in order to inform global cancer burden estimates and cancer control policies.

PO036 SIOP19-0342 | **Elaborating Tools to Enhance Early Diagnosis for Childhood Cancer in Sub-Saharan Africa. A Program of the Institut Jean Lemerle-Dakar, Developed by the GFAOP**

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Background/Objectives: In French speaking Sub-Saharan Africa (SSA), it is estimated that there are 20 000 incident cases of childhood cancer a year. Each year, only 2500 children are reaching a GFAOP unit and half of them are eligible to a treatment protocol. Late diagnosis is one of the main reasons preventing the initiation of a curative treatment, leading to very low survival rates.

Developing early diagnosis tools and materials to reinforce caregivers' capacity and raise awareness among populations is the corner stone of programs intended to improve children survival. As part of the Institut Jean Lemerle - recently created in Dakar with the support of the Bristol-Myers Squibb Foundation - we have been developing a large early diagnosis educational program in collaboration with Health Authorities of SSA countries. The first step was to create tools to enhance caregiver's education and to inform the general population.

Design/Methods: Eleven pediatric oncology experts from ten countries participated in a 5-day-collaborative workshop in March 2019 with Senegalese health authorities - Ministry of Health and National School for Nurses and Midwives - and experts from AMREF.

Results: Training modules on early signs and symptoms of 5 major children curable cancers (Acute Lymphoblastic Leukemia, Wilms, Burkitt and Hodgkin Lymphoma, Retinoblastoma) were developed and harmonized. These modules are intended to nurses and general hospitals doctors. Tools will be developed accordingly: manual for early diagnosis and the way to manage suspicious cases, video and audio supports, posters. This early diagnosis education program will be piloted in Senegal during the summer of 2019, with the guidance and support of the Ministry of Health and in collaboration with AMREF.

Conclusions: Early diagnosis can be developed in SSA using the program developed by the GFAOP. Demonstrating an impact on survival rates will need further development in other regions and countries in 2020.

PO037 SIOP19-1243 | **Accommodating Displaced Syrian Children with Cancer Back in Their Home Country for Treatment: An Initiative by a Local NGO**

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Background/Objectives: War in Syria has resulted in waves of displacement to nearby and distant countries. This caused significant load on the already suboptimal health systems in few nearby countries. International humanitarian funds supported the treatment of Syrian children with cancer in specific institutions in the region. Over the past few months, war ended in Damascus, thus there was a need to support these children in their country for treatment.

Design/Methods: In June 2018, BASMA association started an initiative to accommodate displaced Syrian children with cancer in their home country by being enrolled in BASMA dedicated pediatric oncology unit (if eligible) or by the

transfer of care to another hospital in Syria. Patients and their families eligible for enrollment in the unit received financial and psychosocial support through other programs by BASMA association.

Results: Between June 2018 and March 2019, ten patients were supported by the initiative. All patients were displaced to Lebanon and had the following diseases: osteosarcoma (n=1), Burkitt's lymphoma (n=1), neuroblastoma (n=2), medulloblastoma (n=1), rhabdomyosarcoma (n=1), ALL (n=1), relapsed AML (n=1), retinoblastoma (n=1), brain pleomorphic xanthocytoma (n=1). Nine patients were enrolled for full treatment at BASMA pediatrics oncology unit in Damascus (operated by BASMA association) and one patient with relapsed AML was admitted to a general hospital in Aleppo for palliative care. The care of one patient with pleomorphic xanthocytoma was transferred back to a hospital in Lebanon for family-related issues. All patients are currently alive with no treatment abandonment.

Conclusions: An initiative by a local NGO has successfully supported displaced Syrian children with cancer to return to their home country to receive medical treatment and to get enrolled in others financial and psychosocial support programs.

PO038 SIOP19-1530 | Implementation of a Pediatric Oncology Diploma Program to Address Critical Workforce Shortages in French-Speaking Africa

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Background/Objectives: **Background:** In 2012, the French African Pediatric Oncology Group (GFAOP) established the African School of Pediatric Oncology (EAOP), a training program supported by the Sanofi Espoir Foundation's My Child Matters program. As part of the EAOP, the GFAOP created a Pediatric oncology training diploma, a one year intensive training program accredited by the Mohammed-V Rabat University and the Paris Sud University. We present this training and certification program as a model for subspecialty training for low- and middle-income countries.

Design/Methods: A fourteen-member committee of multidisciplinary experts from Morocco, France, and the USA finalized a curriculum patterned on the French model "Diplôme Inter-Universitaire d'Oncologie Pédiatrique". Learning modules and teaching methods are multidisciplinary, and the program trained 15-25 physician candidates per year. Candidates committed to returning to their home country to work

at their parent institutions. Training included didactic lectures by experts, both in-person, and recorded for online delivery, an on-site practicum, and a research project. Evaluation included candidate evaluation and feedback on the effectiveness and quality of training.

Results: The first cohort began October 2014 and by January 2019, 72 candidates from three cohorts had been trained. Of the first 72 trainees from 19 French African countries, 55 (76%) graduated successfully and returned to their countries of origin. Four new pediatric oncology units have been established in Niger, Benin, Central African Republic and Gabon by the graduates. An e-learning platform www.e-gfaop.org was made available via the program.

Conclusions: This training model rapidly increased the pool of qualified pediatric oncology professionals in low- and middle-income French-speaking countries of Africa. It is feasible and scalable, but requires sustained funding and ongoing mentoring of graduates to maximize impact.

PO039 SIOP19-0569 | Pediatric Cancer Registry in Turkey 2009-2018 (TPOG and TPHD)

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Background/Objectives: Pediatric cancer registries are the essential element of cancer control programs. Each year more than 200000 new cancer cases are expected at global level in children and adolescents aged 0-14. There are still needs the major investments in LMICs for the establishment of pediatric cancer registries. Here we present the most updated results of the pediatric cancer registry in Turkey.

Design/Methods: Turkish Pediatric Oncology Group and Turkish Pediatric Hematology Association has established the Registry in 2002. The childhood cancer cases registered between 2009-2018 was included in this analysis. ICCC System was used for the classification. ICD-O-3 morphology and topography codes & essential demographic findings, were recorded for each case.

Results: Between 2009 and 2018, 15800 cases were registered. For all cases, median age was 6.7 year (0-17; M/F8884/6908, 3 hermaphrodite, 5 unknown). Age distribution was 0-4 yrs, 40.7%; 5-9 yrs, 24.4%; 10-14 yrs, 23.2%; 15-19 yrs, 11.7%) The distribution of the tumor types were [number of cases, percentage of total, median age yrs, M/F]: Leukemia (4405, 27.9%, 5.4, 2538/1867); Lymphoma & other RES tumors (3002, 19.0%, 9.7, 2014/983, 1 hermaphrodite & 4 unknown); CNS (2100, 13.3%, 7.1, 1147/953); Sympathetic system (1248, 7.9%, 2.4, 654/594); Retinoblastoma (360, 2.3%, 1.4, 206/154); Renal (790, 5.0%,

3.3, 369/421); Liver (262, 1.7%, 1.8, 144/118); Malignant bone (1043, 6.6%, 12.6, 573/470); Soft tissue sarcomas (1055, 6.7%, 7.4, 614/441); Germ cell (974, 6.2%, 8.5, 346/625, 2 hermaphrodite, 1 unknown); Carcinoma & other malignant epithelial (462, 2.9%, 13.7, 226/236); Other/non-specific malignant (99, 0.6%, 7.9, 53/46). Five-year survival rate was found as 70.8%

Conclusions: This registry has been a good example for the role of cancer societies on collecting data for registries and used widely among health professionals. Survival rates for children and adolescents has been improved to 70 and shows the level of care in Turkey, as an upper middle-income country.

PO040 SIOP19-0738 | Interest of a Preliminary Meeting for the Participation of Patients in Early Phase Trials (PRIMEP) in a Pediatric Oncology Department

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Background/Objectives: The participation of a patient in an EPT raises many questions. In our pediatric department, most inclusion offers are questioned in a multidisciplinary board named PRIMEP

Design/Methods: After the identification of an eligible patient for an EPT through the oncologic medical board, the PRIMEP meeting discusses the feasibility and the individuality of such a proposition, as well as the appropriate alternatives for care management. The referral physician and nurse, a physician and a staff member from the clinical research team, a member of the home care team, and a palliative care team caregiver are present.

The medical situation, as well as the personal and psychosocial issues at stake are discussed. Administrative, organizational and ethical issues are raised.

Results: From 2016 to 2018, 114 patients were enrolled in an EPT. 48 PRIMEP were organized, which concerned 38 patients (33.3%) with advanced oncologic disease. Most PRIMEP (N=40, 83%) concluded that offers for an EPT was consistent with patient and family condition. In 8 cases, it was either not the right moment or not adapted at all. In only 1 case, an EPT was offered against the PRIMEP consideration. Three case studies will be described to exemplify PRIMEP

discussions focusing on social context, psychologic condition, medical considerations, family management and palliative care considerations. The identification of the patient's environment enable to move towards a reflection favoring its global management, far beyond a simple offer of an EPT.

Conclusions: The opinion of PRIMEP is only advisory and do not usually change the decision to offer an EPT. It's the opportunity to have a comprehensive view of the patient and his environment. Areas of improvement are to make PRIMEP accessible to all patients included in an EPT and to promote its feasibility in order to develop palliative support post PRIMEP.

PO041 SIOP19-1675 | Benefits and Limitations of an International Observer-Ship for Pediatric Oncology Providers

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Background/Objectives: Twinning programs, partnerships between high-income and low-to-middle income countries (LMICs), have been shown to improve pediatric oncology care globally.[1, 2] One key aspect of these programs is provision of education and training to providers from LMICs. International observer-ships were offered as part of a developing twinning partnership between a large referral hospital in Kenya and an academic institution in the U.S.

Design/Methods: Nine pediatric oncology providers, recommended by senior hematologists at University of Nairobi, were funded through a grant from the Conquer Cancer Foundation of the American Society of Clinical Oncology to travel to the U.S. for one-month observer-ships. Participants included 4 physicians who provide pediatric oncology clinical care, 2 oncology pharmacists, 2 pediatric oncology nurses and a palliative care nurse. Participants rotated with counterparts practicing in the same specialties and attended multidisciplinary rounds. All providers completed pre-test, post-test and follow-up surveys to assess retention of knowledge.

Results: Preliminary results from the initial 4 providers show a variety of changes in knowledge from pre-tests to follow-up assessments (range -3% to 23.3%) with an average increase in knowledge of 8.3 percent. All participants returned to Kenya motivated to improve care. One nurse became a patient educator, a newly created position. Another nurse implemented weekly CME trainings for her colleagues on the pediatric oncology unit. Both nurses were hired as research nurses for the grant. Several months after returning home, providers reported increased knowledge about chemo, safe chemo administration and handling of spills, and an understanding of the importance of hygiene and caregiver education

and empowerment. Limitations included training time being too short for further advancement of knowledge and resistance to some proposed changes by the home institution.

Conclusions: While international observer-ships are not sufficient to provide a comprehensive education, there are several important benefits that can be derived, including strengthening of the twinning relationship.

PO042 SIOP19-0479 | Evaluation of Delays in Diagnosis of Pediatric Cancer in a Social Security Institution in the Central Zone of Mexico and Related Factors

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Background/Objectives: In México, pediatric mortality due to cancer is high, attributed mainly to the delay in diagnosis and reference to specialized units. Multiple social, cultural and care-process factors influence this delay.

Objective: Identify factors related to delay in diagnosis and referral of pediatric patients with cancer at the Social Security Institute of the State of México and Municipality

Design/Methods: We Included in a retrospective cohort the records of patients with corroborated diagnosis of childhood cancer. at Hospital Materno Infantil of the Social Security Institute of the State of Mexico. In central zone of Mexico.

We evaluated the intervals between the beginning of the first symptom of cancer and first medical evaluation, as well as the interval between it and the date of diagnosis, the diagnostic interval and the variables related to these: age and type of cancer, age and educative level of the parents, Iatrotropic Index, type of doctor who suspects diagnosis.

Results: We analyzed 114 Records, male 59, female 55, adolescents 54%, maternal age 36 $\pm$ 7 years old, paternal age 38 $\pm$ 7 years old, with high education level, 32% mothers and 28% of parents, leukemias 48% (85% high risk) and solid tumors 59% (48% stage III and 31% stage IV) Interval first symptom-first doctor 57 $\pm$ 128 days, interval between suspected cancer and date of diagnosis 41 $\pm$ 77 days. Doctor who suspect cancer was a pediatrician in 60% of the cases

Total 89 $\pm$ 119 days. 30% with iatrotropic index $>$ 4. Adolescents, solid tumours and high educative level of the mother were significantly associated with greater delay

Conclusions: Knowing the intervals related to the delay in leg time diagnosis of childhood cancer of our environment and the

variables related to it will allow to identify modifiable variables and organizational barriers limiting the diagnosis and timely reference increase the survival and optimize the health resources.

PO043 SIOP19-1171 | Role of Research Associate in Pediatric Oncology Indus Hospital Karachi

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Background/Objectives: Pediatric cancer patients are at a higher risk of life threatening hospital acquired infections (HAI). HAI are cause of high mortality and morbidity, with transmission of infections due to the poor hygienic practices. The research associate (R.A) plays a vital role in compiling data regarding HAI's, and by providing statistical and graphical analysis. The objective of this study is to determine the impact of data analysis in obtaining better findings for HAI through hand hygiene compliance rates.

Design/Methods: Data collection and education was provided by the Infection Control Practitioners (ICPs). After data collection, statistical analysis was performed by the R.A using SPSS version 21. Subsequently, the R.A converted statistics into a graphical form to present the data to hospital directors and departmental heads.

Results: The data was analyzed by the R.A to produce results of hand hygiene compliance; it was found that there is poor compliance among the medical and nursing staff. Comparing the data of hand hygiene with HAI's, the root causes as well as solutions were found for decrease the infection. Additionally, graphical data described the trends of compliance and making comparison of hand hygiene compliance and HAI's. The R.A consequently shared the data with the ICP's, so that further steps can be decided for better compliance and plans can be made to fill the gaps of hand hygiene and decrease the rate of HAI's.

Conclusions: If data is presented comprehensively, further decide the future plans of better hand hygiene compliance for decrease the infections. Through analysis and comparison of hand hygiene compliance and HAI's can easily find out the root causes of the poor compliance of hand hygiene so solutions can be design accordingly and overcome HAIs, achieving better compliance of hand hygiene. Also, there can be reductions in patients' length of stay, the hospital burden and mortality rate.

PO044 SIOP19-0723 | Development of a Pediatric Oncology Program at Calmette Hospital, Cambodia

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Background/Objectives: The incidence of childhood cancer worldwide is 130 new cases per million children under 15 years of age. The population of Cambodia is approximately 16 million, with 33% of the population consisting of children less than 15 years, thus, we estimate 670 new cases of childhood cancer per year. Due to low cancer awareness in the general population and among medical staff, only one third of estimated cases currently reach oncology units. We aim to show how a model of partnership with an existing adult cancer center can lead to successful implementation of a pediatric oncology program.

Design/Methods: In 2014, 1 pediatrician began treating children with cancer in the adult national cancer center. Program development has focused on increasing national awareness of childhood cancer, training specialized pediatric oncology staff, obtaining a dedicated unit, and collaborating with international partners.

Results: As of March 2019, there are 12 beds, a playroom, 2 pediatricians and 3 nurses dedicated for pediatric oncology. One radiation oncologist has received pediatric training. We also received the My Child Matters Award for pediatric nurse training in 2018. International cooperation offered opportunities to join international conferences. Total new cases in 2018 was 46, increased from 5 cases in 2014.

Conclusions: Despite many challenges including lack of human resources and infrastructure, limitation in awareness, and financial constraints, we developed a pediatric oncology unit starting with only one dedicated staff, using facilities of an adult cancer unit and continue to grow. Strong support from the hospital board of directors, commitment and motivation of staffs, together with guidance of overseas experts are the keys to our success. Future work, including building a pediatric oncology multidisciplinary team, capacity building, protocol development and partnering with a local foundation is needed to continue progress and ensure good care of children with cancer in Cambodia.

PO045 SIOP19-1382 | Hereditary Predisposition to Oncological Diseases in Russian Pediatric Patients as Revealed by Clinical Exome Sequencing

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Background/Objectives: About 8-10% of neoplasms in children and adolescents are considered to be caused by germline mutations in genes, involved in cancerogenesis. At the same time, it is believed that genetic determination of tumor development in childhood is substantially underestimated. Thus, a further searching for mutations, associated with oncological diseases in childhood, is actual. Our aim was to investigate genetic variants, associated with high risk to develop cancer, in Russian children with oncological diseases using clinical exome sequencing (CES) as high throughput molecular test.

Design/Methods: CES was performed on 96 children (53 boys, average age 11,4 years) in the course of rehabilitation after oncological diseases. 76 children had acute lymphoblastic leukemia (ALL) (n=45) or lymphoma (n=31), 20 children had brain tumors. Most patients had a family history of benign or malignant neoplasia. The coding regions selection was done using commercial kits from Roche (Inherited Disease Panel) or Illumina (TruSight One Panel).

Results: The bioinformatic analysis revealed more than 200 variants with minor allele frequency less than 1% in *APC*, *BRCA1/2*, *PALB2*, *TP53*, *NF1*, *PTEN*, *RET*, *PTPN11*, *MSH2*, *CHEK2*, *VHL* and other genes, involved in cancer development, most of them were described as variants of uncertain significance (VUS). The pathogenicity of variants was estimated using ClinVar, SIFT, PolyPhen2, MetaSVM databases. In ALL patients, pathogenic mutations in *TP53*, *VHL*, *NBN* genes were found, in one lymphoma patient novel *MSH2* mutation was identified. In patients with brain tumors, pathogenic mutations in the *NF1* gene were revealed more often. Our NGS findings were validated using Sanger sequencing and segregation analysis was done in some cases, if parental samples were available.

Conclusions: CES is powerful tool to estimate the mutational burden associated with cancer. To validate the clinical significance of deleterious mutations or VUS, segregation analysis in the family and a prospective follow-up of the patients are required.

PO046 SIOP19-0236 | Paediatric Cancer Services in a Peripheral Ghanaian Setting: A One Year Review

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Background/Objectives: Ghana has two comprehensive paediatric cancer treatment centres managing averagely, 500 new reported paediatric cancer cases. Families travel long

distances to access paediatric cancer services contributing to increased financial toxicity and treatment abandonment rates. Appropriately resourced shared care centres to bring paediatric cancer services closer to families will help mitigate these risks while ensuring access to care and universal health coverage. The Agogo Presbyterian Hospital, APH is located about 2 hours' drive from the comprehensive paediatric cancer centre in the Ashanti regional capital of Kumasi. A paediatric oncologist has been available at APH since April 2018.

Design/Methods: We retrospectively reviewed paediatric cancer services provided by our district-level hospital from April 2018 to March 2019.

Results: The appointment of a paediatrician with a paediatric oncology background since April 2018 has facilitated the training of 2 nurses in chemotherapy preparation and administration. One pharmacist with similar training was subsequently assigned to support the unit. Chemotherapy is presently prepared in a safety biohazard hood located at a research laboratory within the hospital premises. A standard operating protocol was developed to ensure safe chemotherapy preparation and administration. Ten new cases were diagnosed during the year; doubling the mean new case rates recorded from 2015-2017. There were 5 NHL; 3 Rhabdomyosarcoma; 1 Hodgkin lymphoma, HL and 1 Nephroblastoma. 3 patients have completed their scheduled treatments. Four patients with neuroblastoma (1), nephroblastoma (1), Acute Lymphoblastic Leukaemia, ALL (1), and HL (1) were referred from the comprehensive centres to access shared and palliative care services. Morphine (oral and parenteral) is now available and utilized regularly. Similarly, an algorithm has been adopted for the management of febrile neutropenia. Lack of access to platelets and diagnostic services remain major challenges.

Conclusions: A paediatric oncologist at a peripheral setting can potentially ensure universal access to improved care for paediatric cancer patients.

PO047 SIOP19-1139 | Epidemiological Profile of Children Diagnosed with Cancer in a Period of 18 Years at the Civil Hospital of Guadalajara, Mexico

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Background/Objectives: Cancer is a morbidity factor with an increasing incidence worldwide. The objective of this study is to describe the frequency of patients diagnosed per year in a pediatric oncohematology referral center, that serves 89.3% of cancer patients treated with the Social Protection in Health

System of the state of Jalisco, Mexico and the prevalence of different types of neoplasms.

Design/Methods: This is a retrospective, observational study of patients younger 18 years old with cancer diagnosed in the Pediatric Oncohematology Department of the Hospital Civil de Guadalajara Juan I. Menchaca. All patients with diagnosis of cancer from 2001 to 2018 were included. The descriptive statistical analysis was done using EPIInfo 7.

Results: Children who were diagnosed with cancer were 2043, an average of 113.5 cases per year. The incidence of cases attended showed a significant increased in 2015 in which 205 patients were diagnosed, since 2016 the number of patients diagnosed per year has decreased reporting 158 cases by 2018. The most frequent cause in all the years was Acute lymphoid leukemias in 41% of the cases, followed by tumors of the central nervous system in 14.5% and lymphomas with 10% in the third place. Solid tumors represent 23.8% of all cases, with bone tumors being the most common.

Conclusions: Cancer is a major cause of morbidity and mortality children worldwide and its incidence tends to increase. The number of new cases diagnosed with cancer in the state of Jalisco, Mexico increase until 2015 comparable to that reported worldwide, year from which the number of patients with this diagnosis is decreased. The prevalence pattern of cancer is similar to that reported in Latin America, with the most common cancer were Acute lymphoid leukemias, tumors of the central nervous system and lymphomas.

PO048 SIOP19-0891 | Blood Stream Infections in a Pediatric Hematology Oncology Unit

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Background/Objectives: Bloodstream infections (BSI) are a major cause of morbidity and mortality in children with malignancy. The objective of this study is to evaluate the pathogens involved in BSI in children that were treated in a single Pediatric Hematology Oncology unit from July 2017 until March 2019.

Design/Methods: A retrospective study of positive blood cultures involving the period between July 2017 and March 2019 was carried out. All laboratory data and clinical records for 6,000 children admitted in the Unit at this period were recorded. Antibiotic stewardship program and nosocomial infection prevention plan has been adopted in our unit since 2013.

Results: During the study period 57 episodes BSI occurred in 27 boys and 30 girls. The mean age of the patients was 7.04 years old and 84% of children had Central Venous

Line. The underlying malignancies were Leukemia 51%, solid tumors 30%, brain tumors (9%), aplastic anemia (5%), Langerhans Cell Histiocytosis (4%) and lymphoma (1%). Among the 57 BSI episodes, 51 (90%) were monomicrobial and 6 (10%) polymicrobial. Central line-associated bloodstream infection (CLABSI) were 16 episodes (28%). Gram-negative bacteria accounted for 51% of the cases, followed by Gram-positive bacteria (44%) and fungi (5%). The bacteria included Coagulase negative staphylococcus (31%), Pseudomonas species (14%), Klebsiella species (13%), Enterobacter species (6%), Escherichia coli (6%), Candida species (5%). Single episodes BSI were due to Acinetobacter, Staphylococcus aureus, Enterococcus, Listeria, Micrococcus, Rhizodium radiobacter, Chryseobacterium, Citrobacter and Lactococcus.

Conclusions: Despite prevention programs BSI remains a significant cause for morbidity. The awareness of the etiology of BSI and sensitivity of antibiotics is a necessary tool for regular update of the guidelines for the management of febrile episodes in pediatric oncology patients

PO049 SIOP19-1579 | Podcasting Delivers Global Pediatric Oncology Education in Low- and Middle-Income Countries

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Background/Objectives: We piloted an educational podcast called *Global Health & Childhood Cancer* (GHCC) to explore the feasibility of podcasting as an education medium for healthcare workers interested in global pediatric oncology (GPO).

Design/Methods: Episodes were designed as interviews with content experts in an area relevant to GPO. Episodes were posted on www.GHCCpod.com and promoted on social media accounts of www.cancerPOINTE.com. Podcast download statistics were obtained via the subscription podcast hosting platform Blubrry.

Results: From November 2018-March 2019, 7 podcast episodes were released and downloaded 253 times. Median file size was 30.7 megabytes (range=14.3-37.5). Estimated download time for the median episode on a 2G wireless network is 40 minutes (m), 56 seconds (s) at 0.1 megabits/second (Mbit/s) (range=19m11s-50m0s) and for a 4G network is 16s at 15Mbit/s (range 7s-20s). Median downloads per episode

was 30 (range=14-56). Episodes were downloaded by listeners in 42 different countries, including 11 Asian, 7 African, and 7 Central/South American countries. Listeners from low- and middle-income countries (LMIC) accounted for 26 total countries (62%) and 92 episode downloads (36%). Mobile applications accounted for 153 (60%) of total downloads, with the iOS platform (iPhone, iPad) used for 87 downloads (34%), the Android platform for 61 downloads (24%), and other platforms for 5 (2%). Ninety-five (37.5%) of remaining downloads were from computers via web browsers and 5 were unclassified. The podcast website received 1867 total page views from 743 unique visitors in 79 different countries. Visitors to the website from LMIC accounted for 220 visits (29%).

Conclusions: This pilot project demonstrates that podcasting is a feasible and promising platform to deliver free GPO education resources to people in LMIC. The pilot episodes reached a wide geographic distribution, especially in LMIC. As mobile technologies and high-bandwidth internet resources become more available to healthcare practitioners around the world, podcasting will become an increasingly valuable education medium.

Haematology - Acute Lymphoblastic Leukaemia

PO050 SIOP19-1592 | IS 6-Mercaptopurine Suspension Therapeutically Equivalent to Tablet in Children with Acute Lymphoblastic Leukemia During Maintenance Therapy?

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Background/Objectives: Xaluprine®, a 6-mercaptopurine (6-MP) suspension, has obtained its market authorization in 2012. The bioequivalence study performed on adult healthy volunteers revealed a different absorption profile (maximal concentrations of 6-MP plasma concentrations (>39%)) compared to tablet and a comparable exposure (the area under the curve > 13%). The European medicines agency justified this authorization in front of benefits for pediatric patients (a more accurate dosing and an ease of taking adapted for the child) and specified that the dose for children should be adapted.

The aim of this study is to assess therapeutic equivalence for this suspension compared to tablet in the target population.

Design/Methods: This was a retrospective monocentric cross-over study. We obtained a local ethical agreement. Patients who received both formulations throughout maintenance therapy at a protocol dosage (75 mg/m²/day, adapted to leukocytosis) were included.

Intracellular metabolites concentrations named 6-thioguanine nucleotides (6-TGN) and methylated derivatives (6-MMPN) were measured, after each formulation introduction, at steady-state by HPLC-UV. Wilcoxon tests were performed.

Results: Seven patients (3 boys) were included in this study. The median age was 6 (3-14) years old at the maintenance therapy initiation. Compared to tablet, the ratio of 6-TGN/dose for suspension was higher in 4 patients (median $(6\text{-TGNXaluprine/dose})/(6\text{-TGNtablet/dose}) = 1.4$ (0.8-1.9)) and the ratio of 6-MMPN/dose was higher in 3 patients (median $(6\text{-MMPNXaluprine/dose})/(6\text{-MMPNtablet/dose}) = 0.9$ (0.5-1.4)), not statistically different.

Conclusions: This study highlighted that therapeutic drug monitoring after a 6-MP formulation change is essential to optimize the individual 6-MP dose.

PO051 SIOP19-0064 | Pediatric Nurses Knowledge on Chemotherapy at Komfo Anokye Teaching Hospital

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Background/Objectives: BACKGROUND Chemotherapy (anti-cancer drug) is one of the effective treatments for most oncological conditions. It targets cells that grow and divide quickly as cancer cells do. It is important to know whether general nurses know about chemotherapy as this can impact what they tell patients. This study was undertaken to evaluate the knowledge of staff nurses on chemotherapy at the pediatric wards of the Komfo Anokye Teaching Hospital (KATH).

Design/Methods: METHODS This study was a hospital based cross sectional descriptive study. Nurses' knowledge of chemotherapy was evaluated using a structured questionnaire with both open and closed ended questions. Systemic random sampling was used in selecting 100 respondents from the various wards in the Directorate of Child Health at KATH.

Results: A total of 100 nurses participated in the study. The male respondents were 60 (60%) while female respondents were 40 (40%). Most of the respondents (60%) said they didn't have knowledge about chemotherapy. However, only 40% of the respondent had knowledge about chemotherapy. Regarding the side effects of chemotherapy, 45% of respondents had some knowledge while the remaining 55% said they didn't have any knowledge about side effects of chemotherapy. For the specific chemotherapy for treating specific types of oncological conditions, 30% of respondents were able to give a correct answer while 70% of the respondents were not able to give correct answers.

Conclusions: Evidence from this survey suggested that nurses have insufficient knowledge about chemotherapy and

its side effect. It is recommended that more education about paediatric cancers and chemotherapy should be added on to the nursing curriculum. Also, workshops and in-service training session on chemotherapy should be organized for nursing staffs of the pediatric wards at Komfo Anokye Teaching Hospital.

PO052 SIOP19-1371 | A Case Study on Cardiorespiratory and Muscular Functions in a Child with Acute Lymphoblastic Leukemia: Consolidation Phases of Chemotherapy

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Background/Objectives: Acute lymphoblastic leukemia (ALL) is the most diagnosed cancer for children younger than fifteen years old. Studies showed that children in maintenance chemotherapy have lower cardiorespiratory fitness and muscular strength than normal children, and that they engage in physical activity less frequently. Expectation of weakness and fear of over exertion contributed to a lack of data on their ability to engage in vigorous physical activities prior to maintenance. The aim of our project was to evaluate the cardiorespiratory fitness, with a maximal oxygen uptake (VO₂max) test and muscular function of a child with ALL during the first six months of chemotherapy.

Design/Methods: An eleven years old female with low-risk B-cell ALL under the DFCI-16-001 protocol took part in two cardiorespiratory function testing sessions during her consolidation 1A (T1, 38th day of treatment) and consolidation 2 (T2, 154th day of treatment). The VO₂ was assessed following the James protocol and the American Heart Association recommendations for cardiorespiratory exercise stress testing. Body composition, grip strength, moment of force of the knee extensors and ankle dorsiflexors were also evaluated in both treatment phases.

Results: From T1 to T2 the participant had a 12.3% weight gain with a 32.4% increase in body fat. Her VO₂max increased from 884.6 ml/min to 1366.9 ml/min (+54.5%). The moment of force of the knee extensors and the ankle dorsiflexors increased on average by 105.7% and 36.6%, respectively. Grip strength increased by 31.8% on the left and decreased by 2.9% on the right.

Conclusions: Although the participant's overall performance was slightly better during consolidation, she achieved no more

than 60% of her age-predicted VO₂max, and strength values were under the norms. These results underlined not only the fact that some children with ALL can be unconditioned early into chemotherapy, but most importantly that some would benefit from adapted physical activity during consolidation.

PO053 SIOP19-0351 | Childhood Acute Lymphoblastic Leukaemia and Obesity Risk: An Evaluation of Healthy Eating and Exercise Advice Through Treatment

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Background/Objectives: Survivors of Acute Lymphoblastic Leukaemia (ALL) in childhood are at an increased risk of health problems including Cardio-Vascular Disease (CVD) (Fidler et al. 2016). Around 1 in 3 children complete treatment as overweight or obese (Zhang & Parsons 2015). Obesity is also associated with developing CVD and other chronic conditions (PHE 2017). The aim of this project was to evaluate healthy eating and exercise advice offered to families of childhood ALL patients and ascertain how useful health promotion is considered as part of treatment.

Design/Methods: Bespoke questionnaires were developed. Professional opinion was sought from Leukaemia Clinical Nurse Specialists (CNSs) within each Paediatric Principal Treatment Centre (PTC) in the UK (n=20). Parent / carer opinions were sought when attending follow up appointments with their child (n=22).

Results: Eleven professionals and 20 families completed questionnaires. All teams delivered healthy eating advice but only half delivered exercise advice (n=6, 55%). Fourteen families received exercise advice (70%) and thirteen received healthy eating advice (65%). Consultants, Nurses, Dieticians and Physiotherapists were delivering support. Most parents wanted input from the beginning and throughout treatment, which only one family received and one centre delivered. Parents wanted a non-judgemental, proactive approach at the appropriate time with better guidance, better hospital food and an online forum. Professionals wanted a structured approach, better hospital food and more resources. Barriers were a lack of time, resources and staff training. Both professionals and parents think health promotion is a useful part of treatment.

Conclusions: Delivery of health promotion throughout treatment was inconsistent and parents wanted more support with the challenges their child faced. There is a need for a standardised pathway for professionals where health promotion advice is embedded throughout the treatment journey. Better use of literature, websites, mobile apps and signposting to

other teams is indicated. Professionals need more time, training and funding.

PO054 SIOP19-0829 | Deep Venous Thrombosis (DVT) in Pediatric Patients Diagnosed with Acute Lymphoblastic Leukemia (ALL). Comparison Between Two National Protocols

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Background/Objectives: Pediatric patients with ALL have an increased risk of developing DVT due to numerous factors, such as central venous lines, asparaginase and corticosteroid use. Objective: review of the characteristics of children with ALL and DVT in our center, analyzing whether there are differences according to the protocol used (LAL SHOP-2005 or SEHOP-PETHEMA-2013).

Design/Methods: Retrospective, descriptive study of clinical data of children diagnosed with ALL who developed a DVT between January 2005 and February 2019 in a tertiary hospital.

Results: One hundred and twenty-six ALL were diagnosed: 60 treated with LAL-SHOP-2005 protocol (Group A) and 66 with SEHOP-PETHEMA-2013 (Group B). Seven presented a DVT (5.55%): 3 from group A and 4 from B. Fifty percent older than 10 years, mostly males and with precursor ALL; no statistically significant factors. All occurred during the induction, only one had received Pegylated Asparaginase, the rest native E. coli. Eighty-six percent had received more than half of the protocolized doses. Extracerebral thrombosis was the most frequent: 80% in lower extremities, of which 80% were central venous line related. One patient (T-ALL with mediastinal mass on debut) receiving prophylaxis with LMWH, presented DVT in the jugular/left subclavian vein in the context of thrombophlebitis due to *S.aureus*. Two patients that developed cerebral venous thrombosis were diagnosed with ALL-T and presented hyperleukocytosis at diagnosis. None had previous thrombophilia study, but it was performed later in 60% of patients that developed DVT. One presented heterozygosis gene *FII 20210A*.

Conclusions: In our series, the highest incidence of DVT in children with ALL was confirmed in the induction phase and increased risk with a history of CVC of peripheral insertion. Prospective studies with a larger number of cases are needed to help determine which patients would benefit from thrombophilia studies and antithrombotic prophylaxis.

PO055 SIOP19-1547 | Avian Myeloblastosis Viral Oncogen Homolog (MYB) Overexpression is Associated to Diagnosis in Childhood B-Cell Acute Lymphoblastic Leukemia

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Background/Objectives: B-cell acute lymphoblastic leukemia (B-ALL) is characterized by immature cells proliferation that arises from stem cells in bone marrow. In Mexico leukemia represents priority health problem, being the most frequent type of cancer in pediatrics; representing 52% of diagnosed cases in children under 15 years old. Moreover, Mexico has more cases of poor prognosis than other countries. Currently, B-ALL whole transcriptome allows identifying genes that could be involved in cancer development. Additionally, transcriptome tools promise to be useful identifying patients with high risk of poor prognostic at diagnosis in order to implement specific treatments. **Objective.** Evaluate MYB expression and the impact of the clinical correlation in B-ALL.

Design/Methods: We obtain 82 bone marrow of pediatric patients with B-ALL at diagnosis and seventeen peripheral blood of healthy donors, we obtain total RNA and subsequently cDNA synthesis. All samples were evaluate using RT-qPCR. The analysed was performed with 2^{-ΔΔCT} method. The statistics analysis was archived using U-Mann Whitney, Kruskal-Wallis and the receiver operating characteristic (ROC) curve.

Results: We include in this study 70 samples, the comparative analysis of the MYB expression showed that MYB is overexpressed in B-ALL $p < 0.0001$. We identify that the expression over 1.46-fold is associated to leukemia disease. Finally, we observed a tendency of MYB overexpression is potentially maker of die.

Conclusions: MYB overexpression in B-ALL could be used as diagnostic molecular marker.

PO056 SIOP19-0195 | The Influence of Methionine Synthase 2756 A>G Polymorphism on Methotrexate Induced Toxicities in Children with Acute Lymphoblastic Leukemia

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Background/Objectives: Methotrexate induced toxicities vary considerably between patients implying the necessity to study factors that may contribute to such interindividual variability. Pharmacogenetic markers, like gene polymorphisms, may offer a strategy to help identify patients who are more likely to suffer the toxicity of MTX. The Methionin synthase (MS) 2756 A>G polymorphism have been reported to be associated with methotrexate toxicities with still controversial results. The objective of our study was evaluation of the correlation of MS 2756 A>G polymorphism with the occurrence of toxic effects during therapy with high doses of methotrexate.

Design/Methods: Our study comprised of 65 children with ALL treated with high doses of methotrexate (5g/m²) during protocol M, part of the ALL BFM 2000 protocol. Genotyping for MS 2756 A>G polymorphisms of MS gene was performed using the PCR-based restriction fragment length polymorphism assay. Toxic effects were analyzed according to the criteria for toxicity from the protocol ALL BFM 2000 (absence or presence of toxic effects) in correlation with the type of present polymorphism.

Results: Subjects with MS 2756 AG manifested more often thrombocytopenia [OR (95%CI) 1.658 (0.54 – 5.06) RR (95%CI) 1.446 (0.64 – 3.27), $p=0.025$] than patients with MS 2756 AA and GG. Skin toxicity in patients with MS 2756 AG [OR (95%CI) 2.833 (0.48 – 16.73) RR (95%CI) 2.571 (0.51 – 13.05), $p=0.709$] and also intestinal mucositis in patients MS 2756 AG [OR (95%CI) 2,040 (0.32 – 13.13) RR (95%CI) 1.929 (0.35 – 10.77), $p=0.709$] were more common, but without statistical significance. No other toxic effects in correlation with this polymorphism were registered.

Conclusions: The present study suggests that MS 2756 A>G polymorphism can be considered as markers for predicting toxicity in childhood ALL. Further multicenter studies with larger data should be performed for future personalization of treatment in childhood ALL in combination with this pharmacogenetic markers.

PO057 SIOP19-0544 | Strategies for Reducing Mortality in Induction in Patients with Acute Lymphoblastic Leukemia in a Pediatric Public Center in Brazil-NE

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Background/Objectives: Acute lymphoblastic leukaemia (ALL) mortality is less than 10% in developed countries, whereas in low/median income countries it may exceed 60%, mainly due to infectious complications. The study's goals were: to evaluate general and Induction mortality, and global survival at three years in a public reference oncology center in the northeast of Brazil; to compare these results with the ones of previous study in the same center after the implementation of simple conducts for reducing deaths by infection during Induction.

Design/Methods: All patients with ALL up to 19 years-old treated with a standardized protocol were prospectively evaluated. The following interventions were adopted: 1) Keeping clinically stable patients but who are living in remote places housed in the Supporting Houses, at least during the first two weeks of treatment; 2) Providing guidance to caregivers for temperature admeasurement and, in case of fever, coming back to hospital immediately; 3) Encourage contact by phone with the multidisciplinary team; 4) Conduct training to emergencist-doctors in order to standardize conducts for diagnosis and management of complications; 5) Immediate administration of the first dose of antibiotic in suspected febrile neutropenia. Overall and Induction mortality, major complications during treatment and global survival at three years were evaluated.

Results: We studied 52 patients. There was a decrease in general (38.5%) and Induction (13.5%) mortality in relation to the results of the previous study in the same center (45.3 and 22.6%). Infection was the leading cause of death (75%). Global survival after three years was 59.6%.

Conclusions: There was reduction in general and Induction mortality rates after the implementation of simple measures aimed at protecting patients in situation of social vulnerability as well as reducing deaths from infection in the first weeks of treatment. The results obtained justify the maintenance and improvement of these measures as a routine in that center.

PO058 SIOP19-1535 | Association of CD 45 Expression with Risk Staging in Pediatric Patients with Acute Lymphoblastic Leukemia

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Background/Objectives: Acute lymphoblastic leukemia (ALL) is the most common cancer in children. There are studies that have shown the association of CD 45 expression for flow cytometry (FC) with ALL with worse prognosis.

Objective: This study evaluates the association between the expression of CD45 with the risk of the disease in a cohort

of patients diagnosed with ALL of the HOMI Foundation Bogotá Colombia.

Design/Methods: 254 patients under 18 years of age diagnosed with B and T ALL diagnosed between 2014 and 2018, treated with ALLIC 2009 protocol. The risk group was assigned to each patient according to the following criteria of ALLIC 2009 protocol. For this study, patients with standard and intermediate risk were analyzed as patients of low risk since they have a very good survival rate. Analysis of the variables was performed by square CHI and association measures.

Results: We analyzed 254 patients, 137 children (54%), reviewed the CD45 report in the CF at diagnosis and divided it into 3 groups 75 (29%) patients had CD45 less than 10%, 79 (31%) 10 to 50% and 100 (40%) greater than 50%, the risk of relapse was classified as low in 154 (60%) and high in 100 (40%), performing the bivariate statistical analysis it was found that having CF with CD45 expression less than 10% has OR of 0.49 (IC95% 0.27-0.88) p 0.16 and CD45 expression greater than 50% has OR of 2.08 (95% CI 1.24-3.48) p 0.005.

Conclusions: CD45 expression higher than 50% in the diagnosis CF was associated with high risk ALL, which is associated with a worse prognosis, which shows the usefulness of this marker as disease prognosis.

PO059 SIOP19-1745 | Overweight and Obesity and its Relationship with Positive MRD on Day 14 in Children with Acute Lymphoblastic Leukemia in a Third Level Hospital in Mexico

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Background/Objectives: Studies have demonstrated that overweight and obesity at the time of diagnosis of kids with acute lymphoblastic leukemia (ALL) has been associated with an increased risk of relapse and poorer event-free survival (EFS), an strong oredictor for this outcome is the day 14 minimal residual disease (MRD) in the bone marrow. It is believed this relationship is due to altered pharmacokynetics of chemotherapy in obese people, owing to an increased expose of leukemia cells to adipokines, reduced the efficacy of chemotherapy agents (vincristine, dexamethasone, asparaginase, and daunorubicin) in in vitro coculture and increased risk for treatment-associated hepatic and pancreatic organ damage.

Objective: To determine if the association between overweight or obesity in children with acute lymphoblastic leukemia affects the the results of day 14 MRD.

Design/Methods: Restrospective analysis of children between the ages of 1 and 18 years diagnosed with ALL between January 2014 and January 2019 at hospital Civil de Guadalajara, Mexico. Height and weight at diagnosis were used to calculate each child's body mass index (BMI) and classified nutritional status as malnutrition (BMI <5th percentile), eutrophic (BMI 5-85 percentile), overweight (BMI 85-95 percentile) and obese (BMI >95 th percentile).

Results: A total of 250 patients were diagnosed with ALL, the final cohort consisted of 216. Overweight was found in 36 (14.4%) and overweight in 18 (7.2%). We did not found a relationship between overweight/obesity and positive MRD at day 14 (OR= 0.95, p=0.5, and OR= 0.74, p= 0.5), nor did the presence of obesity (OR= 0.7, p=0.018). Girls who were overweight at diagnosis presented a higher risk of positive MDR (OR=4.69, IC95% 1.77-12.4, p= 0.001), being eutrophic act as a protective factor (OR= 0.34, IC 95% 0.13-0.86, p= 0.01).

Conclusions: Assesment of nutritional status at diagnosis can ameliorate the treatment approach, especially in obese girls.

PO060 SIOP19-0163 | Down Syndrome and Acute Leukemia- Analysis of Cases in West of Paraná- Brazil

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Background/Objectives: A child with Down Syndrome (DS), characterized by trisomy of Chromosome 21, is at high risk of developing hematological disorders such as anemia, transient myeloproliferative disease, and acute leukemias (AL). The development of AL is about 10 to 20 times more common than in the general pediatric age group, and may account for about 1 to 3% of pediatric patients with LA. Objective: To evaluate the cases of acute leukemia associated with Down syndrome in Paraná- Brazil.

Design/Methods: Descriptive study, data regarding sex, age, clinical manifestations, morphological diagnosis and immunophenotyping of leukemia attended from January 2008 to January 2018 in Cancer Hospital of Cascavel, Paraná, Brazil

Results: 180 cases of AL were diagnosed and 10 (5,5%) had Down syndrome (SD), 3 (30%) in children under 4 years old; 7 (70%) above 4years old. 8 (80%) were male and 2 (20%) female. Signs and symptoms: microadenopathies, hepatosplenomegaly, fever, abdominal and lumbar pain, hyporexia and mucosal cutaneous pallor. The mean time between onset of signs and symptoms at diagnosis was 13 weeks. 6 (60%) were Acute Lymphoid Leukemia ALL-pre B and 4 (40%) Acute Myeloid Leukemia AML-M7. Of the patients with ALL, 5 (83%) patients achieved remission after D28 of induction chemotherapy with negative DRM. Of the

patients with AML-M7, 3 (75%) presented remission after induction. The 9 (90%) patients in the study remained alive and being followed up by the institution.

Conclusions: There was a higher incidence of acute leukemia in children with Down syndrome than in the literature. There was a predominance of male and histological subtype of ALL. We must emphasize the importance of a multiprofessional team trained and specialized in the care of patients with Down syndrome and AL, since the complications and difficulties of initial therapeutic management may have a direct influence on the survival of these children.

PO061 SIOP19-1100 | Involvement of MTHFR C677T Polymorphism in the Susceptibility to Acute Leukemia in Tunisia

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Background/Objectives: The 5, 10-methylenetetrahydrofolate reductase (MTHFR) acts as a critical juncture in the folate metabolism by directing folate metabolites toward the DNA methylation pathway and away from the DNA synthesis pathway. MTHFR C677T is the most important polymorphisms in the MTHFR gene contribute to the reduction of enzyme activity and may expose to leukemia.

To assess the risk of acute leukemia in Tunisian population according to the MTHFR C677T genotype.

Design/Methods: It was a case-controls study which includes thirty five patients with acute leukemia (AL) applied to the Departments of Hematology, and 35 age matched non-AL controls.

Genomic DNA was extracted from EDTA-anticoagulant blood samples according to the salting methods. After DNA extraction, the polymerase chain reaction using specific primers and Restriction Fragment Length Polymorphism using the HinfI.

Results: The *MTHFR* 677CT genotype increase the risk of acute leukemia (RR=2.3; p=0.001).

Conclusions: Despite the limit of this study (size and duration); our finding highlights the impact of the C677T variant of MTHFR on leukemogenesis. Awareness of folate metabolism is mandatory to prevent leukemia, especially in childhood.

PO062 SIOP19-0884 | Pulmonary Function Tests in Childhood Cancer Survivors

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Background/Objectives: There is a growing population of childhood cancer survivors with long term adverse effects. Pulmonary morbidity is one of the important long term complications of treatment. Present study was carried out to assess pulmonary functions in survivors of hematological malignancies.

Design/Methods: Treated cases of Hodgkin's lymphoma (HL) (24), acute lymphoblastic leukemia (ALL) (18) and controls (17) were included in the study. Inclusion criteria were: age 8 to 18 years, ≥ 1 year after completion of chemotherapy, no pre-existing pulmonary or cardiac disease. Exclusion criteria were: relapsed patients. Cases and controls were subjected to detailed clinical examination including anthropometry, examination of respiratory system and pulmonary function tests (PFT). Forced vital capacity (FVC), forced expiratory volume in one second (FEV1), ratio of FVC and FEV1 and peak expiratory flow (PEF) was measured for all patients.

Results: Mean present age was 12.40, 12.22 and 12.20 years respectively in the three groups. Mean age at diagnosis was 8.67, 7.47 years in HL and ALL groups respectively. Seven patients (16.7%), 4 in HL group and 3 in ALL group had abnormal PFT with restrictive type of abnormality. In HL group, mean age at diagnosis in patients with abnormal and normal PFT was 6.3 ± 1.53 versus 10.0 ± 2.45 ($p=0.02$). There was no significant difference in gender, present age, stage of disease, interval from diagnosis and cumulative dose of bleomycin in the two groups. On multivariate analysis age at diagnosis ≤ 6 years was found to be a significant risk factor (RR 9.00, 95% CI 1.52-58.73, $p=0.035$). In ALL group, patients with abnormal and normal PFT were comparable in relation to age at diagnosis, gender, interval from diagnosis, risk stratification and cumulative dose of Methotrexate.

Conclusions: Pulmonary function abnormality is a significant long term adverse effect of treatment in childhood cancer survivors. Regular pulmonary function tests should be carried out in follow up.

PO063 SIOP19-1041 | Cytogenetic and Immunophenotypic Profile of Acute Lymphoblastic Leukemia in Children

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Background/Objectives: The objective of our work is to determine the frequency of lymphoblastic leukemia B and T and cytogenetic abnormalities in ALL in a Moroccan population.

Design/Methods: This is a descriptive study that included patients aged less than 20 years with ALL who were followed in the Pediatric Hematology and Oncology department at the hospital on August 20 during the period from January 2006 to December 2016.

Results: During the study period, 395 cases of ALL were diagnosed, the median age was 11 years (0-20), with a sex ratio M / F of 1.8, the immunophenotypic study was performed in 353 cases. The phenotype was B in 221 (56%) and T in 174 (44%) cases. The karyotype was performed in 277 (70%) patients; it was normal in 97 (35%) cases and found cytogenetic abnormalities in 121 (43%) cases. This was abnormality in number in 67 (55%) cases and structure in 54 (45%) cases. A culture failure was noted in 59 (21%) cases. Hyperdiploidy was the most common cytogenetic abnormality 51 (18%) associated with the highest rate of complete remission and the lowest rate of relapse.

Conclusions: In our work the phenotype B was the most common. The results of this study contribute to a better knowledge of the biological profile of ALL in Morocco, which makes it possible to develop the currently used chemotherapy protocols.

PO064 SIOP19-1058 | Acute Lymphoblastic Leukemia in Children: NCI Standard Risk

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Background/Objectives: The objective of our work is to describe the epidemiological and evolutionary profile of patients followed for LAL, SR in hematology and Oncology Pediatric Department 20 August 20 hospital.

Design/Methods: This cohort study included patients followed for ALL in our unit during the period from May 2006 to December 2016. Children were classified according to the NCI criteria: Age greater than 1 year and less than 10 years, Leukocytosis less than 50000 / mm³, No initial neurological involvement, phenotype B, absence of t (9, 22), t (4,11) or hypoploidy lower than 44 chromosomes and the correct response to corticosteroids and chemotherapy. Children are treated according to the national protocol for the treatment of ALL (MARALL).

Results: 395 patients were diagnosed ALL, 36 (9%) were stratified ALL SR, the median age was 5 years (1-9 years), sex ratio M / F was 1, ALL was revealed by a tumor syndrome in 18 (50%) patients, the median white blood cells (G / L) was 16.7 (2.7-40.2), 28 patients (77%) were treated according to the MARALL SR protocol, the karyotype was performed in

18 (50%) of the patients, according to the karyotype, 8 (22%) had a hyperdiploidy. Seven patients relapsed (24%) after a median time of four years, the relapse was medullary in 13% of cases, neurological in 6.5% of cases. 7 (19%) of the patients were died, 5 (14%) had disease progression, and (5.5%) were toxic deaths, 1 had septic shock in induction, and the second had a methotrexate toxicity in interphase. The complete remission maintained was 58% after a median time of 6 years.

Conclusions: The rate or frequency of SAR ALL is low in this study, as our center recruits mostly adolescents over the age of 10.

PO065 SIOP19-1710 | Induction Chemotherapy in Children with Acute Lymphoblastic Leukemia (ALL) in Lima – Peru: Outcomes and Complications

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Background/Objectives: The primary objective was to describe clinical characteristics of patients during induction therapy for acute lymphoblastic leukemia. The secondary objectives were to describe causes and factors associated of death in this phase of treatment.

Design/Methods: This study was a retrospective review of children from 1 to 14 years of age who received induction chemotherapy between January 2009 and December 2011. According to our electronic register we have 496 cases of children with ALL, and collecting medical data of 84.3% of all cases. We evaluated the causes of morbidity during induction as: Infection, chemotherapy toxicity. Survival analysis was performed using Kaplan-Meier method.

Results: We included 419 patients, the median age was 6 years (range 1 to 14 years), M/F ratio 1.4/1, the north region of Peru have 48% de new cases of ALL, delay time on diagnostic and starting treatment with chemotherapy was 5 and 9 days, respectively. Median initial white blood cell count (x 10⁹/L) was 65.3 (0.36 to 970). ALL – T lineage represent 8.6% of patients. Of the 419 children, 122 (29.1%) experienced at least one microbiologically documented infection. Fungal infections were 14 patients. Twenty patients (4.7%) died during induction chemotherapy; among these patients, 35% (n = 7) were female, and 40% had high-risk clinical features at diagnosis. The main causes of death were infection and bleeding.

Conclusions: Early mortality was five times higher in the Instituto Nacional de Enfermedades Neoplásicas compared to developed countries, while the causes of death did not differ. We observed high-risk clinical features at diagnosis in an important group of patients.

PO066 SIOP19-0033 | Extramedullary non-CNS (Maxillary and Orbital Mass) Presenting as Proptosis in Acute Lymphoblastic Leukaemia with Concurrent Pituitary Adenoma

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Background/Objectives: Acute lymphoblastic leukaemia (ALL) is the most common childhood cancer with 26% of cancer diagnosed from birth to 14 years old². ALL presenting with ocular/orbital involvement is very rare³⁻⁷. The incidence of haematological malignancy in patient with acromegaly is rare¹.

Design/Methods: October 2018, 4 year old girl EP presented with proptosis of the right eye. She started wearing glasses for squint of the right eye since June 2018. No history of headaches or visual change. Clinically she had proptosis, squint and subtle features of acromegaly. CT head shows appearances of multi-focal Langerhans Cells Histiocytosis with involvement of right orbit, maxillary sinus and pituitary stalk including pancytopenia from blood work up. MRI head and orbit confirmed the CT findings. Bone marrow aspiration was consistent with pre-B ALL. Histology of maxillary sinus confirms leukaemic infiltration. Anterior and posterior pituitary function endocrine work up were normal She was discussed in neuro-oncology MDT as well as endocrinology MDT (multi-disciplinary team) meetings prior commencing on UKALL 2011.

Results: End of induction MRD low risk and MRI revealed 50% reduction in size of extra-medullary mass with complete resolution of proptosis and mass effect. She continues to be on Standard Risk Regimen A in her Interim Maintenance. She will have further MRI assessment at the end of Delayed Intensification phase.

Conclusions: In this patient the existence of two disease is a mere coincidence but emphasised the utility and importance of MDT approach in unusual cases.

PO067 SIOP19-1588 | Hyaluronan-Mediate Motility Receptor (HMMR) Expression Predicts Overall Survival in Childhood B-Cell Acute Lymphoblastic Leukemia

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Background/Objectives: B-cell acute lymphoblastic leukemia (B-ALL) is the most commonly diagnosed childhood malignancy worldwide; represent more than 50% of cases of cancer are diagnosed in México. Although the 5-year survival rate is > 80% and 30% of patients experience relapse with poor prognosis. Cancer-associated gene expression profiles have been identified in several malignancies and some transcripts have been used to predict disease prognosis. The HMMR protein exhibits a variable cellular distribution, has been associated to cancer stem cells and plays roles in proliferation and migration. HMMR has been associated to poor prognosis in breast, lung cancer, chronic myeloid leukemia, among other. **Objective.** Evaluate HMMR expression in patients with B-ALL and clinical correlation.

Design/Methods: We included 80 bone marrow of pediatric patients with B-ALL, HMMR expression was determined by RT-PCRq using $2^{-\Delta\Delta CT}$ method. Additionally, we evaluated HMMR protein by immunohistochemistry in 63 patients with B-ALL and 54 healthy donors of peripheral blood. The statistics analysis was archived using U-Mann Whitney, Kruskal-Wallis and the receiver operating characteristic (ROC) curve.

Results: We found that HMMR protein is expressed in healthy controls. Additionally, we observed a gradient of HMMR expression is correlated with poor prognosis by RT-PCRq and immunohistochemistry analysis.

Conclusions: The HMMR expression could be molecular marker of prognosis in B-ALL. Moreover, HMMR could be evaluate in peripheral blood.

PO068 SIOP19-1211 | Rate and Risk Factors for the Development of Tumor Lysis Syndrome in Childhood Acute Lymphoblastic Leukemia in a Tertiary Centre in Bangladesh

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Background/Objectives: Acute lymphoblastic leukemia (ALL) is the most common hematological malignancy in children. Though cure rate of ALL exceeds 90%, Tumor lysis syndrome (TLS) plays an important cause for early toxic death. TLS is characterized by metabolic abnormalities including hyperuricemia, hyperphosphataemia, hyperkalemia, hypocalcaemia and azotemia at diagnosis or within 7 days after initiation of induction chemotherapy. These metabolic complications may produce clinical toxicities including renal insufficiency, cardiac arrhythmias, seizures and even sudden death. So identifying patients at risk of developing TLS will help in managing this condition thereby improving outcome. A data

regarding the same from Bangladeshi population is lacking. The aim of the study was to detect the rate and identify the risk factors for the development of TLS in children with ALL.

Design/Methods: This prospective observational study, conducted at Department of Pediatric Hematology and Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka for a period of one year from September 2017 to August, 2018. Eighty children of 1-17.9 years with ALL, having no convulsive disorder, chronic kidney disease and congenital heart disease were included. Relevant clinical, laboratory and treatment related data were collected prospectively and analyzed.

Results: Out of eighty patients, ten patients (12.5%) developed TLS. Among the studied cases initial high white blood cell count was found to be an independent risk factor (P value <0.006) but other parameters like age, sex, LDH, mediastinal mass, immunophenotypic pattern and treatment regimen were not found as risk factors. Among the ten patients, six patients (60%) developed TLS at diagnosis. However, no patient was found to have clinical TLS.

Conclusions: In this study, rate of TLS was found to be 12.5% and mostly (60%) at diagnosis. Initial high WBC count was found to be a risk factor for the development of TLS without developing clinical TLS.

PO069 SIOP19-1697 | Profile of Infections During Treatment for Acute Lymphoblastic Leukemia in Children, Real Life Experience from a Single Center

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Background/Objectives: Introduction: Infection is the most common complication during treatment for acute lymphoblastic leucemia (ALL).

Objective: Description of infectious events during treatment since induction to maintenance in children with ALL.

Design/Methods: Retrospective analysis of children with ALL that have completed treatment according to EORTC 58081 CLG protocol since Sept 2012. Exclusion criteria: transplantation in first remission; *BCR-ABL* positive cases; and disease progression during protocol.

Results: We included 68 patients, median age at diagnosis was 6.5 years [range, 1-17], 52% were males and 69% had age between 1 and 11. There was a total of 209 infectious events. Fifty-seven percent of children under 11 years old presented >3 events in the course of treatment, as well as 33% of adolescents. Regarding risk groups, 92% of children in the VHR group presented >3 events. Very High Risk group has more delays in treatment as well which reflects its higher intensity.

This risk group also gives higher odds for infectious events in a multivariate analysis (p 0.041). During the intensive part of treatment, there were 78 events in induction (37%), 70 cases in reinduction (34%) and 29 during interval therapy (14%). Only 15% of infections occurred during maintenance ($n=32$). Patients with infectious events had neutropenia $<500/uL$ in 67% of cases ($n=140$), had central venous access in 81% of cases ($n=159$) and demanded hospitalisation in 64% of cases ($n=134$). There was also need for >1 antibiotic in 70 cases (33%). The most common cause of fever was febrile neutropenia (44%) followed by respiratory infection (22%). There was identification of pathogens in 26% of cases. There were 6 events that required intensive care and 2 children died due to infection.

Conclusions: Infection is very common in patients with ALL, mainly during intensive phase of therapy, but serious infections are fortunately rare.

PO070 SIOP19-0912 | RNASeq Analysis Of Leukemia Cells Treated with Methionine Γ -Lyase Reveals the Mechanisms of Dependence of Methionine

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Background/Objectives: Leukemia cells are found to be absolutely dependent of methionine. Although our previous studies have found that methionine γ -lyase (MGL) can reduce the concentration of methionine in leukemia cells and induce the inhibition of cell proliferation, the mechanism of this reaction remains unclear.

Design/Methods: Here we used RNA-sequencing (RNAseq) to compare the changes of gene expression in leukemia cell lines RS4;11 and NALM6 after MGL treatment of $0.5\mu M$ in 48h. Clustering and differential expression analyses were conducted to identify genes with altered expression.

Results: RNAseq data analysis revealed 520 differentially expressed (DE) genes between MGL-treated group and control group, including 393 genes with up-regulated expression and 127 genes with down-regulated expression. Pathway analysis identified 25 significantly perturbed pathways in MGL-treated cell lines with p53 signaling pathway, DNA replication, cysteine and methionine metabolism, phenylalanine and tyrosine acid metabolism, glutathione metabolism being the most significantly dysregulated. GSEA analysis showed the enrichment of transmembrane receptor, sulfotransferase, GTPase, kinase regulator and inhibitor, cytokine binding and tyrosine kinase-related pathways.

Conclusions: The treatment of MGL causes the deficiency of methionine in leukemia cells, which ultimately leads to cell death. This study provide initial evidence of effect through MGL treatment.

PO071 SIOP19-0940 | Early Life Factors Associated with the Development of Acute Leukemia in Children

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Background/Objectives: Acute leukemia is the most common type of cancer in children, however the aetiology is scarcely known. This review of the literature focuses on maternal factors during pregnancy, pregnancy conditions, obstetrical factors, mode of delivery and perinatal factors in early-life that may affect the development of leukemia in children.

Design/Methods: Original articles investigating the role of early life factors in the development of acute leukemia in children were searched through a systematic review of the literature using Pubmed and Web of Science. A total of 53 studies (5 prospective cohort studies, 48 case-control studies) were included in this review.

Results: Findings from different studies suggest a positive significant association with coffee intake and alcohol consumption for Acute Lymphoblastic Leukemia (ALL). A decreased risk of ALL in the child was observed for mothers with an increased intake of fruits and vegetables during pregnancy and for mothers who took folate, iron or vitamin supplementation. Maternal race other than white was positively associated with the risk of ALL and Acute Myeloid Leukemia (AML). Lower maternal education level was significantly positively associated with ALL risk in most of the studies. A maternal history of any form of fetal loss was significantly associated with the risk of ALL and AML in subsequent children. Among the perinatal factors, long-term breastfeeding had a significant protective effect on ALL, while increasing birth order was associated with a decreased risk of AML. Birth weight greater than 4000 grams was associated with a significantly increased risk of ALL.

Conclusions: Several early life factors may influence the development of leukemia in children, however more research is needed to develop cost-effective evidence-based prevention strategies to combat acute leukemia in children.

PO072 SIOP19-0235 | Socioeconomic Factors Affecting Survival in Pediatric Patients with Acute Lymphoblastic Leukaemia: Experience from a Tertiary Care Centre in North-East India

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Background/Objectives: Acute lymphoblastic leukaemia (ALL) is a highly curable childhood cancer with survival rate nearly 80% in developed countries, but is only around 45% in developing countries. The aim of this study is to analyse the association between demographic and socioeconomic factors with survival in pediatric ALL.

Design/Methods: This was a retrospective observational study. All confirmed cases of pediatric ALL (age <18 years) registered at Dr B Borooah Cancer Institute between 2010 to 2017 were analysed using data collected from hospital based cancer registry and case records.

Results: Seventy five confirmed cases of pediatric ALL were eligible for the study. Median age of presentation was 6 years with male: female ratio 1.9:1. Overall survival (OS) at 4-years was 43.8%, with median survival of 25 months. A trend for higher 4-year OS was seen in female children (54.1% *versus* 37.9%, $p=0.097$). Children from families residing in rural areas tend to have better survival as compared to those residing in urban areas (4-year OS 44% *versus* 39.5%, $p=0.308$). Patients with higher maternal education (4-year OS 83.3% for more than secondary school education *versus* 41.1% for less than secondary school education, $p=0.161$) and patients who did not abandon treatment (4-year OS of 49.1% *versus* 31.2% for those who abandon treatment, $p=0.497$) had better survival, but the differences were not significant. Four year OS in upper-middle, lower-middle, upper-lower and lower class were 85.7%, 74.9%, 38.1% and 7.7% respectively (upper-middle *versus* lower socioeconomic class, $p=0.0001$). Multivariate analyses confirmed a statistically significant relationship between socioeconomic status and survival, with upper-middle group had a 90% decreased risk of death compared to lower socioeconomic group.

Conclusions: There is an urgent need for proper definition of the problems of childhood ALL to introduce appropriate policies for improving survival in developing countries.

PO074 SIOP19-1358 | Changing Lipid Profile in Children with Acute Lymphoblastic Leukemia During Induction Chemotherapy

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Background/Objectives: The two main components of acute lymphoblastic leukaemia (ALL) treatment, steroids and L-asparaginase, cause lipid abnormalities and leading to various forms of morbidity and mortality. If lipid abnormalities are not predicted timely, this might lead to pancreatitis and thromboembolism in acute conditions. Survivors of ALL may also develop hypertension and ultimately increased risk of coronary heart disease in the long run. Hence, this study would give an insight to the spectrum of the problems in our population and might help in planning treatment.

Design/Methods: It was a prospective, observational study carried out from March to November 2013. Thirty-five newly diagnosed children with ALL, aged 3 to 15 years old, were included in the study after obtaining written consent from their parent/guardian. Two patients were lost to follow-up while three died before completing asparaginase (*E. coli*) therapy. Fasting (8-12 hours) serum total cholesterol, TG, HDL, LDL, fasting blood glucose, ALT and creatinine levels, as well as PT and APTT were done before treatment, after completion of asparaginase according to protocol. All the biochemical tests were done by photometric method, Final analysis was done with the data of 30 children.

Results: The mean ($\pm$ SD) age of the study cohort was 6.07 ± 2.95 years. Among them, 66.7% were ≤ 6 years old and 66.7% were male. Pre-treatment mean total cholesterol, TG, HDL and LDL levels were 158.40 ± 42.70 , 184.47 ± 65.32 , 19.93 ± 10.85 and 101.20 ± 35.01 mg/dl respectively. After completion of L-asparaginase, TG and LDL declined significantly, while HDL increased significantly. After completion of induction chemotherapy, the mean values of total cholesterol, HDL and LDL levels increased to 195.43 ± 36.58 ($p=0.003$), 50.20 ± 19.59 ($p=0.001$) and 116.70 ± 27.59 mg/dl ($p=0.186$) respectively, but TG decreased to 140.93 ± 62.80 mg/dl ($p=0.060$). Only one patient had acute pancreatitis

Conclusions: After induction chemotherapy, the mean values of total cholesterol, HDL, LDL levels increased and TG decreased

PO075 SIOP19-0407 | CYP1A1 and CXCL12 Gene Polymorphisms in Childhood Acute Lymphoblastic Leukemia

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Background/Objectives: Despite the high survival rates in childhood Acute lymphoblastic leukemia (ALL), the outcome remains poor in relapse. Recent genetic association studies of leukemogenesis, focused on single nucleotide polymorphisms in genes that regulate inflammation and tumor suppression (chemokines and P450 cytochrome). CXCL12, a chemokine expressed in various tumors, binds to chemokine receptor 4 (CXCR4) and is considered to play an important role in tumor growth and invasion. The polymorphism rs1801157 Single Nucleotide Polymorphism (SNP) of this gene has been investigated concerning its association in tumorigenesis. Moreover, *CYP1A1* gene belongs to family 1, subfamily 1A1 of cytochrome P450. CYP1A1 protein activates the conversion of environmental chemicals into carcinogens. The above gene contains 2 important SNPs, *CYP1A1**2A (rs4646903)

and *CYP1A1**2C (rs1048943), which are associated with increased leukemia risk.

Aims: The study of rs1801157 and rs1048943 SNPs of *CXCL12* and *CYP1A1**2C, respectively, in children with B lineage ALL.

Design/Methods: Genomic DNA was isolated from peripheral blood of 84 children with ALL and 125 healthy individuals, and analyzed for the existence of rs1801157 SNP of *CXCL12* and rs1048943 SNP of *CYP1A1**2C with PCR-RFLPs approach. The PCR products were digested with the restriction enzyme *MspI* for *CXCL12* and *BsrDI* for *CYP1A1* gene polymorphisms. Statistical analysis was performed using Fisher's exact test.

Results: In the *CXCL12* loci, the frequencies of AA, AG, and GG genotype were 10.84%, 60.24% and 28.91% in ALL, whereas 13.44%, 46.21% and 40.33% in control group. In the *CYP1A1* loci, the frequencies of AA, AG, and GG genotype were 60.71%, 39.28% and 0% in ALL, whereas 84%, 15.2% and 0.8% in control group. No statistical significant differences in *CXCL12* polymorphism were revealed between children with ALL and controls. Regarding *CYP1A1* loci, a positive association for the AG polymorphism and ALL was detected [OR: 3.576 (95% CI: 1.855, 6.893), p: 0.0001].

Conclusions: A higher frequency of *CYP1A1* heterozygote allele was observed among children with ALL, whereas no differences was observed regarding *CXCL12* polymorphism. Future studies in larger populations are planned in order to clarify the role of the above polymorphism in childhood ALL.

PO076 SIOP19-0461 | First Report of a Novel Translocation T (5;11) Discovered in Infant Acute Lymphoblastic Leukemia (ALL)

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Background/Objectives: Infant ALL comprises 2% - 4% of paediatric ALL with inferior outcomes. Most infants harbor the KMT2A (MLL) gene on chromosome 11q23 with approximately 94 different partner genes identified. We hereby report a novel translocation; t (5;11) in newly diagnosed infant ALL.

Design/Methods: a case report. Immunophenotyping and MRD done by flow cytometry. Cancer gene panel sequencing done by next generation sequencing.

Results: An eight-month-old boy presented with multiple scalp swellings and testicular enlargement. Bloodwork showed Hb 45g/L, WBC 33 x10⁹/L with 60% peripheral blasts and platelets 14x10⁹/L. He was diagnosed as Infant Pre-B ALL, with extramedullary CNS and testicular disease. G-banding and spectral karyotyping (SKY) analyses showed karyotype as 46, XY, t (5;11) (q35;q23) dic (13;13) (q14;q14) [19]/46, XY[7]. FISH analysis confirmed t (5;11) in 19 of 26 metaphases. The breakpoints were 5q35 and 11q23, wherein no KMT2A partner genes have been previously reported. The 5' portion of KMT2A gene was on the derivative (11) chromosome and 3' KMT2A was transferred to the derivative (5) chromosome. Tumor and germline sequencing by an 864 gene panel was performed through Cancer Sequencing (KiCS) program with informed consent which showed absence of pathogenic variants. RNA sequencing is underway to more precisely define the nature of this translocation. The patient received treatment as per our institutional Infant ALL protocol with good clinical response. Post -induction, he achieved morphological remission with positive MRD of 0.87%, which cleared post consolidation. He continued chemotherapy as per protocol and is currently on maintenance phase and doing well.

Conclusions: This novel translocation in newly diagnosed infant ALL has not been previously reported. MRD positivity post induction was seen; however long-term follow up is needed to determine its prognostic significance.

PO077 SIOP19-0370 | Pain Coping Strategies in 125 Pediatric Patients Diagnosed with Acute Leukemias in the First Month of Therapy: Effects of Treatments and Implications on Procedural Analgesia

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Background/Objectives: Pediatric patients with acute leukemias had to implement pain coping strategies such as distraction, problem-solving, seek for social support and cognitive self-instruction in the first month of therapy. The aims of the study were to assess whether these strategies and/or catastrophizing could be influenced by treatments' factors and whether they were significantly associated with the dosage of sedation-analgesic drugs during the first three bone marrow aspirates.

Design/Methods: One hundred twenty-five patients of both genders (average age = 6.79 years; DS = 3.40) with newly diagnosed ALL (90.4%) and AML (9.6%) and their parents were given, one month after diagnosis, a socio-demographic questionnaire and the Waldon-Varni Pediatric Pain Coping Inventory. Data on the severe treatment effects (days of hospitalization, number of mucositis, fever and nausea episodes) and on the dosage of drugs in sedation-analgesia were also collected

Results: The factors that significantly influenced the use of distraction ($R^2=0.25$), weighing the age factor ($F=3.47$; $df=3$; $p=0.02$), were the number of episodes of fever ($F=4.78$; $df=1$; $p=0.03$), nausea ($F=4.71$; $df=1$; $p=0.03$) and mucositis ($F=5.81$; $df=1$; $p=0.02$). Cognitive self-instructions ($R^2=0.22$) were influenced by the number of hospitalizations ($F=5.14$; $df=1$; $p=0.03$) and by episodes of mucositis ($F=8.48$; $df=3$; $p=0.004$), as well as by the age of the child ($F=3.76$; $df=3$; $p=0.01$). Finally, children who sought parental support more frequently ($F=9.7$; $df=2$; $p=0.0001$) and who tended not to succumb to catastrophic attitude ($F=13.33$; $df=2$; $p=0.001$) during Induction treatment phase seemed to require lower drug dosages, especially for propofol.

Conclusions: Clinical application of these results could be to encourage the use of coping strategies such as cognitive self-instructions and search for social support, avoiding catastrophizing.

PO078 SIOP19-0873 | Severe Psychiatric Disturbances During Therapy in Pediatric Acute Lymphoblastic Leukemia

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Background/Objectives: Corticosteroids are an essential component of the treatment for children with Acute Lymphoblastic Leukemia (ALL). Corticosteroids are administered repeatedly, first during the "induction" phase and then in multiple subsequent pulses. During corticosteroid use behavioral changes can be observed.

Design/Methods: In this retrospective study, we reviewed all the records of 145 patients with ALL, treated in our Unit during the last 6 years (2013-2018), and identified the patients who experienced significant behavioral and/or psychiatric changes. All patients were treated according to BFM-ALLIC protocol.

Results: Ten children (7 boys, 3 girls) with ALL, (mean age 12.3 years) were included in the analysis. Seven out

of 10 patients experienced this event during the phase of reinduction (Prot. II, phase 1) while being treated with dexamethasone 10mg/m². The adverse effects noticed included severe depression, withdrawal, visual hallucinations, mood swings and thought problems. One patient classified into IR group had experienced a psychotic crisis during reinduction (Prot. II, phase 2) with aggression and violence towards others and had to be treated immediately with intramuscularly haloperidol and diazepam. Patients who had symptoms of depression were treated with fluoxetine, risperidone and escitalopram at a range of 5 days to 6 months. Two out of 9 patients classified into the High Risk group presented with behavioral effects such as psychosis, disorientation, and behavioral outburst, one at the second HR2 block and one at the phase of reinduction, respectively. All patients are alive and in remission, 8 post chemotherapy and 2 on maintenance therapy. All patients experienced psychiatric effects after administration of dexamethasone and not during prednisolone therapy.

Conclusions: Transient serious behavior changes may occur during therapy for ALL. Most of the episodes occur while patients are treated with corticosteroids and usually a the reinduction phase, where dexamethasone is used. Timely treatment of these events and proper parental education are essential for optimal outcome.

PO079 SIOP19-0650 | Height Deficit in Brazilian Children and Adolescents with Acute Lymphoblastic Leukaemia at Diagnosis: Impact on Overall Survival

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Background/Objectives: Although having decreased in the last few decades, height deficit, also known as stunting, is still prevalent in around 6% of Brazilian children, varying greatly throughout the country. The objective of this study was to investigate the impact of height deficit at diagnosis of acute lymphoblastic leukaemia (ALL) on overall survival (OS) in a sample from a tertiary hospital in Sao Paulo, Brazil.

Design/Methods: This is a cross-sectional study that included children and adolescents diagnosed with ALL, treated with the Brazilian cooperative group treatment protocols GBTLI-99 (OS: 74.2%±1.7) or GBTLI-09 (OS: 79.3%±2.1). Patients with Down syndrome were excluded from the analysis. Height at diagnosis was collected from patient charts from 2007 to 2016. Stunting was defined according to the World Health Organization (height-for-age z-score smaller than -2). The

Kaplan-Meier method was used to estimate the overall survival function.

Results: There were 115 patients from 0 to 16 years old (median=5.8), 49.6% female. The prevalence of height deficit was 3.6%. While the estimated 5-year probability of overall survival for children with the height-for-age z-score above -2 was 70%, no stunted child has completed 5 years of overall survival ($p=0.000$). This result corroborates with previous Brazilian studies that found stunted children to be at greater risk of relapse and have a worst prognosis. This may be due to socioeconomic factors, which play a predominant role in the unfavorable prognosis of leukaemic children.

Conclusions: Patients with height deficit at diagnosis had reduced overall survival compared to non-stunted patients.

PO080 SIOP19-1262 | Childhood Cancer in 16–18 Year of Age Group in Yogyakarta, Indonesia

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Background/Objectives: The incidence of childhood cancer is increasing in our center and worldwide. We have already developed Yogyakarta Cancer Registry since 1995 located in Dr. Sardjito Hospital, Yogyakarta, Indonesia. We studied childhood cancer within age group of 15-18 years of old as early group of adolescence young adult oncology population (AYAO).

Design/Methods: Data of children with cancer in early AYAO population were analyzed retrospectively from our registry. We compared the number and proportion of cases within this age group to all children with cancer during the last 2 decades.

Results: The number of childhood cancer cases during 1998-2007 and 2008-2017 periods were increasing from 993 to 1788 (180%) with children within 15-18 years of age group was 11 (1.1%) and 112 (6.3%), respectively. The 4 common type of malignancy in this age group were acute lymphoblastic leukemia (63.6% vs. 37.5%), acute myeloblastic leukemia (28.2% vs. 31.3%), chronic myeloblastic leukemia (9.1% vs. 6.3%) and osteosarcoma (9.1% vs. 6.3%).

Conclusions: The proportion of children with cancer in early group of AYAO population are increasing significantly. We have to pay attention in this age group and may develop suitable protocol for their biological characteristics and better prognosis.

PO081 SIOP19-1411 | Cytogenetic Features of Acute Leukemia Patients Treated at a Single Center at East Mediterenian and South Region of Turkey

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Background/Objectives: To determine the cytogenetic features and survival of patients with acute leukemias at our institution

Design/Methods: Between February 2005 and 2019; 96 patients admitted with leukemias. Age, gender, type of leukemia and cytogenetic features as well as date of diagnosis, date of event, and date of last visit were recorded.

Results: 96 patients admitted with acute leukemia. Median age was 60 months. (2 - 204 months) Male to female ratio was 1,27. Sixty one patients had B cell ALL (63,5%); 9 had T cell ALL (9,4%); and 22 had AML (22,9%) and 3 had granucytic sarcoma (3,1%). Chromosome analysis could be studied in 64 patients (n=96) In 38, chromosome analysis was normal. There were 47XY in 5, 47XX in 3; 45XY in 3, hyperdiploidy in 8, kompleks karyotype in 5, monosomy 7 in 3 patients. Due to technical and social-economic issues, chromosome analysis and FISH studies could not be studied in 32 and 23 patients, respectively. FISH cytogenetic studies were normal in 51 cases. Cytogenetic anomalies of t (12;21) were positive in 10; hyperdiploidy in 3; Inv (16) in 2; FLT3-ITD in 2 patients. Respectively, t (8;14); t (1;19), t (9;22) Phi; t (8;16); t (8;21) were detected in each one patient. In B cell-leukemia patients most common anomaly was t (12;21)(%16). A total of 71 patients were remained at follow-up. For 3 years overall survival was 93,5% (n: 41) in B cell ALL;%100 (n=9) in T cell ALL; and 58,5% in AML (n=21).

Conclusions: Most common cytogenetic anomaly was t12;21 in B-ALL although its frequency is low compared with literature. On the other hand it is of note that there were many cases in whom cytogenetic studies could not be done due to technical, social-economic issues. Marrow sampling, study technique and economic issues should have contributed to this condition.

Haematology - Lymphomas

PO082 SIOP19-1522 | Epidemiologic, Clinical and Therapeutic Characteristics: About 46 Cases of Childhood Burkitt Lymphoma in Center of Tunisia

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Background/Objectives: Burkitt lymphoma (BL) is the most common Non-Hodgkin's Malignant Lymphomas and accounts for 30 to 60% of childhood cancers in Africa. Its management requires a multidisciplinary collaboration between oncologist, surgeon, anatomopathologist, radiologist and biologist. This study aimed to describe the epidemiological characteristics and survival of children presenting with BL in the center of Tunisia.

Design/Methods: This is a descriptive retrospective study of 46 children with BL treated from 1998 to 2018 treated at the department of medical oncology Farhat Hached hospital with LMB 89, LMB 96 and LMB 2001. Risk groups were stratified into classes A, B, or C according to the definition of the LMB group. Results were analyzed with Spss 19. Survival curves were analyzed with Kaplan Meier method.

Results: The median age was 6 years with male predominance sex ratio 3.18. The abdomen was the most common primary site followed in 82.6%. The most common symptom at diagnosis was abdominal pain (34.7%). According to the Murphy classification, stage I, stage II, stage III and stage IV were observed respectively in 4.3%, 26.1%, 50% and 19.5%. Patients were treated according to SIOP protocols LMB89 LMB96, LMB 2001 respectively in 74%, 4% and 22%. The therapeutic groups A, B and C were respectively 0%, 95, 7% and 4, 3%. Forty one patients achieved complete clinical remission and all of them were alive at the last contact. Death occurred in 5 of our patients: One patient died due to another cancer, two died from toxicity, and two died after relapse. Overall survival for 5 years was 89.1%, 77.8% for stage IV and 91.9% for others stages.

Conclusions: Our findings confirm the favorable prognosis of children with Burkitt lymphoma with multi agent chemotherapy. Childhood cancer, particularly Burkitt's lymphoma, should no longer be a fatality in Tunisia.

PO083 SIOP19-1027 | Management and Outcome of Children with Stage 4 Non-Hodgkin's Lymphoma: A Report from a Single Institution in Algeria

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Background/Objectives: Improvement of treatment results for NHL has been achieved during recent years, espe-

cially by intensifying therapy for advanced disease. However, resources remain still limited in Algeria.

Objectives: This study aimed to analyze treatment results of children with B stage 4 NHL regarding our working conditions.

Design/Methods: A retrospective study including all patients aged less 16 years old initially diagnosed with B stage 4 NHL was performed from January 2005 to December 2018. Patients were staged and treated according to adapted LMB protocol regimens. Survival rate was studied by Kaplan-Meier method.

Results: Of out 76 patients registered for a NHL, 18 (23.6%) were identified as having a stage 4; 10 boys and 8 girls with an age ranging from 12 to 138 months Primary tumor sites were bone marrow (n=8), abdomen (n=3), thorax (n=4), tonsil (n=3). Fifteen patients had bone marrow involvement and 3 had CNS involvement at diagnosis. Burkitt's lymphoma was the commonest histological type. High Dose methotrexate was administrated at 3 or 5 g/m²/day. No one underwent CNS radiotherapy. Sixteen patients (89%) achieved complete remission while two died rapidly of refractory disease. Secondly, three other patients died as a consequence of disease relapse. Overall survival is 72% with a follow up time ranging 12 to 120 months, without evidence of disease.

Conclusions: Algerian children seem to be more sensitive to High Dose Methotrexate administration. Our strategy based on reducing chemotherapy related mortality seems to be effective in management of stage 4 NHL.

PO084 SIOP19-1625 | Non Hodgkin Lymphomas in Tunisian Children: A Clinicopathological Study

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Background/Objectives: Non Hodgkin lymphomas (NHL) are the third most common group of malignant tumors in children representing about 10% of childhood cancer. Its pathological spectrum in this age category is smaller than in adults but with much faster growth and earlier spread in the bone marrow and central nervous system. Our aim was to describe the epidemiological characteristics and to study the pathological aspects of these lymphomas.

Design/Methods: Retrospective study of 99 cases of NHL collected at our department over a period of 9 years. Our study population was patients under 16 years old.

Results: The median age at diagnosis was 8 years with male predominance (sex ratio=2). The diagnosis was made mainly on lymph node biopsies (57,6%). Extra-nodal speci-

mens accounted for 42, 4% of cases with predominantly digestive biopsies (15%) and bone marrow biopsies (13%). The macroscopic appearance was variable depending on the location. Histological and immunohistochemical study revealed lymphoblastic lymphoma in 42,5% of cases, Burkitt lymphoma in 34,5% of cases, anaplastic lymphoma in 13% of cases, large B cell lymphoma in 8% of cases and T cell lymphoma in 2% of cases.

Conclusions: NHL in children represents a heterogeneous group of high-grade malignancies requiring urgent and adequate diagnosis for multidisciplinary treatment. Morphology and immunohistochemistry remain the corner stone to establish the diagnosis. Molecular biology may be a powerful tool in challenging circumstances.

PO085 SIOP19-0166 | Lymphomas non Hodgkin - Retrospective Study of 17 Years in Hospital of Reference in Pediatric Oncology in the South of Brazil

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Background/Objectives: Non-Hodgkin's lymphoma (NHL) represents 5% of childhood cancer, which is considered the most common in children. They are classified into histological subtypes and the clinical manifestations are variable according to the type of lymphoma and the site affected.

Objective: To evaluate and describe the clinical and laboratory characteristics of lymphomas in children under 19 years of age at a referral hospital in pediatric oncology in south of Brazil.

Design/Methods: Descriptive study, data regarding sex, age, clinical manifestations, histopathological diagnosis and evolution between January 2001 and May 2018 in Cancer Hospital of Cascavel, Paraná, Brazil.

Results: 32 cases were recorded. 21 (66%) males and 11 (34%) females. The mean age of diagnosis was 11.38 years. 8 patients (25%) with less than 5 years, 8 (25%) between 5 and 10 years, 7 (22%) between 10 and 14 years, and 9 (28%) between 14 and 19 years. The most frequent initial clinical manifestations were: lymphadenopathy, abdominal pain and weight loss. The mean time between the onset of symptoms and diagnosis was 62.5 days, with 19 (59%) patients diagnosed in the first 30 days and 13 (41%) under 30 days. Twelve cases (37.5%) were Burkitt's Lymphoma, 12 (37.5%) Lymphoblastic, 4 (12.5%) Diffuse Large B Cells, 1 (3.125%) Diffuse High Diffuse, 1 (3.125%) Diffuse Anaplastic Large Cells, 1 (3.125%) Diffuse Convolute Cells, and 1 (3.125%) Others. The Burkitt and Lymphoblastic subtypes predominated.

Of the 32 patients, 16 (50%) remained alive and followed up by the institution.

Conclusions: The most common subtypes were Burkitt and Lymphoblastic lymphomas, compatible with national and international data. Although childhood and juvenile cancer is difficult to recognize in early stages, NHL manifestations serve as a warning to health professionals in order to identify malignancy and refer early to referral centers, thus improving the life expectancy of these patients.

PO086 SIOP19-0679 | Castleman Disease Prevalence, Practice Essentials and Outcome Among Children Cancer Hospital of Egypt (CCHE) Patients

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Background/Objectives: Castleman disease (CD) describes a group of heterogeneous hematologic disorders with characteristic histopathological features. CD can present with unicentric or multicentric (MCD) regions of lymph node enlargement. Some cases of MCD are caused by human herpesvirus-8 (HHV-8), whereas others are HHV-8-negative/idiopathic (iMCD).

Design/Methods: this retrospective study included all patients diagnosed CD. either Unicentric or multicentric From 7/2007 till 12/2017 at CCHE, Any sex, Age below 18 years at time of diagnosis. Pathology confirmed Castleman from any body site, Age, Sex, Clinical presentation, CBC, Kidney, liver functions, CRP, IL6, HIV PCR, HHV8, Histopathology CT Whole body, Echo, Line of treatment received.

Results: A total of 12 patients were enrolled. age ranging from 4 to 17 years. 66.6% were males & 33.3% were females. 9 of them were unicentric & the remaining 3 were multicentric. Unicentric patients were presented with Lymphadenopathy either Cervical, supraclavicular, Axillary LN, 2 of them were having retroperitoneal and paravertebral soft tissue lesion which was excised completely, the 3 multicentric patients were presented with immune Cytopenia (anemia and thrombocytopenia) with small bowel thickening forming mass& Splenomegaly in first patient&Respiratory distress with extensive pulmonary involvement in second one& last

patient presented with pleural effusion&Ascites. Whole body CT scan done for all patients, BMA done only for patients with Cytopenia, viral screening was done (HIV Ab) for all patients&it was negative, HHV8 was not available so, not performed, IL6 done only for 2 patients out of the 3 multicentric &was very high in one of them & normal in the other patient, histopathology for all patient confirming castlman either hyaline vascular or plasma cell variant. unicentric patients underwent surgical excision&no further treatment was received&they do well. Multicentric patients received systemic treatment including Steroids, single agent Rituximab, RCHOP (rituximab-cyclophosphamidexorubicin-vincristine-prednisone)&AntiLL6 and they improved much apart from the patient with Pulmonary involvement still with uncontrolled systemic manifestation & RD.

Conclusions: unicentric castleman is localized disease cured with surgical excision only while Treatment of iMCD is challenging, and outcome is poor because no uniform treatment guidelines exist.

PO087 SIOP19-1595 | Diagnostic and Therapeutic Difficulties Concerned with the Treatment of Children with Blastic Plasmacytoid Dendritic Cell Neoplasm

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Background/Objectives: Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is an extremely rare subtype of hematopoietic malignancy in children, which is clinically less aggressive than the majority of acute leukemias.

Diagnosis, clinical course, and optimal treatment are not homogeneous. Worldwide standard of treatment is not yet established.

Some patients are treated with regimens dedicated to acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), or non-Hodgkin lymphoma (NHL), whereas some undergo stem cell transplantation (SCT).

Design/Methods: There were seven patients (3 girls and 4 boys) with BPDCN registered by Polish Pediatric Leukemia/Lymphoma Study Group during the period of 33

years (1986-2019). Their age at the moment of the diagnosis ranged from 8 months to 15 years.

Clinically in general they presented with lesions in the skin, and the involvement of bone marrow, lymph nodes, liver, spleen, bones, testes, and central nervous system. It is difficult to make diagnosis, because there is no single test to prove it. Microscopy examination with typical immunohistochemistry or flow cytometry triad of CD4, CD56, CD123 is observed in most of the cases.

Results: Six of the patients underwent treatment according to protocols dedicated to lymphoblastic proliferative diseases; while two of them subsequently underwent SCT. All of them are alive in complete remission (4-172 months after the diagnosis, median 80 months). The seventh patient underwent treatment for acute myeloid leukemia, and she died in second relapse after SCT (26 months after the diagnosis).

Conclusions: Clinical course of BPDCN in children is heterogeneous, which may make the diagnosis difficult. Our observations demonstrate that in patients diagnosed with BPDCN, the regimens dedicated to lymphoblastic neoplasms are more effective and create opportunity for long lasting remission. In contrast to the case of adults, where SCT improves outcome, SCT in children is not essential in first remission.

PO088 SIOP19-0850 | PET-CT +2 Metabolic Response Guided Treatment in Pediatric Hodgkin Lymphoma Patients

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Background/Objectives: The prognostic value of post 2 chemotherapy blocks PET-CT scan metabolic response has established validity for adult Hodgkin Lymphoma (HL) patients. The Pediatric Protocol EuroNet-PHL STUDY evaluates patients with CT/MRI imaging and PET-CT scan following 2 OEPA chemotherapy blocks in an effort to avoid irradiation. We aim to present preliminary imaging and outcome results of a Greek pediatric patient cohort.

Design/Methods: From 2/2009-6/2018 29 patients with newly-diagnosed HL were treated according to the EuroNet-PHL STUDY. PET-CT scan was performed at diagnosis, following 2 OEPA cycles (PET+2) and at the end of treatment. Three Therapy-Groups (TG) were defined. Treatment plan: Initially 2 OEPA for all patients; 2 or 4 COPP/COPDAC blocks followed for TG2 and TG3 patients, respectively. Irradiation of the initially involved sites 20-30Gy was prescribed

only for patients with inadequate response following 2 OEPA blocks.

Results: Total 29 newly diagnosed patients diagnosed were treated according to groups TG1 (3), TG2 (4) and TG3 (22). Good PET+2 metabolic response was documented in 3/3, 4/4 and 16/22 patients, respectively. Irradiation was prescribed to 13/29 patients. Six TG3 patients had disease progression (3) or no complete response (3) following 6 chemotherapy blocks. All 6 received second line treatment, (IEPx2-ABVDx2) and with responsive disease 5/6 underwent autologous stem-cell transplantation (ASCT) with BEAM cytoreduction, without irradiation in 6/6, due to good response.

Conclusions: PET+2 inadequate metabolic response was observed in patients who had relapsed/resistant disease. Patients with adequate mass regression and metabolic response can be managed without irradiation, while they achieve good outcome. Patients with resistant/relapsed disease can be rescued with second line chemotherapy and ASCT $\pm$ irradiation. The effectiveness of intensification of chemotherapy following the initial 2 OEPA cycles, in PET+2 scan positive patients, while diminishing the number of patients receiving irradiation, is under investigation.

PO089 SIOP19-1078 | Large Cell Anaplastic Lymphoma: Results in a Single Institution in Argentina

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Background/Objectives: Large cell anaplastic Lymphomas (LCAL) represent 15% of pediatric lymphomas. Event-free-survival-probability (EFSp) has increased to 75%; however the most adequate regimen is still not clear.

Objectives: 1-To evaluate demographic and biological features of LCAL. 2-To analyze different chemotherapy regimens 3-To compare outcome of patients treated with chemotherapy strategy for B-Non-Hodgkin lymphoma (B-NHL) versus adapted schedule for LCAL.

Design/Methods: We retrospectively analyzed the records of 41 patients from April-1991 to March-2019. The evaluated variables were: age, sex, markers, response to treatment and EFSp. From these 41 patients, 3 were excluded from the analyzes of survival due to protocol violation, death before treatment, or HIV diagnosis. Of the 38 remaining patients, 19 were treated with B-NHL strategy and 19 with an adapted schema, with the main difference being the dose and duration of Methotrexate infusion (3 g/m² in 4 hs).

Results: The median age at diagnosis was 10.5 (2-19) years and M/F distribution 1.75:1. Extranodal compromise was observed in 84%. The distribution of stages showed: 6 stage II (15%), 28 stage III (68%) and 7 cases stage IV (17%). CD30 was positive in 100% of analyzed cases. ALK mutations were not available in 35% of biopsies. From 38 eligible patients for treatment evaluation, 31 achieved complete remission (CR), 5 patients died during induction and 2 presented null response. From the 31 patients who achieved CR, 3 relapsed and 1 died in CR. EFSp (SE) was 66 (7)% for the total population, 68 (10)% for B-NHL strategy and 72 (10)% for adapted therapy (p-value: 0.98).

Conclusions: 1-EFS of our patients was slightly lower than described, probably related to a high rate of patients with disseminated disease. 2-No significant differences were observed with the different treatment strategies. 3-A more accurate diagnostic approach is needed in our setting.

PO090 SIOP19-1223 | Outcome of Pediatric Lymphomas in Estonia from 2009-2018

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Background/Objectives: The objective of this study was to describe the incidence and treatment outcomes of Estonian children treated with lymphoma in the last 10 years.

Design/Methods: This study was a retrospective study based on electronic medical records of Estonian children aged 0-18 diagnosed in Tallinn Children's Hospital and Tartu University Hospital.

Results: During 10 years 52 children were diagnosed with lymphoma.

Non-Hodgkin lymphoma (NHL) was diagnosed in 27 patients (52%). The median age 11.3 years. The most common subtype was Burkitt lymphoma (38.1% of NHL). The disease was diagnosed in stage I or II in 40.7% and stage III or IV in 59.3% of cases.

There were 25 patients diagnosed with Hodgkin lymphoma (HL) (48%). The median age of children diagnosed with HL was 15.4 years. The most common subtype of HL was nodular sclerosis (72%). The disease was diagnosed in stage I or II in 52% and stage III or IV in 48% of cases.

All children received chemotherapy according to current protocols. Radiation treatment was given to 3 patients with HL with bulky disease and to 1 patient with NHL with a testicular mass. Two patients with NHL needed hematopoietic stem cell transplantations due to relapsed disease and one patient with HL due to refractory disease.

The 5-year overall survival (OS) of patients with HL was 100%, the 5-year event free survival (EFS) was 90%. The OS of patients with NHL was 88.9% and EFS 77.8%. Two patients died from disease progression.

Conclusions: Lymphoma was diagnosed in an advanced stage in about 50% of our patients. Still, the treatment outcomes of Estonian children are comparable to those reported from other European countries.

PO091 SIOP19-0055 | Bowel Obstruction and Perforation in Pediatric Intestinal Mature B Cell Lymphoma: Incidence, Clinical Features, and Outcome in CCHE

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Background/Objectives: Bowel perforation or obstruction is life-threatening complications of intestinal lymphoma. Our aim was to define incidence, clinical features, and outcome associated with bowel perforation or obstruction in pediatric intestinal lymphoma.

Design/Methods: A retrospective, non-randomized study was included all newly diagnosed pediatric intestinal mature B cell lymphoma patients who were operated out of intestinal obstruction or perforation from July 2007 till end of July 2017 in CCHE.

Results: Intestinal obstruction or perforation developed in 34 patients (7.5%) out of 456 patients with intestinal mature B cell lymphoma. Median age is 4.85 years. All of them were treated accordingly to NHL LMB 96 protocol [1]. The 5 years OS among patients were operated out of intestinal obstruction, and who were operated out of perforation were 87.7%, 62.9% respectively with no significant statistical differences. Five years OS among patients with viable malignant cell versus no malignant cell was 65.2%, 90.9% respectively with significant P value. The five years OS for patients didn't have surgery, and who had surgery was 87.9%, 78.6%, respectively, with no significant statistical differences. Multivariate analysis on EFS and OS was done for the overall group and the subgroup. Including age, sex, pathology, clinical stage, elevated LDH, presence of ATLS, showed statically no significance.

Conclusions: Intestinal complication in the form of obstruction with or without intussusception, or obstruction perfora-

tion followed by exploration is not adverse prognostic factor for survival in pediatric patients with intestinal mature B cell lymphoma. Operation with viable malignant cell was associated with significant lower outcome.

PO092 SIOP19-0497 | Chemo-Sensitivity to Salvage Chemotherapy Determines Outcome Survival in First Relapse of Paediatric Hodgkin Lymphoma

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Background/Objectives: Hodgkin lymphoma (HL) is the sixth most common cancer of pediatric age group with survival outcome between 80-90%. However, 10% to 15% with localized disease and 25% with advanced classical HL relapse after first line treatment.

Patients with relapsed HL have a substantial chance of cure unlike other malignancies. All salvage regimes use different drug combination with or without radiation.

High Dose Chemotherapy (HDCT) with Autologous Stem Cell Transplant (ASCT) has been shown to improve outcome in relapsed HL.

Objectives: To assess the outcome of children with first relapse of HL in a large cancer care hospital. To evaluate the prognostic significance of variables including time to relapse, stage at initial diagnosis and at relapse, chemo responsiveness and chemo regimen.

Design/Methods: All children with relapse HL, who received primary treatment at our center between Jan 2001 to Dec 2010 were included in this study. Data were analyzed retrospectively. Relapse was confirmed histologically. Majority of our pts were given salvage chemotherapy with Etoposide, Prednisolone, Ifosfamide and Cisplatin (EPIC) chemotherapy with or without Involved field radiotherapy (IFRT).

Kaplan –Meier's method were used to calculate the event free and overall survival rates.

Results: In our report OS and EFS at 10 years were 54% and 35% respectively. On univariate analysis treatment responsiveness at initial two cycles and at the end of treatment assessment, initial stage at disease, stage at relapse, treatment protocol, were statistically significant factors. Multivariate cox regression analysis revealed stage at relapse (p=0.004), chemotherapy regimen (p=0.25) and end of treatment disease evaluation (p=0.005) as most significant variables.

Conclusions: Our results are encouraging to document negative impact of chemo resistance, stage 4 at initial diagnosis and at relapse on outcome following relapse. EPIC is an

effective salvage regimen particularly for late relapse >24 months and showed superior outcome in regards to median long term survival.

PO093 SIOP19-0269 | Modified Escalated BEACOPP Regimen, an Acceptable Alternative to ABVD for the Management of Hodgkin's Disease (HD) in Developing Countries!

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Background/Objectives: In early 2000's, the BEACOPP regimen, both basic and escalated, has emerged as an acceptable alternative to ABVD for the management of Hodgkin's Disease (HD) both in terms of efficacy and cost. In the present study, the cost-effectiveness of modified escalated BEACOPP regimen was studied in Indian context. The modified escalated BEACOPP regimen differed from the standard one in having higher Adriamycin at a dose of 30 mg, administration of Bleomycin on day 8 in addition to day 1, and no support of growth factors.

Design/Methods: From April 2000 to January 2003, 20 children with biopsy proven HD with clinical stage I to IV and adverse clinical features like B symptoms, extranodal or bulky mediastinal disease were selected for treatment with modified BEACOPP regimen. Ten patients with bulky disease received IFRT with a dose of 30 Gy.

Results: median follow up was 97 (range, 71-147) months. median age was 11 (range, 4-15) years, 14 were male and 6 female. Three patients had stage I, 6 patients stage II and 11 stage III HD, with 0, 2 and 5 having B symptoms respectively. Most common subtype was nodular sclerosis seen in 10 (of which 6 had mediastinal disease) followed by mixed cellular in 6, lymphocyte predominant in 3 and lymphocyte depleted in 1 patient. All patients were compliant to prescribed treatment. Grade III anemia, neutropenia, and thrombocytopenia were seen in 2, 2, and 1 patient respectively. One patient developed locoregional recurrence while another one developed distant relapse, the remission rate was 90%. Overall survival was 95% as one patient died at 103 months due to secondary AML.

Conclusions: The modified BEACOPP regimen has shown excellent results in terms of prolonged clinical remission with acceptable morbidity. The lesser treatment cost and duration are desirable for both patients as well as caregivers in Indian scenario.

PO094 SIOP19-0835 | Safety and Efficacy of Intrathecal Rituximab in Children with Non-Hodgkin Lymphoma: A Retrospective Study

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Background/Objectives: This study demonstrated that the efficacy and safety of intrathecal (IT) rituximab in the treatment of NHL in children.

Design/Methods: We reported 12 children were diagnosed with histologically proven CD20+ NHL from 2015 to 2019 who received IT rituximab in Pediatric Hematology/Oncology of Sun Yat-Sen Memorial Hospital were retrospectively analyzed.

Results: In total, 12 patients were enrolled; they were predominantly 10 male and 2 female. The median age was 8.25 years. All the 12 patients were initially located outside the lymph nodes. Burkitt lymphoma (BL) constituted 75% of 12 patients, diffuse large B-cell lymphoma (DLBCL) constituted 16%, and lymphoblastic lymphoma (LBL) constituted 8%. According to the IPNHLSS, there were 1 case (8%) in stage 3 and 11 cases (92%) in stage 4, and CD20 was positive with immunohistochemistry all patients. There were 5 cases of CNS invasion, including 3 cases of multiple vertebral body (25%) and 2 cases of brain invasion (16%). ALL patients received the modified NHL-BFM95, while IT rituximab was arranged the day before the chemotherapy, which was simultaneously used with the intravenous infusion of rituximab. The median time of doses received by each patient was 5 times, every three weeks, with the IT dose of 10mg, 15mg, and 20mg in increments. We didn't use both methotrexate and/or cytarabine in combination with rituximab, and no adverse reactions occurred in all 12 cases. Among the 5 patients with CNS invasion, 4 (80%) cases were in complete remission, and only 1 (20%) had disease progression. Two cases of infantile cells were found in cerebrospinal fluid, and all of them were turned negative after the first rituximab IT.

Conclusions: We concluded that IT rituximab was safe in the treatment of children with NHL, it had a good effect on children with CNS invasion, especially for children with infantile cells of cerebrospinal fluid turned negative after the first IT rituximab.

Haematology - Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes

PO095 SIOP19-0583 | Pediatric Acute Promyelocytic Leukemia Presenting as Tongue Chloroma: A Case Report Olfat Ahmed, Ala'A Remawi, Amal Abu Ghosh

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Background/Objectives: Chloroma also known as Myeloid Sarcoma (MS), Granulocytic Sarcoma or Myeloblastoma is a rare extramedullary tumor consisting of immature myeloid cells occurring in 1-2% of patients with acute myelogenous leukemia (AML). In a significant proportion of cases, it displays myelomonocytic or pure monoblastic morphologic features which correlate with the French-American-British (FAB) classification of M4 and M5 respectively. Cytogenetically, MS has been found to occur in association with a variety of chromosomal abnormalities, including MLL rearrangement, inv (16) and t (8;21). Usual sites include the skin, soft tissue and lymph nodes. Tongue chloroma is extremely rare especially as an initial presentation of Acute Promyelocytic Leukemia (APL) in children. Here we report the first case of pediatric APL presenting with tongue chloroma at our institution.

Design/Methods: Three-and-a-half-year-old girl was referred to our cancer center with one month history of recurrent tonsillitis, fever and fatigue followed by one-week history of growing painful tongue masses and abnormal CBC.

Results: Blood film showed myeloblasts with Auer rods. Bone marrow examination and flowcytometry were consistent with AML M3 and FISH study was positive for PML-RARA in 91% of interphases. Cytogenetic testing was positive for t (15;17) and the diagnosis of Acute Promyelocytic Leukemia was made. Induction chemotherapy was started with Tretinoin (ATRA), Idarubicin and dexamethasone. Tongue lesions responded rapidly and completely dissolved within one week therapy.

Conclusions: Although it is unlikely for APL to present with chloromas and exceedingly rare to present with tongue chloromas, still it may occur. Biopsy of the tongue lesions was not done in our patient as the bone marrow was positive for APL and the lesions responded well to standard Induction therapy. Increased awareness of the oral cavity as a site of chloromas will result in earlier referrals to specialized Pediatric Oncology Centers.

PO096 SIOP19-1390 | Nutrition Status of Children with Acute Myeloid Leukemia Admitted to 57357 Children Cancer Hospital Egypt

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Background/Objectives: Nutritional status plays an important role on the prognosis and quality of life in patients with cancer. Malnutrition and weight loss are often contributors to

the morbidity and mortality of patients with Acute Myeloid Leukemia (AML). In pediatric oncology, rapid rate of growth and high nutritional requirements represent challenges during the course of treatment. The aim of the study was to determine the nutritional status at time of diagnosis and throughout the nutrition journey in pediatric and adolescent children with AML to identify those patients who may require specialist nutritional intervention and more appropriate referral to such services.

Design/Methods: It was observational descriptive, retrospective study. The study population included pediatric and adolescent patients who were newly diagnosed with AML and admitted to the Children's Cancer Hospital- Egypt (CCHE-57357) in the year 2012 and followed to the end of treatment. The patients aged ≤ 18 years were divided into 5 subgroups according to their age categories. Available patients weight (in kg) and height (in cm) measures were recorded from diagnosis until the end of therapy, they were taken at (diagnosis, end of first induction, end of second induction, end of first intensification, end of second intensification, end of third intensification). Age and sex specific weight, height and BMI standard deviation scores were calculated based on the reference standard of WHO growth charts.

Results: Weight loss is more prominent at the beginning of therapy, after the second induction fifty five point six percent (55.6%) of children had more than ten percent (10%) weight loss from the initial weight. Height velocity was decreased at the end of therapy in all age groups especially in children less than two years. BMI Z score was decreased in all age groups

Conclusions: The intensive course of chemotherapy affects the weight and height velocity of in children treated with AML.

PO097 SIOP19-0775 | Drastic Immunophenotype Change and Acquisition of a Rare MLL Rearrangement T (10;11) (KMT2A-MLLT10) Observed at Late Relapse, in Parvovirus B19 Positive Boy with Acute Megakaryoblastic Leukemia

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Background/Objectives: Acute parvovirus B19 infection has long been linked to acute myeloid leukemia (AML). Certain leukemia sub-clones at initial diagnosis may become predominant at relapse. The gain of a distinct population of leukemia cells at relapse is presumed a rare type of immunophenotype change. Such an alteration accompanied by the acquisition of a rare MLL rearrangement is quite scarce in the literature.

Design/Methods: A case report

Results: The nineteen months old boy admitted to our department with a three weeks history of fever, pallor, rhinitis, sore throat, cough and mild hepatosplenomegaly. CBC demonstrated moderate anemia, thrombocytopenia, slight lymphocytosis, and elevated ESR. Lab test showed high LDH and CRP levels, parvovirus B19 IgM proved positive. Initial bone marrow (BM) aspirate was hypercellular, without abnormalities, flow cytometry (FC) found increased counts (<20%) of myeloid and lymphoid blasts. The patient was given a symptomatic treatment of IVIG, blood component transfusions and antibiotics. Repeated CBC revealed 7% of blast cells, BM morphology showed 24% of myeloid blasts, and FC identified 32% of CD34+ blasts expressing CD45, CD41a, CD61 receptors, positive cytoplasmic staining for CD41a (72%) proved the Acute Megakaryoblastic Leukemia (AMKL) phenotype with negative MPO and positive PAS cytochemistry stains. No chromosomal or karyotype abnormalities were reported. The patient was diagnosed with AMKL and started treatment according to AML-BFM-2004. After 4 years from initial diagnosis, the patient was readmitted with BM relapse (40%), although FC showed dramatic immunophenotype change towards non-AMKL AML phenotype. Molecular genetics identified a rare MLL rearrangement t (10;11)(KMT2A-MLLT10).

Conclusions: Considerable immunophenotype change accompanied by the acquisition of a rare MLL rearrangement KMT2A-MLLT10 at relapse may suggest selection and emergence of chemo-resistant sub-clones that are undetectable by routine methods at initial diagnosis. Exceptional plasticity of MLL-rearranged leukemic blasts in response to their microenvironment perturbations may favor the selection and survival of these cells in the context of parvovirus B19 infection.

PO098 SIOP19-1324 | Leukemia in Down Syndrome

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Background/Objectives: Children with Down syndrome (DS) manifest multiple haematological disorders: transient myeloproliferative disorder (TMD)/transient abnormal myelopoiesis (TAM) at birth, acute myeloid leukemia (ML-DS), and acute lymphoblastic leukemia (ALL).

Objectives: Determinate the distribution of hematologic disorders in DS and to study the clinical-biological, treatment and evolution features.

Design/Methods: Retrospective study from 2000 to 2010 and prospective study from 2011 to 2019 concerning patients hospitalized in the pediatric department

Results: We have collected 25 cases with a mean age of 3 years, The sex ratio is 1,5. These patients are distributed as follows: 8 ALL, 11 AML, 5MDS, and one transient leukemia. Consanguinity is present in 30% of cases. The reason for consultation was hemorrhagic syndrome (45,5% of cases) and / or mucocutaneous pallor (45.5% of cases). The diagnosis was made by bone marrow study and confirmed by Immunophenotyping. All cases of leukemia received chemotherapy;. 11 patients who had leukemia died, 2 still in treatment, 4 are on remission, 4 MDS received chemotherapy, all them have evolved well

Hematological disorders are common in DS, and probably underestimated in the absence of screening. Near an SD on 100-300 develops acute leukemia, with a slight male predominance. What joins our results. ALL is the usual type, but a higher proportion of AML has also been reported There are no clinical or biological features in DS-LA, but they are more likely to have thrombocytopenia; and less likely to have a mediastinal mass, Adenopathy or Splenomegaly and this is the case of our patients.

Conclusions: Today we have a better knowledge of the haematological disorders in the DS than we had in the past decades, but children continue to die of leukemia and its complications mainly infections. Better stratification of risk and targeted therapies may reduce the toxicity of treatment

PO099 SIOP19-1632 | Congenital Juvenile Myelomonocytic Leukemia (JMML) Presenting with SH2B3 Germline Mutation and Good Response to Mercaptopurine: Case Report

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Background/Objectives: JMML is a rare leukemia associated with poor prognosis, treatment usually requires hematopoietic stem cell transplantation for cure. JMML is characterized by mutations on the Ras pathway gene: NF1, NRAS, KRAS, PTPN11, and CBL. We present a case with congenital JMML with a new mutation and good response to chemotherapy.

Design/Methods: Case report presenting in Stollery Children's Hospital.

Results: We describe a newborn, 33 weeks gestation age, born from C section, Cree ancestry and consanguinity likely, mother 19 years/old, G1P0, smoking and gestational diabetes (treated with diet), prenatally presented with intrauterine growth retardation and intrabdominal calcifications. Clinically, he was small for gestational age, no dysmorphic features except for absence of 4th right finger, splenomegaly, imaging confirmed diffuse intracranial and liver calcifications, splenomegaly and portal hypertension. TORCH was ruled

out. Genetic work up ruled out syndromes including Down and Noonan. Multiple cell blood counts (CBC) revealed anemia, thrombocytopenia, both transfusion dependant and progressive leucocytosis ($>70 \times 10^9/L$) with blasts. He met criteria for JMML: splenomegaly, absence of the BCR-ABL1 fusion gene, monocytosis, $<20\%$ blasts in the peripheral blood and bone marrow, circulating myeloid precursors, no evidence of mutation in the RAS pathway, a germline SH2B3 mutation (homozygous) was found, both parents had the same mutation (heterozygous). He was treated with cytarabine (3mg/kg/dose) twice weekly with no response, mercaptopurine 2.5mg/kg/day was instituted with improvement on the CBC and transfusion independence and resolution portal hypertension. He is currently 12 month old with normal development and thriving well, on weaning dose of mercaptopurine with normal CBC.

Conclusions: We report a case of congenital JMML with homozygous germline mutation of SH2B3 with unknown significance (implicated with leukemogenesis), who responded well to mercaptopurine. An archive of these new mutations with clinical follow up is required to further understand the significance of this mutation.

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PO100 SIOP19-0648 | Clinical Profile and Management of Chronic Myeloid Leukemia in Children: 15-Year Experience in Single Institute

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Background/Objectives: Chronic myeloid leukemia (CML) is a relatively rare hematologic malignancy in children. Since recently tyrosine kinase inhibitor (TKI) is the mainstay of management of CML, the necessity of bone marrow transplantation (BMT) is significantly decreased. However, the clinical profile and information on long-term outcome are limited in children. To evaluate the clinical profile, long term treatment and outcome in children with CML at King Chulalongkorn Memorial Hospital (KCMH)

Design/Methods: We retrospectively analyzed children who were diagnosed with CML at KCMH, Bangkok, Thailand from January 2004 to December 2018.

Results: 17 CML patients were included in this study. The median age at presentation was 10 years. There was a prevalence in male:female 1:1.1. The initial WBC and platelet counts with the median (XD) were 334,502 (237,930) cumm and 627,176 (342,127) cumm, respectively. Enlarged abdomen and abdominal discomfort were the most common presenting symptoms (100%) followed by fatigue (75.5%), and burr vision (11.7%). All of them were chronic phase at

the time of diagnosis. Fourteen patients (82.3%) and 3 patients (17.7%) were received imatinib and nilotinib, respectively. As the first line treatment, our study showed 16/17 patients (94%) achieved complete hematologic response (CHR) at 3 months and 14/17 patients (82.4%) showed complete cytogenetic response (CCyR) at 12 months. Seven of 10 patients (70%) achieved molecular response at 12 months. 1 patient who was initially treated with imatinib with suboptimal response at 1 year, and then switch to nilotinib with optimal response. Only 2 patients underwent match-related BMT; 1 patient underwent BMT after 8 months of diagnosis with good response and the other patient who developed blast crisis after 6 months of imatinib treatment. He was initially treated with induction chemotherapy and then followed by BMT with successfully outcome. All of them survive.

Conclusions: TKI therapy in CML children confirmed good outcome; therefore, the necessity of BMT is declined significantly.

PO101 SIOP19-0881 | Chronic Myelogenous Leukemia in Children and Adolescents – A Seven Years Tyrosine Kinase Inhibitor's Experience

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Background/Objectives: Chronic myelogenous leukemia (CML) in children is relatively rare. After the introduction of the tyrosine kinase inhibitor (TKI) imatinib approximately 15 years ago, the treatment paradigm for CML changed considerably.

The second-generation TKIs Dasatinib and Nilotinib produce more rapid and deeper molecular responses compared with Imatinib in adults. Effectiveness of TKI therapy is established by achieving timely hematologic, cytogenetic, and molecular response, as previously defined.

The purpose of the study is to present our recent experience on the response to TKIs treatment of CML pediatric patients

Design/Methods: All children and adolescents with CML who were diagnosed in our clinic during the period 2012-2019 were included in this retrospective study. The safety and efficacy of the treatment with first generation TKIs and the reason to switch therapy with 2nd generation TKIs were recorded. Monitoring of the disease was made by standard methodology, quantitative RT-PCR for BCR / ABL.

Results: Four patients (9-18 years old, mean age of diagnosis 12.4y - 3 girls, 1 boy) were diagnosed with CML in chronic phase. Treatment was initiated by administering Imatinib mesylate to 3 out of 4 patients while one patient received

Nilotinib in the diagnosis. Two of three patients on Imatinib experienced a non-molecular response at 30 and 18 months respectively, and were therapeutically upgraded to Dasatinib. Both patients responded within the next 3 months to the second-generation treatment. All 4 patients are still in therapy with 1st and 2nd generation TKIs with Major Molecular Response without the occurrence of adverse effects and with an excellent quality of life.

Conclusions: Efficacy of current therapeutic approaches in pediatric CML parallels the one observed in adults and renders allogeneic bone marrow transplantation obsolete for most of the patients. Long term safety in pediatric population needs to be established.

Haematology - Stem Cell Transplantation

PO102 SIOP19-0957 | Outcome of Relapsed/Refractory Pediatric Leukemia after Allogeneic Stem Cell Transplantation: A Single Centre Experience from India

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Background/Objectives: Relapse is the major reason for treatment failure in childhood leukemia. We hereby describe outcome of relapsed/refractory leukemia following allogeneic Stem Cell Transplantation (alloSCT) from a center in India.

Design/Methods: Retrospective data of 19 children (mean age 10 yr and male/female-2:1) with relapsed (16)/refractory (3) leukemias who had undergone SCT at our center was analyzed. The diagnosis was ALL-68.5%, AML-16%, CML-10.5% and MPAL-5%. One patient was in complete remission (CR1), 14 in CR2, 2 in CR3 and 2 were not in CR. Matched sibling donor (MSD) SCT was performed in 26% whilst 74% underwent haploidentical SCT with post transplant cyclophosphamide (PTCy). Conditioning was Myeloablative-31.5%, Reduced intensity-37% and Non-myeloablative-31.5%. Graft source was PBSC in all.

Results: Eighteen patients engrafted (Neutrophils on mean 16.78 days & platelets on mean 14.57 days). Median follow-up was 275 days (39-1662 days). At a median of 142 days post SCT; 53% patients (5 haplo, 5 MSD) relapsed. One CD20 positive ALL with relapse post haploSCT is in CR with monthly Rituximab for 30 months. Eleven patients died, 9 with progressive disease and 2 with GVHD (acute-1, chronic-1). Transplant-related mortality was 10.5%. Out of 14 haploSCT patients 6 died (4 had progressive disease, 2 GVHD) and all MSD patients relapsed and died. No patient in CR1 (0/1), 7/13 patients in CR2, 2/3 in CR3 and 2/2 patients not in CR, died. Overall survival (OS) was 42%, OS haploSCT-

57.14% and OS MSD SCT- 0% (p value <0.001). Acute GVHD developed in 6 and chronic GVHD in 7 patients (skin involvement in all 7 with lungs in 3 and liver in 1). Viral reactivations were seen in 5 patients. Event free survival was 37%.

Conclusions: AlloSCT is a curative option for children with relapsed and refractory leukemia. Outcomes post haploSCT with PTCy are superior to MSD SCT.

PO103 SIOP19-1744 | Neurologic Complications after Hematopoietic Stem Cell Transplantation in Children, Results from a Third Level Hospital in Mexico

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Background/Objectives: Complications affecting central nervous system are considered an important cause of morbidity and contribute to the mortality posterior to an hematopoietic stem cell transplantation (HSCT). The frequency is reported around 11-59% of all patients. Clinical syndromes include seizures, encephalopathy, focal neurologic deficit. Known risk factors for this complication include type of HSCT, drug toxicity, coagulopathy, graft versus host disease and inappropriate immune response.

Objective: To determine the frequency and characteristics of neurological complications and the associated risk factors.

Design/Methods: From January 2003 to December 2018 we investigated patients undergoing HSCT for malignant and nonmalignant hematologic diseases at Hospital Civil of Guadalajara, in Guadalajara, Mexico. All patients were 20 years of age or younger at the time of HSCT. We investigated those who had a new onset neurological symptom.

Results: At the study time 119 transplants were performed. A total of 74 neurological occurred, As reported in literature, the main complaint was headache (73%), followed by seizures (20%), hemorrhagic stroke (5%) and encephalopathy (2%). Medium age at transplant were 8.7 years (0-20), we found a relationship between age older than 5 years and occurrence of a neurological complication (OR: 1.9, p=0.04). Type of transplant were not related to this outcome (allogenic OR= 0.91, p= 0.4, cord blood unit OR 0.82, p= 0.4, autologous OR= 0.82, p= 0.3), although administration of antithymocyte globulin has been implicated in another series we did not found this to be a cause. As a risk factor we identified the development of GVHD (OR 2.08, p= 0.02) however grade of GVHD did not influence. As outcome the presence of a neurological complication did not affect the mortality.

Conclusions: Recognize the risk factors for the development of neurologic complications in this populations is key in taking preventing measures.

PO104 SIOP19-1256 | Collection of Peripheral Blood Progenitor Cells in Low-Weight Child Donor - Single Center Experience

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Background/Objectives: Peripheral blood stem cell (PBSC) collection became a widely-adopted technique for obtaining donor progenitor cells in cases requiring allogenic or autologous HSCT. In comparison to bone marrow harvesting, PBSC collection significantly expanded the indications for stem cell donors. However, this procedure in low-weighting donors (<10 kg) remains a reason for discussions, considering volume shift associated complications.

Design/Methods: A five-years-old patient with ALL (weight = 17 kg) was admitted to the transplantation department after completion of treatment using the ALL-REZ 2012 protocol to perform alloHSCT from a matched related donor. The only possible donor was full-matched sibling (weight = 8.9 kg, age = 10 months).

Femoral and subclavian central venous catheters were inserted. For five-day mobilization, donor received 10mcg/kg twice a day of G-CSF (Granocyte®). Collection performed on Spectra Optia Apheresis System © in 2 rounds (day5 - day6) with the reach goal of 5.4 donor's blood volume processing. System's contour was filled with 200ml of RBC concentrate. Dexmedetomidine 0.01% i.v. was used for sedation. The patient was given mask oxygen alongside infusion support.

Results: Throughout the processing, donor remained stable, without any signs of hypovolemic condition. Post-procedure average platelets count - $101 \times 10^9/L$ (range: 64-140). Donor was discharged the next day in satisfactory condition. Overall processing duration was 386 minutes, with 5.8 total blood volume processed and average sampling rate = 10.1 ml/min. As result, concentration of CD34+ cells was $4.1 \times 10^6/kg$ of recipient body weight, $CD3+ = 5.83 \times 10^7/kg$.

AlloHSCT with obtained PBSC performed the next day. Patient received all 3 engraftments by day 27.

Conclusions: PBSC collection in low-weight donor with decreased blood sampling rate (10ml/min) can be safe and efficient procedure. Enhanced procedure duration regimen allows receiving an appropriate concentration of CD34+ cells in donor's material. However, it requires sustainable anesthesiological and transfusional support. We recommend to perform PBSC collection under experienced team surveillance.

PO105 SIOP19-0228 | Successful Engraftment of Haploidentical Bone Marrow with Post Transplantation Cyclophosphamide in Patients with Severe Aplastic Anemia

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Background/Objectives: Patients with severe aplastic anemia (SAA) may benefit from hematopoietic stem cell transplantation, but many of them lack a matched donor. We report two pediatric patients with SAA who experienced successful engraftments of haploidentical stem cells with post transplantation cyclophosphamide (PTCy). This approach appears to be an acceptable alternative for patients who need a transplant but lack a fully matched donor.

Design/Methods: Case Series and review of the literature

Results: We present two cases of pediatric patients with SAA who experienced successful engraftment of haploidentical related bone marrow. Both patients received conditioning consisting of rabbit ATG, cyclophosphamide, fludarabine, and total body irradiation pre-transplant (200 cGy), with post-transplant cyclophosphamide. The conditioning regimen was well tolerated by both patients and they achieved full donor engraftment (Time to ANC 500 = 13-16 days; Time to platelet transfusion independence = 18-54 days). Acute GVHD maximum grade was Stage IV gut in one patient and Stage II skin in the other patient. Chronic GVHD was extensive in one patient but resolved with treatment and was negative in the other patient. Both patients were weaned off all immunosuppressants with no evidence of recurrent GVHD and are alive and well 12 and 11 months post transplant.

Conclusions: Haploidentical stem cell transplantation in patients with SAA may be an effective alternative when fully matched donors are not available. It can facilitate successful engraftment and therefore expand the pool of eligible donors for patients with aplastic anemia

PO106 SIOP19-1727 | Cytomegalovirus in Patients with Related Unmanipulated Haploidentical Stem Cell Transplantation

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Background/Objectives: Acute Lymphoblastic Leukemia (ALL) in Mexico is most frequent oncological condition: 12,765 cases (2007 - 2015). Incidence: 79.8 per million. Indications we use are from the American transplant group. Different factors influence risk of infections during this process: Immunosuppressive scheme, conditioning regimen, immune reconstitution, Graft Versus Host Disease: grade and severity. Using Unmanipulated Haploidentical Transplantation (UHT) cytomegalovirus infection is a point to be considered, establishing guidelines for follow-up; prophylactic, preemptive or symptomatic treatment according to risk for serological status. We evaluated frequency of infections associated with CMV, as well as risk according to serological status and treatment guidelines

Design/Methods: Cohort study. Patients with ALL underwent to UHT. Assigned in a nonrandomized consecutive way to two groups: A) Donor - / Receptor - and B) any positive combination D + / R +; D - / R +; D + / R -; PCR monitoring of viral loads for CMV. Initiating preemptive therapy with more than 500 copies. Antiviral therapy in disease. Therapy was stop achievement >2 negative viral loads after starting treatment with ganciclovir 10mg/kg/d. Flow cytometry lymphocyte subpopulations monthly follow-up: CD19+ / CD3+ / CD3+ / CD4+ / CD+ CD8+ / CD16+ 56+

Results: Seven binomial were included 3 binomials: D - / R -. The Incidence of viral replication was 1/3 (33.3%) none of these with disease 4 binomials (2 with D + / R +) (2 with D + / R -). Replication incidence 4/4 (100%), pneumonitis 1/4 (25%) Fisher's test $p=0.146$ Median replication 35 days (18-39). Mortality none. Treatment time with ganciclovir 24 days (15-35 days) Full count NK achieved at 45 days (20-60) Full count CD8+ achieved at day 60 (40-90) Low levels for CD4 and CD19 in all patients.

Conclusions: In the context of Unmanipulated Haploidentical Transplantation in the pediatric population negative serological status is frequent. It is important to select sero-negative donors for CMV, thus decreasing the frequency of viral infections, decreasing associated mortality.

Solid Non Brain Tumours - Bone Tumours

PO107 SIOP19-1159 | LAG Time, Abandonment of Treatment and Survival in Mexican Children with Osteosarcoma: 15-Year Experience at a Single Institution

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Background/Objectives: Osteosarcoma (OS) is the most common primary malignant bone tumour. The aim of the study was to evaluate predictors influencing survival at a single institution.

Design/Methods: A cross-sectional, retrospective cohort study of children <18 years diagnosed with OS between 2004 and 2018 at Pediatric oncology unit of Centro Medico Nacional "20 de Noviembre". Medical records 46 patients with osteosarcoma. Patients with abandonment of treatment were included in the survival analysis. Time to diagnosis (TTD) was defined as time from initial symptoms to the start of treatment for cancer. Descriptive statistics and univariate survival analysis was performed with Kaplan-Meier-Analysis and compared with Log-Rank-Test.

Results: There were 24 males and 22 females. The average age 11.3 years. Of 46 patients, 28 (60.9%) had localized disease, and 18 were metastatic (39.1%) at diagnosis. Most common tumor location was distal femur and proximal tibia (73.9%). Histological subtypes were Osteoblastic (63%) and Chondroblastic (17.4%). Local control: amputation: 29 (60.9%) limb-salvage surgery: 5 (10.9%). 11 patients (23.9%) abandoned treatment. The average TTD were 4 months. 5-year OS rate 57.7% mean survival time 100 months. Patients with localized disease had a 5-year OS rates of 60.7% while for metastatic disease was 56%. Lag time < 3 months had a 5-year OS rate of 26.1%

Conclusions: Epidemiology data is similar to reported in literature. Most of our patients' local control is radical surgery. Abandonment is a big problem in our population. We have to improve our treatment in order to raise OS. We found that lag time isn't really related to a better survival rate, so we have to improve our knowledge in biology tumor so we can understand and personalize our medicine. Further studies are needed.

PO108 SIOP19-0204 | Clinico-Demographic Characteristics and Prognostic Parameters in Pediatric Patients with Ewing Sarcoma

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Background/Objectives: Ewing Sarcoma is the 2nd most common bone malignancy under 15 years. There is limited clinical data on pediatric Ewing sarcoma from developing countries. The aim of this study was to evaluate the demographic characteristics and identifying prognostic factors for survival in patients with Ewing Sarcoma.

Design/Methods: We retrospectively reviewed 66 patients with pediatric Ewing sarcoma. Overall survival was analyzed with the Kaplan Meier method and log-rank test. To identify prognostic factors for overall survival, multivariate survival

analyses using a Cox proportional-hazard regression model was performed.

Results: In this study, majority of patients were found between 6 to 18 years of age group (n=48/66, 72.7%) with a median age of 10 years. Male: female ratio was 1:1. Femur was the most common site of involvement in 13.6% (n=9/66) patients. The median survival in this study was 52 months. Three and 5-year survival rate of these patients was 52% and 45% respectively. Among three-fourth (n=48/66) of patients from below poverty line, 60% (n=29/48) were alive at the time of analysis. One out of 7 patients (14.2%) who refused treatment, 4 out of 8 (50%) patients with incomplete treatment and 35 out of 51 patients (68.6%) who completed treatment were alive at the time of analysis and the difference was significant (p<0.001).

Conclusions: Patients who completed the treatment protocol had a better survival as compared to those who defaulted or refused treatment. Compliance of treatment hinges on literacy and socioeconomic condition of patient and family. However, no significant impact of age, gender, site of tumor and socioeconomic status on overall survival were seen in this study. As completion of therapy strongly correlates with the improvement in survival, our focus should be directed towards efficient delivery of treatment protocol.

PO109 SIOP19-0894 | Uncommon Case of Pediatric Ovarian Tumor

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Background/Objectives: Ovarian masses occur in female pediatric patients and can be discovered based on symptoms (bloating, abdominal pain), physical and imagistic examination (abdominal mass). The ovarian sex cord-stromal tumors are a heterogeneous group of benign or malignant tumors which include 1.2% of all primary ovarian cancers. Granulosa cell ovarian tumors are the most common type of malignant ovarian sex cord-stromal tumor, and the Juvenile granulosa cell ovarian tumor (JGCOT) represents 5% of all granulosa cell neoplasms. JGCOT is hormonally active and occurs in premenarchal girls or young women, with higher proliferation rates than the adult subtype.

Design/Methods: Case report

Results: We report the case of a 5-year-old girl admitted to the Pediatric Surgery Department with a hypogastric mass and abdominal pain. A history of right ovarian cyst resection seven months prior, with benign histopathological features is

noted. Clinical features of precocious pseudo-puberty such as thelarche and vaginal bleeding were observed, with no other clinical signs of virilisation. Computed tomography of the abdomen and pelvis revealed a large, 100/74/111mm mass developing on the topography of the right adnexa, and ascites. A right salpingo-oophorectomy was performed along with peritoneal lavage and histopathologic examination. The histological evaluation with extensive immunohistochemical staining of the specimen helped establish the diagnosis of JGCOT. Cytology of the ascites revealed malignant cellularity, justifying the staging of tumor as IIIA according to the International Federation of Gynecology and Obstetrics (FIGO) classification for ovarian tumors. The patient underwent adjuvant therapy, four courses of combination chemotherapy with bleomycin, etoposide and cisplatin.

Conclusions: Although standard adjuvant therapy for advanced-stage is not well established because of the rarity of JGCOT in pediatric patients, adjuvant chemotherapy appears to contribute to stable and complete remission. Long-term follow-up using clinical examination, inhibin B and imagistic assessment is needed since recurrences may take place many years after initial diagnosis.

PO110 SIOP19-1296 | Extracranial GCTs in Saudi Children

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Background/Objectives: Pediatric germ cell tumors (GCTs) are rare neoplasms arising predominantly in the gonads and sacrococcygeal, mediastinal, and intracranial localizations. Only a few studies, related to Extracranial GCTs in Saudi Arabian children, have been performed. We report epidemiologic data and our clinical experience at the department of Pediatric Hematology Oncology (PHO), King Fahad Medical City (KFMC), Riyadh, KSA.

Design/Methods: A retrospective observational study of all patients, with diagnosis of extra cranial GCT, who attended PHO-KFMC from July 2006 to Dec 2016 was performed. The survival periods (overall survival OS and disease-free survival EFS) and the final outcomes for patients treated and followed at KFMC were recorded. The survival data was statistically correlated with the clinical, pathological and biological features of patients and tumors and compared to national and international cohorts.

Results: 10-year data was available for the 30 patients of which 6 (20%) were male and 24 (80%) were females. Age at diagnosis ranged 0-149 months with a mean and median of 61 and 65 months respectively. 50% of patients were under 5 years. 23 patients had gonadal tumors, of whom 19 cases were ovarian in origin. 17 patients had Teratomas

of which 12 (70%) were MT which was the most common pathology. 50% of them received BEP and the other half received JEB including stage IV cases. The EFS and OS rates were 93.3% and 100% respectively.

Conclusions: Our results are very similar to known published international cohorts, with excellent outcome for Pediatric GCT. Study number was small to draw any robust epidemiologic data on the characteristics of Saudi patients. However, this is the case worldwide, leading to lack of consensus between different national groups, which resulted in variable treatment protocols. We believe that the JEB based protocols are effective as the BEP based ones, and less toxic.

PO111 SIOP19-1591 | Endodermal Sinus Tumor of the Vagina, a Rare Localization About Two Case Reports

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Background/Objectives: Endodermal sinus tumor (EST) of the vagina is quite rare and develops exclusively in children under 3 years of age. Historically, typical treatment protocol has consisted of operative excision with adjuvant radiation therapy and/or chemotherapy. More recently, a few cases have been reported to be treated by chemotherapy alone, without surgical removal of the vagina.

The aim of this report is to emphasize the role of conservative treatment.

Design/Methods: We report in this study 2 cases EST of the vagina

Results: The age at diagnosis of our patients was 14 and 17 months. Vaginal bleeding was the main symptom considered as haematuria in one of them. Vaginal masses were found on physical examination with palpable lymphnodes in one case. Ultrasonography and pelvic MRI revealed a solid mass in the vagina. The imaging assessment (thoracic tomography and bone scanning) was extended to reveal no other localization of the tumor in both cases. Serum AFP level was elevated in the 2 cases (5044 and 2113 ng/ml). Both patients underwent vaginal biopsy. The diagnosis was confirmed by pathology and immunohistochemical staining. Both patients received chemotherapy. The first patient had 99% of tumor regression after 4 cycles of chemotherapy with negative AFP and persistence of tumor remnant revealed by pelvic MRI. Excision of the remnant was then realized and was tumor free on histology. He is now 5 years tumor free with negative imaging and AFP. The second patient had 6 cycles of chemotherapy. We didn't perform surgery. AFP are now negative and imaging didn't show any remnant. He is tumor free since few months.

Conclusions: In accordance with recent literature, we believe that conservative management of endodermal sinus tumor of the vagina has proved its reliability. Partial surgical resection should be a last resort to maintain fertility and sexual function in the future.

PO112 SIOP19-0819 | Favourable Outcomes for South African Children and Adolescents with Mature and Immature Teratomas (1990-2015): First Report by the South African Children Cancer Study Group

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Background/Objectives: Outcomes of rare paediatric teratomas have not previously been reported, and treatment regimens have not yet been standardised in the middle income setting. We sought to evaluate treatment outcomes of children and adolescents with biopsy-proven mature and immature teratomas in preparation for harmonisation of management approaches.

Design/Methods: Retrospective data by folder review was collated from nine South African paediatric oncology units. Kaplan-Meier analysis with Cox regression was performed to determine 5 year overall survival (OS) and prognostic factors.

Results: From January 1990 to December 2015, 64 patients were diagnosed with mature teratomas, 15 males (median 3.47 months) and 47 females (median 10.83 months). Eighty four patients were diagnosed with immature teratomas, 20 males (median 0.85 months) and 64 females (median 30.02

months). Definitive primary resection was performed in 58/62 patients with mature teratomas. In patients with immature teratomas, 62/84 had primary surgery which was definitive in 53.3% (33/62). The five year OS for patients with mature teratomas was 92.5% and 80% for those with immature teratomas. For the combined group outcome was significantly influenced by stage: Stage 1 (97.3%), Stage 2 (100%); Stage 3 (64.4%) and Stage 4 (55.5%) ($p=0.00001$). Five patients with mature teratomas died: 2 from post-operative complications, 1 from disease, 1 from infection and 1 unrelated. Fourteen patients with immature teratomas died, 11 from disease progression, 2 unrelated and 1 from infection. Loss-to-follow-up was reported in 21/62 (38%) of patients with mature teratomas and 11/8 (13.1%) with immature teratomas. All had stage 1 disease and underwent surgery alone.

Conclusions: Five year OS for the entire group was 84.7%, with poor outcomes for Stage 4 disease. This is the largest cohort of its kind reported in sub-Saharan Africa. Harmonisation of a national protocol will assist in standardising surgical approaches, indications for chemotherapy and follow-up guidelines and is intended to improve prognosis.

PO113 SIOP19-1412 | Growing Teratoma Syndrome and Gliomatosis Peritonei in 15-Year-Old Girl with Immature Ovarian Teratoma

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Background/Objectives: Gliomatosis peritonei (GP) is a rare clinical condition characterized by presence of mature glial cells in peritoneum. Growing teratoma syndrome (GTS) is related with the occurrence of ovary and testicular teratomas. The diagnosis is based on following three criterias: 1) normalization of tumor markers after initially high concentrations 2) enlargement of tumor masses or appearance of new masses situated retroperitoneally or in different locations, observed during or after chemotherapy applied because of the malignant non-seminoma tumor derived from primitive embryonic cells, 3) presence of only mature teratoma cells in the removed mass. Continuation of chemotherapy does not have any effect on tumor mass reduction.

Design/Methods: We present the case of 15-year-old girl treated for an immature ovarian teratoma of left ovary.

Results: Initial concentration of AFP was 1500 ng/ml, beta-HCG, LDH, Ca-125, HE-4, ESR – in norm. Histopathology of the removed tumor arising from left ovary with left ovary and part of the fallopian tube, revealed the presence of immature teratoma with epithelial elements. Normalization of the AFP concentration was obtained 8 weeks after surgery (without

chemotherapy, according to TGM-95 protocol). Five months after the surgery, progressive growth of the AFP concentration was noted. Upon MRI and CT of pelvis local relapse was diagnosed. Evaluation of the remission after 2 blocks of preoperative chemotherapy VIP (etoposide, ifosfamide, cisplatin) revealed huge tumor mass in pelvis minor despite normalization of the AFP concentration. The remaining mass was removed – histopathology showed presence of mature teratoma. During surgery, after the opening of abdominal walls, a presence of a great number of white, abnormal small tumor masses spread across the peritoneum was found. Histopathology confirmed presence of mature glial tissue. Patient continued postoperative chemotherapy.

Conclusions: Now, stays under ambulatory control in laboratory and radiological remission.

PO114 SIOP19-0184 | Intrapericardial Teratoma: Fetal Diagnosis and Neonatal Management

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Background/Objectives: Intrapericardial teratoma is an extremely rare form of primary cardiac tumor. Till date, less than 100 cases have been reported in the literature.

Design/Methods: We report a male fetus with an early diagnosis of intrapericardial teratoma, due to prenatal ultrasound, which permitted an optimal post-partum planning.

Results: A male fetus was diagnosed to have a mediastinal mass on ultrasound at 26 weeks' gestation. Fetal echocardiography showed a heterogeneous multi-lobed mass compressing the right atrium with moderate pericardial effusion. Fetal cardiac MRI showed a large mediastinal mass of heterogeneous signal with an intimate contact with the right heart cavities. The 33-year-old mother was then referred to a tertiary level maternity. Delivery was planned at term. However, at 35 weeks' gestation, the mass increased in size with appearance of a pericardial effusion of average abundance. Delivery was then anticipated after a course for fetal lung maturation. It was a caesarean birth of a boy, clinically term, eutrophic with good adaptation to the extra-uterine life. He had transient respiratory distress. Computed tomography showed a large anterior mediastinal mass with predominant cystic component. Post-natal echocardiography confirmed the huge pericardial tumor in the right atrium which evokes a teratoma. Alpha foeto protein returned very high. The parents were seized prenatally for a pediatric cardiovascular surgery. Chemotherapy was also planned. The baby boy turns 2 years old now and he is clinically well.

Conclusions: Fetuses diagnosed with pericardial teratomas almost die in utero from hydrops fetalis. Prenatal diagnosis,

close monitoring for hydrops fetalis, antenatal pericardiocentesis for cardiac obstruction, and early neonatal tumor resection provide a good prognosis.

PO115 SIOP19-1677 | Neurogenic Bladder after Resection of Sacrococcygeal Teratoma and its Management: About 2 Cases

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Background/Objectives: Urologic complications are an underappreciated sequelae of the mass effect of sacrococcygeal teratoma (SCT) and its resection.

Design/Methods: We present two cases of patients who were treated for SCT and presented after resection a neurogenic bladder.

Results: Case presentation:

The age at surgery of our patients was 2 and 4 months. It was Altman type 3 and they had complete surgical resection including removing the coccyx by combined abdominal and posterior sacral approach. Post-operatively, they presented bladder-voiding disorders and acute urine retention suggesting a neurogenic bladder confirmed by urodynamic findings which showed a poorly compliant high-pressure bladder. They were managed with clean intermittent catheterization and anticholinergic medications. Since they developed many urinary tract infection, a vesicostomy was performed in the two cases with good functional results.

Conclusions: Neurogenic bladder, when identified, should be aggressively treated in the patient with SCT to prevent the development of renal injury over time.

PO116 SIOP19-1163 | Pre Pubertal Germ Cell Tumors: Varied Presentations, Management Strategies and Outcomes in a Resource Challenged Setting

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Background/Objectives: Pre pubertal germ cell tumours are rare in children. They are unique for their varied clinical presentations and differences in management approach. We present our experience over 2.5 years.

Design/Methods: This was a retrospective analysis of teratomas operated between June 2016 and December 2018. We studied clinical presentation, surgical management and outcomes and financial / socio economic conditions of these patients.

Results: There were 7 boys and 12 girls. Age ranged from 1 weeks to 13 years. Sixteen patients had CT Scan and MRI was

done in the rest. Preoperative AFP levels range from 2 to 4.2 lakh ng/ml. There were 6 gonadal (3 testicular and 3 ovarian) and rest extragonadal GCTs. Four were sacrococcygeal teratomas, 4 retroperitoneal, 2 mediastinal, 1 pelvic and 1 patient had a presacral teratoma. One patient presented as a fetus in fetu. All patients underwent complete surgical resection of the tumor. 5 out of those 19 lesions were found to be malignant and 4 received adjuvant chemotherapy. AFP and USG was done on follow-up. One patient of malignant SCT has neurogenic bladder and one of mediastinal tumor has plateaued AFP levels. Rest are all asymptomatic on a follow up between All patients are doing well on a 6 months to 2.5 years follow up. Most patients are from a low to moderate socio economic strata.

Conclusions: Pediatric germ cell tumors may have varied presentations and require a tailored surgical approach. Complete excision and occasionally post-operative chemotherapy is curative in most patients. AFP can be used in addition to clinical and radiological parameters for a close follow up. Low socio economic strata causes a great deal of financial burden on the caregivers

PO117 SIOP19-0148 | Germcell Tumor with Bone Involvement in Children. Five Years Experience at the Instituto Nacional De Pediatria, Mexico

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Background/Objectives: Introduction: Germ Cell Tumors (GCT) are the most common solid neoplasm in adolescents. Bonemetastases are infrequent, and causes are still unknown.

Objectives: Present the experience at the Instituto Nacional de Pediatria, Mexico City (INP) of patients with GCT bone metastases.

Design/Methods: Materials and Methods: Retrospective review of patients under 18 years old with GCT bone metastases treated at the INP, from January 2013 to September 2018.

Results: Four male patients were included in this study: two patients with gonadal primary tumor and two with extragonadal tumor at diagnosis. All the patients with non-seminomatous components. We found 2 with choriocarcinoma histology and 2 with mixed components, one with carcinoembryonic / Yolk Salk tumor (primary mediastinum) and the other one with mature teratoma / Yolk Salk tumor (primary retroperitoneum). In 2 patients there were progression of the disease that led to death, 2 patients are alive and without disease. Overall survival was 50% after a mean follow-up of 15.5 months.

Conclusions: GCT bone metastases are a rare presentation, occurring 3-9% as the primary site at diagnosis, and 1-2% as progression of GCT, being this with a null survival, markers are essential for diagnosis or progression of the disease.

PO118 SIOP19-0135 | The Experience of Diagnosis and Treatment of Malignant Extracranial Germ Cell Tumor in Children: A Single Center Study

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Background/Objectives: Summarize the clinical features, therapeutic effects and prognostic factors of extracranial malignant germ cell tumor (MGCT) children.

Design/Methods: The clinical information, diagnosed and treated in hematology-oncology center in Beijing Children's Hospital, from 2008 to 2018, were analyzed retrospectively, analysis the risk factors affecting the prognosis.

Results: 35 patients were collected, 19 girls, 16 boys, median age 71 months, The primary tumors were located at gonad in 9 (6 ovary, 3 testis), and 26 at extragonad (8 pelvic cavity, 8 mediastinal, and 10 sacral tail); 5 stage II, 16 stage III, 14 stage IV, and 11 intermediate-risk-group, 24 high-risk-group. The median follow-up time is (25.43±4.82) months. All children were given standard treatment, combined with surgical and chemotherapy. C-PEB protocol for high-risk-group, PEB or EP/IE for intermediate-risk-group. The two-year OS and EFS were 87.4% and 67.1%, respectively. The OS and EFS (93.8% and 80.4%) for stage II and III were significantly higher than those in stage IV (66.7% and 45.1%), $P < 0.05$; The EFS in children with distant metastasis at the beginning of the disease was 43.8%, and 86.9% in the non-metastatic-group, $P < 0.05$; At the beginning of the disease, The CR rate with whole tumor resection was 100% and 71% in intermediate and high-risk-group, respectively. Patients diagnosed after puncture, and go throw with 2-4 cycles of chemotherapy, the CR rate was 73%. 40% with incomplete resection have tumor progression, and CR can be reached again by increasing chemotherapy, secondary surgery, and autologous stem cell transplantation.

Conclusions: The extracranial MGCT in children is relatively rare, treated with surgical and chemotherapy, the overall prognosis is good, even if there is distant metastasis in the early stage, there is a hope for survive; Incomplete surgical resection and slow decline of AFP during treatment are the factors of poor prognosis. Children with tumor progression can be further improved by increasing chemotherapy courses and autologous stem cell transplantation.

Solid Non Brain Tumours - Liver Tumours

PO119 SIOP19-0516 | Combined Targeted Therapy in the Treatment of Recurrent Fibrolamellar Hepatocellular Carcinoma: Clinical Case Description

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Background/Objectives: Fibrolamellar carcinoma (FLC) is a variant of hepatocellular carcinoma (HCC). FLC most often affects younger patients with no underlying liver disease. FLC intrinsically has poor response to chemotherapy. This disease is characterized by extremely low 5-year recurrence-free survival with lymph node metastasis is the only significant negative prognostic factor.

Design/Methods: We describe a girl of 17 years old who was diagnosed with fibrolamellar carcinoma in March 2018. Initially, she had a massive lesion (9x6x7.5 cm) in the V/IV segments of the liver, moderately hyperintense on T2 weighted MRI. In addition, heterogeneous masses were found in the porta hepatis, with axial size of 7 x 5 cm and in a craniocaudal dimension of about 9 cm (fig. A, B).

Results: In April 2018, the patient underwent surgery of hemihepatectomy (segments 5-8), ligamentous lymphadenectomy with an excellent result. In June 2018, the progression of the disease was noted in the form of the appearance of intraperitoneal nodes with a diameter of up to 60 mm in the greatest dimension with a rapid growth. In this regard, the patient was prescribed sorafenib at a dose of 800 mg/day from August 1, 2018. This resulted in reducing the size of intraperitoneal lymph nodes to 43 mm in the greatest dimension. In November 2018, the disease progression was noted in the form of choledoch compression by a conglomerate of lymph nodes. The patient underwent endobiliary stenting and was prescribed regorafenib at a dose of 120 mg/day. Since December 2018, nivolumab was added to the therapy at a dose of 150 mg once a week. Despite this, there was a further negative trend in the progression of the malignant process. The patient died in February 2019.

Conclusions: This observation indicates the need for further search for effective treatment of patients with fibrolamellar carcinoma.

PO120 SIOP19-0567 | Relapsed Hepatoblastoma with a Normal Alpha-Fetoprotein Level: Description of Two Clinical Cases

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Background/Objectives: Relapses of hepatoblastoma with a normal alpha-fetoprotein (AFP) level in previously AFP-positive tumors are considered as a rare situation. The purpose of this analysis is the description of AFP-negative relapses of hepatoblastoma.

Design/Methods: Two patients with AFP secreting hepatoblastoma who experienced relapses with a normal AFP levels were included in the analysis. Immunohistochemistry (IHC) for AFP expression was done on the paired tumor samples at diagnosis and relapse.

Results: Case 1. 3-year-old boy was diagnosed with hepatoblastoma of the right hepatic lobe, PRETEXT II, M1 (lung metastases). IHC showed AFP expression. Initial AFP - 24701 ng/ml. The patient received therapy per SIOPEL-4 resulted in complete response (CR). Evaluation because of prolonged fever 19 months after therapy discontinuation revealed a normal AFP level (1.6 ng/ml) and a right lung lesion with mediastinal lymphadenopathy. Complete surgical resection of intrathoracic lesions was done, histology confirmed relapsed HB with weak AFP expression. Adjuvant therapy consisted of vincristine/irinotecan was carried out. The child is alive in without disease 26 months after completion of therapy. Case 2. 6-month-old boy was diagnosed with hepatoblastoma of the right hepatic lobe, PRETEXT III. Initial AFP - 124983 ng/ml. Therapy per SIOPEL-3 standard-risk protocol with subsequent right hemihepatectomy was carried out. Implant metastasis in the post-biopsy area on the abdominal wall was observed and resected in the postoperative period. PLADO chemotherapy was initiated but terminated because of poor tolerability. CR was achieved. Relapse with involvement of lung, liver remnant and peritoneum was observed in 3 months. AFP level was normal (2.9 ng/ml). Histology confirmed HB with no AFP expression. Therapy according to ICE scheme was carried out with subsequent palliative care because of the unresectable disease.

Conclusions: Hepatoblastoma relapses with no AFP elevation emphasize the importance of chest X-rays and abdominal ultrasound as elements of follow-up examinations.

PO121 SIOP19-0147 | Glissonean Pedicle Transection in Surgical Treatment of Pediatric Hepatic Tumors

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Background/Objectives: To study the application of glissonean pedicle transection method of Ken Takasaki in surgical treatment of pediatric hepatic tumors.

Design/Methods: We conducted a retrospective review of all cases operated in Children Hospital 1 between August 2013 and August 2016.

Results: There were 20 cases, 13 boys and 7 girls from 10 to 139 months old. 16 cases were malignant tumors, 4 cases were benign. Mean operation time was 175 ± 74 minutes (35-315), mean blood loss was $16,7 \pm 8,5$ ml/kg body weight (3,5-26,7), mean postoperative stage was $8,68 \pm 2,08$ days (6-14). Complication rate was 5%.

Conclusions: Pediatric hepatic tumors is rare. The glissonean pedicle transection method introduced by Ken Takasaki can be applied effectively in surgical treatment of pediatric hepatic tumors.

PO122 SIOP19-1342 | Hepatoblastoma Experience in Terms of Surgery

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Background/Objectives: The most common primary malign liver tumor in children is hepatoblastoma. We aimed to present the patients with hepatoblastoma who had undergone surgery.

Design/Methods: Patients who were operated for hepatoblastoma in the last 12 years at Çukurova University Hospital were included in the study.

Results: We operated on 22 patients with hepatoblastoma in the last 10 years. We have access to 17 patients' data. The mean age of the patients was 22.4 years (4 months - 8 years). Seven patients were male and 10 were female. Fourteen patients presented with abdominal distention and swelling. One was admitted to the hospital with weight loss, one with diarrhea and one with fever. In the first evaluation, 8 patients were stage 2 and 9 patients were stage 3 according to PRETEXT staging. Two patients had a tumor in the caudate lobe. AFP levels were high in 16 patients. The mean size of the mass was 11.5 cm in the first evaluation. We did not have a stage 1 patient, so trucut biopsy was performed before taking neoadjuvant chemotherapy later underwent to surgery. One patient was undergoing surgery for trans-arterial chemo-embolization hence the tumor could not be excised after chemotherapy, and then tumor was totally removed. In one patient, the surgical margin was excised positively due to invasion of the vena cava. Two patients had portal vein thrombus and were removed during surgery. Three of the patients had right extended hepatectomy, 3 had left extended

hepatectomy, 1 had 6 and 7 segmentectomy, 7 had right hepatectomy and 3 had left hepatectomy. The distant metastasis was in 2 patients (lungs). Mortality was in 1 patient.

Conclusions: Multidisciplinary approach is very important in hepatoblastoma treatment. In appropriate patient, treatment options such as trans-arterial chemo-embolization should be evaluated.

PO123 SIOP19-1401 | A Case of Relapsed Hepatoblastoma Presenting with Occipital Condyle Syndrome

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Background/Objectives: Occipital condyle syndrome is a rare clinical syndrome due to the involvement of the occipital region on the base of the head characterized by a headache spreading from the unilateral occipital to the temporal region and accompanying hypoglossal nerve paralysis. It has been reported most commonly related to prostate, lung, myeloma and renal cell carcinoma and rarely hepatocellular carcinoma. Here, we present a case of hepatoblastoma diagnosed in remission, AFP (alpha-feto protein) levels were found to be gradually increasing, but there was no focus in their scans and he had headache and hypoglossal nerve paralysis.

Design/Methods: A seven-year-old girl who was healthy previously had swelling on her abdomen. His biopsy pathology resulted in well-differentiated hepatoblastoma with high AFP level (117260 mg/dL). A delayed primary surgical resection was performed after three cycles of neoadjuvant chemotherapy according to SIOPEL protocol. Mass pathology was reported as compatible with epithelial-fetal type hepatoblastoma. After postoperative chemotherapy, AFP returned to normal and no residual images were detected. Six months after the treatment, AFP levels started to increase gradually. Abdominal, thoracic and cranial cross-sectional views of the patient and PET-CT were not detected. He was followed-up by intermittent imaging and AFP. He developed headache and right hypoglossal nerve palsy 10 months after treatment.

Results: Repeated imaging revealed a bone mass in the right occipital condyle, with a 26x35x25 mm metastasis, holding the skull base and hypoglossal canal. The patient was evaluated at the tumor board and radiotherapy was initiated with Ifosfamide-Carboplatin-Etoposide chemotherapy.

Conclusions: Hepatoblastoma is the most common malignant liver tumor of childhood. Although 10 to 20% lung metastasis

is reported in patients, cranial and bone metastasis are rare. Skull base metastasis has not been reported in the literature. AFP is a highly sensitive marker in the diagnosis and follow-up. It was aimed to emphasize the importance of systemic findings and rare metastasis sites in pediatric hepatoblastoma patients.

Solid Non Brain Tumours - Neuroblastoma

PO124 SIOP19-1664 | Management of Ganglioneuroma: When Benign Is Not So Benign

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Background/Objectives: Ganglioneuroma (GN) represents a surgical challenge. Despite being benign, GN can both cause significant morbidity and involve a high surgical risk.

Design/Methods: Review of cases of GN diagnosed in our Institution between April 2017 - July 2018.

Results: Four cases were reviewed, with median age of 10 years (8-12). Three were female. The primary tumour was abdominal in three, thoraco-abdominal in one. None had metastases. Patient 1: ten year-old girl, who presented with abdominal distension, then developed shortness of breath and psychological issues, related to body shape changes. The tumour was deemed inoperable because of vascular risk (the IVC surrounded the tumour). She underwent two courses of cryoablation with improvement. Patient 2: Eight year-old girl, with incidental finding of a small mass posteriorly to the left renal vessels. The decision was to do surveillance only. Patient 3. Ten year old girl, presenting with back pain. A large thoraco-abdominal mass was diagnosed. Two expert surgical teams reviewed her and both concluded that the surgical risks would be superior to the possible benefit. Spinal fusion will be offered if the scoliosis progresses further. Over the last 10 months, since diagnosis, the pain has worsened to the extent that the girl has now whole body pain and requires a wheelchair to mobilize. She is followed by the local chronic pain team. Patient 4. Thirteen year-old boy, with an incidental finding of abdominal mass, which was considered unresectable without a significant risk of nephrectomy. Ultrasound surveillance continues to show hydronephrosis, with normal renal function.

Conclusions: Ganglioneuroma constitutes a significant clinical challenge. The risks of major surgery must be weighed against the potential benefits. A multidisciplinary approach with active involvement of the parents in decision making is vital in the management of these cases.

PO125 SIOP19-1033 | Paraneoplastic Neurologic Syndromes in Children with Neuroblastoma

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Background/Objectives: Neuroblastoma (NBL) is the most common extra cranial solid tumor in childhood. It's a tumor characterized by a large spectrum of clinical and biological heterogeneity. However, if classical manifestations are well known, neuroblastoma continues presenting with atypical and exceptional symptoms that makes it a real enigmatic disease.

A series of patients with neuroblastoma is reviewed to report on atypical clinical characteristics at initial diagnosis within evolution, and to analyze treatment features.

Design/Methods: We retrospectively analyzed the data of children diagnosed in the Pediatric Oncology Unit from 1st January 2005 to 31th December 2018 as having NBL with paraneoplastic manifestations. They were evaluated by biochemical and imaging investigations, classified and treated according to the conventional protocol regimens.

Results: Five patients are identified including 2 males and 3 girls with a median age of 40 months, ranging from 12 to 108 months. Opsoclonus -myoclonus syndrome (OMS) was present in 3 patients. Primary tumor was unidentified in the first patient, while the second patient had an age older than that classically reported in the literature, with a thoracic enlarged and metastatic tumor. Two patients presented respectively with bulbar syndrome as initial complaint and polyneuritis with unknown primary tumor also. Curiously, our patients experienced with disseminated disease, aggressive and unresponsive tumor in two cases.

Conclusions: Patients with paraneoplastic symptoms exhibit most frequently a delay in diagnosis. Despite major improvement realized in the comprehension of its underlying mechanism, neuroblastoma continues to fascinate us by its revelation modes.

PO126 SIOP19-1044 | Particular Resolution of Dilated Cardiomyopathy in a Children with Neuroblastoma: A Case Report

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Background/Objectives: Dilated cardiomyopathy is a redoubtable complication rarely described in children with neuroblastoma, and therefore less well known.

Objectives: To report on a case of a spontaneous regression in a child presenting with neuroblastoma and dilated cardiomyopathy.

Design/Methods: We report on a case of a children admitted with a neuroblastoma associated with a dilated cardiomyopathy. We describe management and outcome.

Results: We report on the case of an 11-month-old infant, admitted for adrenal neuroblastoma and dilated cardiomyopathy of incidental discovery. Treatment was based on chemotherapy plus digital- diuretics resulting in a discreet improvement. As the parents refused surgery, this one was not performed, chemotherapy was also stopped at their request and only inotrope with diuretics were continued. During follow-up, we found progressive cardiac function improvement, with satisfying growth. Two years later, dilated cardiomyopathy has completely disappeared, and adrenal tumor was entirely calcified. Key words: cardiomyopathy; neuroblastoma; maturation

Conclusions: Despite pejorative nature of dilated cardiomyopathy observed in children with neuroblastoma, a possible regression can occur spontaneously with a favorable behavior outcome.

PO127 SIOP19-0038 | Neuroblastoma Mimicking as Infantile Hepatic Haemangioma

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Background/Objectives: Neuroblastoma is the third most common neurogenic, extracranial solid tumor of infancy and childhood emerging anywhere along the peripheral sympathetic nervous system (1,2). The prevalence of neuroblastoma is approximately 1/7000 live births (3) In Northern America and the United Kingdom, the prevalence is approximately 1/650 and 1/100 live births, respectively. It mostly originates from the adrenal gland, nerve tissues of the neck, chest, abdomen, or pelvis. (4,5,6)

Design/Methods: We presented the 4 months old girl, who admitted to paediatric ward with distended abdomen. She was feeding well, thriving and otherwise no concerns. On abdominal examination she had a small umbilical reducible hernia. She had a large irregular surface nodular liver which was non-tender with irregular border. Rest of general examination was normal

Results: USS which showed the likely possibility of infantile haemangioma. Her platelet count was 663, AFP was 159 iu/L, AST was 86, Gamma GT was 69, LDH and ferritin were normal. She had normal thyroid function. The biopsy of liver lesions revealed that it is a poorly differentiated metastatic neuroblastoma. Urinary VMA results VMA is 652.4 (normal being 0-15) and HVA is 201.0 (normal being 0-22). Bone marrow aspiration revealed presence of neuroblastoma in the marrow but involvement was less than 10%. Her MIBG was

negative. Only abnormality MRI abdomen is liver Hence she had stage MSIV She completed chemotherapy as per Lines protocol (7)

Conclusions: Neuroblastoma originates from neural crest cells of the adrenal medulla or sympathetic ganglia. Neuroblastomas likely present as an asymptomatic mass in a child Neuroblastoma treated depends on staging by BMT, multiagent chemotherapy and surgical incision. (8) Neuroblastoma has varied prognosis depending on stage and age at presentation. This case highlights the importance of surgical biopsy. She is presently 2 year off therapy and continues to be in remission.

PO128 SIOP19-0976 | Combination of HDCT with MIBG I Radiotherapy in Poor-Risk Neuroblastoma Patients Treatment

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Background/Objectives: Poor-risk neuroblastoma treatment is still a challenge because of high relapse rate. Combination of HDCT with MIBG I¹³¹ radiotherapy is a relatively new strategy for consolidation regimens in some patients with neuroblastoma. Our goal was assessment of safety and efficacy of such a complex consolidation in a treatment of high-risk neuroblastoma patients in a pilot clinical trial.

Design/Methods: We analyzed toxicity along with 2- and 4-years OS and EFS in a cohort of 12 patients who got a consolidation based on Treo/Mel HDCT in combination with MIBG I¹³¹ as a part of high-risk neuroblastoma treatment protocol since 2014 till 2018.

Results: We saw grade 1-2 cumulative organ toxicity in all but 1 patient. There was no treatment-related mortality. OS for 2 and 4 years was $87,5\% \pm 11,7\%$. EFS for 2 and 4 years – $61,4 \pm 15,3\%$ and $49,1 \pm 16,4\%$, respectively.

Conclusions: Consolidation regimen based on Treo/Mel with MIBG is safe. As a part of treatment program, it provides 4-years EFS for about a half of patients with poor-risk neuroblastoma with active residual tumor at the moment of consolidation.

PO129 SIOP19-0528 | Brain Metastasis in Children with Stage 4 Neuroblastoma: Risk Factors and Characteristics

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Background/Objectives: **Background:** Neuroblastoma (NBL) is the most common extracranial solid tumor in children. Involvement of the central nervous system (CNS) is rare, ranging from 1% to 16%. We describe a series of 6 patients suffering from stage IV NBL who presented a cerebral metastasis This series of 6 cases among 54 NBL patients treated in our department during a period of 5 years.

Aim: Describe series of 6 patients with stage 4 neuroblastoma and brain metastasis, analyze their characteristics and probable risk factors.

Design/Methods: Retrospective study, 6 patients with stage 4 NBL with brain metastasis from the department of pediatric hematology and oncology in University Hospital Mohamed VI of Marrakesh from January 2019 to January 2015.

Results: We recorded 6 patients with stage 4 neuroblastoma who developed brain metastasis, the median age at diagnosis was 4 years, all patients were female. Three patients had the brain metastasis at the time of the diagnosis and three at the time of relapse. All Patients had high lactate dehydrogenase levels. 5 patients had supratentorial metastasis, one had infratentorial metastasis. Neurologic signs were present in 5 patients. 5 patients had multiples lesions only one had solitary frontal lesion. 4 patients died, 3 had relapsed and one progressed under induction chemotherapy, the other 2 patients are now in consolidation phases (Topotecan) with good response until now.

Conclusions: Relatively rare, brain metastases from extracranial neuroblastoma usually result from direct extension of skull or dural metastatic lesions. Primary cerebral metastases without evidence of intracranial extension from adjacent bone are even rarer. these cases emphasize the utmost importance of detecting brain metastases in high-risk patients with neuroblastoma,

PO130 SIOP19-0581 | Persistent Bone Marrow Minimal Residual Disease is a Poor Prognostic Marker for Neuroblastoma

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Background/Objectives: To investigate the clinical features of patients with neuroblastoma (NB), and analyze associations between minimal residual disease (MRD) and clinical features.

Design/Methods: A retrospective analysis was performed for the clinical data, including age, sex, primary tumor site, INRG staging system (INRGSS) and treatment response of 23 patients receiving standard chemotherapy. Flow cytometry was utilized to detect CD56+CD81+GD2+ cells in bone marrow before and after treatment.

Results: A total of 23 patients (13 males and 10 females; mean age, 4.5 ± 3.5 years; age range, 0-12 years) were enrolled in this study. There were 19 patients in the INRGSS stage M (82.6%). Unilateral adrenal gland was the common primary tumor site, with a total of 14 cases (60.9%), followed by mediastinal masses (6 cases, 26.1%), spine and neck. 14 patients with MRD > 0.01% before chemotherapy and most of the patients initially responded to induction therapy and reached MRD-negative status. The level of the MRD before chemotherapy was not associated with INRGSS, treatment response and tumor relapse ($P > 0.05$). Remarkably, patients with persistent positive MRD had poor chemotherapy response ($P = 0.037$) and a higher recurrence rate ($P = 0.01$) than the MRD-negative.

Conclusions: There is a significant correlation between persistent positive MRD and chemotherapy response, highlighting the possibility of consecutive MRD monitoring to enable an early detection of tumor relapse in high-risk neuroblastoma patients.

PO131 SIOP19-0597 | Role of Radiotherapy in the Treatment of Advanced Pediatric Ganglioneuroblastoma

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Background/Objectives: Purpose: Local failure is always a significant concern in high-risk neuroblastic tumors (NTs). Ganglioneuroblastoma (GNB) is one category of NTs with a high rate of residual disease after chemotherapy and surgical resection. The aim of this study was to evaluate the local control outcomes in children with GNB receiving radiotherapy (RT).

Design/Methods: Methods: After receiving dose-intensive chemotherapy and resection, 33 patients older than 18 months with GNB underwent radiotherapy to the primary site and residual disease. Radiotherapy consisted of 21.6 Gy to 41.4 Gy based on extent of resection in a once-daily fraction of 1.8-2.0 Gy each. The Kaplan-Meier method and the Cox proportional hazard model were used to calculate the probability of progression-free survival (PFS) and overall survival (OS) and for univariate analysis.

Results: Three patients developed local failure. Distant failure occurred in the bone, bone marrow, liver, brain or distant lymph node in nine patients. The 3-year PFS and OS rates were 67% (95% CI 57%-77%) and 70% (95% CI 61%-79%), respectively. The International Neuroblastoma Staging System (INSS) stage, but not the age, tumor size, surgery extent or encasement of blood vessels, was a significant predictor of local or distant failure and survival.

Conclusions: Our data suggest that local RT contributes to local disease control of GNB. More patients and longer

term follow-up are needed to survey complications after radiotherapy.

Keywords: Ganglioneuroblastoma; Radiotherapy; Local control rate; Prognosis

PO132 SIOP19-1688 | Myelodysplastic Syndrome, Which Develops Ten Years After Neuroblastoma Treatment and Turns into Acute Myelomonocytic Leukemia: Importance of Long-Term Follow-Up

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Background/Objectives: Modern treatment protocols including use of cyclophosphamide and an epipodophyltoxin for high-risk neuroblastoma have improved survival rates, but the long-term sequelae, including development of secondary malignant neoplasms (SMN), are just now appear.

Design/Methods: We presented a case of MDS evolving to acute myelomonocytic leukemia in a patient with neuroblastoma who was treated 10 years ago.

Results: Ten years ago, when the patient was 11 months of age, the patient admitted to the hospital with a mass in the abdomen and diagnosed as Stage IV; n-myc positive, high-risk neuroblastoma with bone involvement. He treated according to Turkish Pediatric Oncology Group (TPOG) Neuroblastoma protocol. After induction therapy, he received surgery and strengthened maintenance therapy. In June 2018, neutropenia was detected during follow-up. Bone marrow aspiration was made due to increasingly developed pancytopenia (Hb: 7.1 g/dL, WBC: 3150 109/mm³, PLT: 99 600 109/mm³) and myeloblasts and monoblasts were found in 15% and 9%, respectively. The patient was followed up with a diagnosis of MDS and was hospitalized due to febrile neutropenia in November 2018 and repeated bone marrow aspiration showed that increased myeloblasts and monoblasts rate as 57%. In the immunophenotype study, high CD13, CD33, CD 11b, CD117 expression were detected. t (15,17), t (8,21), inv (16), FLT-3 expressions were negative. The CSF pathology was normal. Remission was achieved after AIE chemotherapy given as induction therapy. In December 2018, FLAG treatment was given without Idarubicine due to cumulative Adriamycin dose was 240 mg/m². Successful allogeneic stem cell transplantation was performed from a matched sibling donor after FLAG therapy.

Conclusions: High-risk neuroblastoma who were treated with intensive induction chemotherapy showed that the 10 year cumulative incidence of SMN was 16.5% including acute myeloid leukemia (AML)/myelodysplastic syndrome (MDS). The risk of developing an SMN will increase due to

exposure to epipodophyllotoxins and a high cumulative dose of alkylating agents these patients received during the long-term follow-up.

PO133 SIOP19-1045 | An Unusual Respiratory Presentation in a Patient with Paired-Like Homeobox 2B (PHOX2B) Associated Metastatic Neuroblastoma

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Background/Objectives: Neuroblastoma (NBL) is the commonest extra-cranial childhood tumour, originating from the neural crest. Several mutations in PHOX2B, a neurogenesis regulator gene, have been identified in patients with NBL. PHOX2B is also a disease defining gene in Congenital Central Hypoventilation Syndrome (CCHS). We report a case of an unusual respiratory presentation in a patient with NBL with a PHOX2B mutation.

Design/Methods: Case report.

Results: A six-year old male with a family history of NBL received intensive treatment for refractory stage 4 NBL with primary thoracic disease and bone and bone marrow involvement. A non-polyalanine repeat expansion mutation in PHOX2B was identified. The patient was enrolled on the SIOPEN HR-NBL-1 trial but had a poor initial response and went on to receive further chemotherapy, followed by MIBG (Iodine-131-metaiodobenzylguanidine) therapy resulting in clearance of metastases. After twelve months he suffered a metastatic relapse and received further chemotherapy followed by a Busulfan/Melphalan Autograft. This was consolidated with anti-GD2 immunotherapy and retinoic acid. There was minimal toxicity associated with chemotherapy. During his first anti-GD2 infusion, he developed periodic breathing resulting in low oxygen saturations. Polysomnography revealed a significant number of central apnoeas, and no evidence of hypoventilation, unlike other patients with CCHS. MRI head was normal. The results from the sleep studies were similar in the presence and absence of opioids.

Conclusions: This case highlights that patients with PHOX2B mutations can present with variable respiratory phenotypes, not only as classical CCHS. The type and severity of the mutations might result in different respiratory presentations and clinicians should be aware of the risk of disease evolution in these patients. Preclinical data also suggest that PHOX2B functions as a suppressor of neuroblastoma progression, further research is needed to address the challenges in treatment of patients with PHOX2B associated NBL.

PO134 SIOP19-0604 | Evaluation of the Results of 12 Patients who Underwent Laparoscopic Adrenal Neuroblastoma Excision

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Background/Objectives: Adrenal gland is the most common localization for neuroblastoma. In appropriate cases, laparoscopic adrenal mass excision is a recommended method.

Design/Methods: The records of 12 patients with laparoscopic adrenal neuroblastoma excision were performed between 2009-2019 years were evaluated. The Turkish Pediatric Oncology Group protocol was applied in the treatment.

Results: Seven of the patients were male, 5 were female, the mean age was 17.5 (3-156) months. Two patients underwent trucut biopsy from mass, 1 was inadequate and the other was evaluated as neuroblastoma. Bone marrow aspiration and biopsy were performed in 11 patients. Five were reported as neuroblastoma, 1 as inadequate and 5 as normal. At the time of diagnosis, two patients had liver, 1 had spleen and 3 had bone metastasis. Eight of the masses were in the right, 4 were in the left side. Seven patients received neoadjuvant chemotherapy. The largest mass size before surgery was 41 x 22 mm and the smallest was 17x10 mm. According to the International Neuroblastoma Staging System, 5 were stage 4, 4 were stage 1, and 3 were stage 4s. Eight were favourable, 2 were unfavourable and 2 patients could not be evaluated because of necrotic tissue in Shimada Classification. MYCN was negative in 8 patients. Histopathological evaluation were detected as 6 neuroblastoma, 2 ganglioneuroma, 2 ganglioneuroblastoma intermix, 2 necrotic tissue (identified as neuroblastoma with bone marrow biopsy). No Image Define Risk Factor was detected. The median operation time was 120 (95-195) minutes. There was no complication during the operation and pre-operative or postoperative blood transfusion was not required. Postoperative surgical site infection was not detected. Two patients developed relapses and 1 died. Nine patients are followed up without disease. The median follow-up period was 15.5 (3-53) months.

Conclusions: Laparoscopic excision is a safe method for the treatment of adrenal neuroblastoma.

PO135 SIOP19-1038 | MYCN Amplified Relapse Following Resolution of MYCN non-Amplified 4S Neuroblastoma with Placental Involvement

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Background/Objectives: Congenital neuroblastoma with placental involvement is exceptionally rare, but mortality is high. Relapse following resolution of the disease is exceptional, especially MYCN amplified relapse after initial MYCN-non amplified disease.

Design/Methods: Case report and review of literature.

Next Generation Sequencing including WES (comprehensive cancer panel) and RNAseq.

Germline DNA was sequenced using a custom pediatric cancer panel targeting 15,000 exons across 886 genes (1000x coverage).

Results: An infant with antenatally detected adrenal mass was diagnosed with MYCN non-amplified congenital neuroblastoma on placental histology and elevated urine HVA and VMA. Due to the life-threatening clinical condition, treatment was initiated as per COG ANBL0531 cycle 3 with resolution of the primary disease and normalisation of urine catecholamines. Age 20 months of age, there was a recurrent adrenal lesion on ultrasound with elevated urine catecholamines. Biopsy revealed MYCN amplified neuroblastoma.

Additional SCAs included copy number loss at 1p and 16p and gain at 7q and 17q. Germline sequencing using a large comprehensive cancer panel did not reveal variants in candidate cancer predisposition genes. Comprehensive cancer panel sequencing and RNAseq of the relapse tumor specimen did not reveal potential tumor drivers.

Treatment as per the current COG ANBL12P1 for high-risk neuroblastoma was initiated, with 5 cycles of induction chemotherapy, surgical resection of the adrenal mass, single high-dose chemotherapy with busulfan/melphalan and autologous stem cell rescue, abdominal radiotherapy and immunotherapy with dinutuximab, GM-CSF and IL-2. He achieved complete response after surgery and remains in complete remission 12 months after completing therapy.

Conclusions: Placental involvement is extremely rare, however provides an unique opportunity to obtain tumor biology without the need for invasive biopsy. MYCN amplified relapse in a previously non-amplified primary tumor is extraordinary. Further understanding of germline and somatic findings as well as heterogeneity of primary, progressive and relapsed tumors in very young infants may help guide management and follow-up in the future.

PO136 SIOP19-0346 | Thymic Neuroblastoma with the Syndrome of Inappropriate Antidiuretic Hormone Secretion in a Child

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Background/Objectives: Neuroblastoma (NB) is the most common extracranial solid tumor of childhood. Most tumors are located along the sympathetic chain and in the adrenal gland. Thymus as a primary location of NB is extremely rare, usually is observed in adult patients and often associated with paraneoplastic syndrome of inappropriate antidiuretic hormone secretion (SIADH).

Description of the clinical case of the development of thymic NB with SIADH in a 9-year-old child.

Design/Methods: for the period 02.2012 – 04.2019 (87 months) 578 patients with NB were treated in Dmitry Rogachev National Research Center of Pediatric Hematology, Oncology and Immunology. Thymic NB was diagnosed in 1 patient (0.2%).

Results: 9-year-old boy with previous unremarkable medical history presented with tonic-clonic seizures as a result of arterial hypertension and hyponatremia. Blood tests revealed hyponatremia (121 mmol/l), low plasma osmolality (208 mOsm/kg) which were in line with the diagnosis of SIADH. Initial work-up revealed a thymic mass. MRI showed a cystic-solid lesion in the thymus (volume – 120 cm³). 18F-FDG PET/CT showed pathological uptake in the right anterior mediastinum (SUVmax = 13.2). Bone marrow was free from tumor cells. The child underwent an open biopsy with suspected lymphoma. Histology revealed poorly differentiated NB. FISH showed normal status of MYCN gene, 1p and 11q loci. Pathological uptake only in the mediastinal mass was detected on MIBG scintigraphy. Thoracotomy and thymectomy was done, resulted in macroscopic complete resection and normalization of the sodium level and blood osmolality within 48 hours. According to German NB 2004 protocol guidelines the child was stratified to observation group.

Conclusions: Thymic NB is extremely rare in children, but should be included in the differential diagnosis of thymic masses, especially when associated with SIADH. Complete tumor resection is essential for correction of SIADH.

PO137 SIOP19-0812 | Adrenal-Derived Malignant Neuroblastoma is Susceptible of Progression after Surgery

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Background/Objectives: Neuroblastoma is the common solid cancer in children. As a tumor that forms in nerve tissue, it most frequently originates from adrenal glands or spinal nerve root. However, little research has been done on the association between tumor origin and clinical features of neuroblastoma.

Design/Methods: Pearson's chi-squared test, Cochran-Mantel-Haenszel test and Kaplan-Meier test were used to conduct statistical analysis. The results were considered statistically significant when $P < 0.05$.

Results: All information was obtained from 116 patients with neuroblastoma, which was confirmed by radical operation at the Department of Pediatric Surgery, Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, from 2012 to 2017. In all malignant neuroblastomas (neuroblastoma and ganglioneuroblastoma, $n=99$), tumor origin was associated with postoperative disease progression ($P=0.047$). Subgroup analysis implied that in all adrenal-derived malignant neuroblastomas ($n=74$), the 3-year overall survival rate of infants (less than 12 months at diagnosis, 88.8%) was significantly higher than the 3-year overall survival rate of children over the age of 12 months (58.3%, $P=0.036$). Meanwhile, the 3-year postoperative progression-free survival rate of infants was 84.0%, which was also significantly higher than 55.4% of children over the age of 12 months ($P=0.037$). In these adrenal-derived malignant neuroblastomas, patients with stage III and IV had poor prognosis ($P=0.002$), higher risk level ($P=0.001$), and were more susceptible of progression after surgery ($P=0.001$). Their 3-year overall survival rate was 51.6%, which was significantly lower than 94.4% of children with stage I, II and IVs ($P=0.006$). Their 3-year postoperative progression-free survival rate was 46.4%, which was also significantly lower than 93.2% of children with stage I, II and IVs ($P=0.004$).

Conclusions: Adrenal-derived malignant neuroblastoma is susceptible of progression after surgery. For adrenal-derived malignant neuroblastoma, age at diagnosis and clinical stage are promising indicators of disease progression and prognosis.

PO138 SIOP19-1398 | A Childhood Neuroblastoma with Hypercatecholaminemia: A Case Report

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Background/Objectives: Neuroblastoma is the most common extracranial solid tumor in children. Mild hypertension is a frequent symptom, presumably an effect of catecholamines that tumors release. Reported herein is the rare occurrence of hypertension and subsequent heart failure attributable to adrenal gland neuroblastoma.

Design/Methods: A 3-year-old girl presented with retroperitoneal neuroblastoma. Physical examination revealed severe hypertension and fast heart rate.

Results: Abdominal MRI scan showed a 49.9mm×61.3mm×51.3mm solid mass arising from right adrenal gland. The patient underwent a biopsy and was pathologically diagnosed with neuroblastoma. According to the INSS staging system, this patient was divided into stage 4. Metanephrine (MN), normetanephrine (NMN), 3-methoxytyramine (3MT), epinephrine (E), norepinephrine (NE) and dopamine (DA) levels in serum were increased obviously, the patient was received injected intravenously esmolol 100ug/kg.min and ebrantil 4mg/kg.h, and was given oral amlodipine 5mg once daily and metoprolol 25mg three times a day. Both hypertension and heart rate improved after medicine. Subsequently, the patient was underwent surgery. Meanwhile, she was received Arsenic trioxide plus 2 VAC (CTX200mg/m² d1-3, VCR0.67mg/m² d1-3, THP 9mg/m² d4) and 2 PVP (CBP25mg/m² d1-3, VP16 100mg/m² d1-2) chemotherapy regimens, and both hypertension and heart rate were resolved. The specific transitions (for NSE: 298→29.3 ng/ml, for MN: 1.09→0.18 nmol/L 1.51→0.37 nmol/L, for NMN: >20.56→7.37 nmol/L, for 3MT: 1.51→0.37 nmol/L), and their deuterated internal standards (for E: 32.27→53.26 pg/ml, NE: 2241.31→624.19 pg/ml and for DA: 211.79→85.17 pg/ml) had dropped significantly. There were no serious side effects during chemotherapy.

Conclusions: We concluded that children with neuroblastoma characterized by hypercatecholaminemia should be treated with antihypertensive drugs and antiarrhythmic drugs at the beginning of treatment, and chemotherapy or surgical treatment should be given as soon as possible.

PO139 SIOP19-1317 | Stage IV Neuroblastoma: Single Center Experience: Treatment Consolidation

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Background/Objectives: Except treatment with high dose chemotherapy-stem cell rescue and maintenance with dinutuximab immunotherapy; prognosis of stage 4 neuroblastoma is dismal. In this report cases with stage 4 neuroblastoma treated with conventional chemotherapy were evaluated.

Design/Methods: Between January 2007-January 2018; 25 patients with stage 4 neuroblastoma were retrospectively evaluated. Age, gender, date of diagnosis, primary site, bone marrow involvement, molecular genetic features, treatment regimen; additive treatments to conventional high risk treatment backbone, date of last visit, date of event, and outcome were recorded. Turkish Pediatric Oncology Group Neuroblastoma protocol 2003 and 2009 had been used during study period. All of patients were treated according to conventional high risk treatment regimen; in patients after 2012, modifications had been done using repeated MIBG treatment, temozolamid irinotecan consolidation and propranolol. Frequency, mean, median values and Kaplan Meier curves with log rank test were used.

Results: Fourteen of the patients were male; median age was 31 months (6 -84 months) Before 2012; 15 patients were treated. Bone marrow involvement was seen in 13; (%52); tumors site was abdomen in all patients. In 13, besides conventional treatment, MIBG treatment or vinkristin, irinotekan, temozolamid and/or propranolol were added (%52). Beta blocker was given to 9 patients (%36). N myc was positive in 7 (%28). In whole group overall event free survival for four years was %35; overall survival was %39,7. Before 2012; overall survival for 4 years was %26,6. After 2012 there were 6 patients alive with a median follow up of 36 months (p=0,1)

Conclusions: With conventional high risk therapy, the patients with stage 4 disease were treated with 25% survival. In our country, immunotherapy is still not accessible and high dose chemotherapy and stem cell rescue had been reported comparable with conventional high risk chemotherapy. Study with high patient numbers are necessary for alternative consolidation treatments.

PO140 SIOP19-0390 | Neuroblastoma Treatment in Kazakhstan: Single Center Experience

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Background/Objectives: The incidence of neuroblastoma (NB) in children under the age of 18 in the Republic of Kazakhstan is 6-7 cases per 1 million. Significant prognostic factor affecting the outcome is the stage of disease. Despite the implementation of modern methods of treatment, the results of treatment in high risk group patients remain disappointing worldwide.

Design/Methods: Retrospective review of 129 patients with neuroblastoma treated in Scientific Centre of Pediatrics and Pediatric surgery between February 2013 and February 2018 was done. There were 69 (53.5%) boys and 60 (46.5%) girls. The median age was 3.45 years (ranging from 5 days to 17 years). Distribution by stages: I stage - 12 (9.3%), II stage - 11 (8.5%), III stage - 16 (12.4%), IV stage - 79 (61.2%) and 4S stage - 11 (8.5%). Patients were treated according to Neuroblastoma 2004 Protocol, all requirements of which were followed, including autologous peripheral stem cell transplantation. MIBJ is not available in our country yet.

Results: The overall survival rate (OS) among the patients with I and II stages was 100%, for 4S stage - $91.0 \pm 9.0\%$, for stage III - $53.3 \pm 13.3\%$, IV stage (81) - $28.4 \pm 5.0\%$. OS in low- and intermediate risk groups was $97.0 \pm 2.9\%$, while for high risk amounted to $32.3 \pm 4.7\%$. OS for the all patients was $48.8 \pm 4.4\%$. The mortality rate was $51.2 \pm 4.4\%$.

Conclusions: The incidence of NB in our country is slightly lower compared to data from the developed countries, which might be due to the underestimation of patients. The implementation of the international protocol contributed to increasing of survival among the low- and intermediate risk patients. Poor survival rate in high risk group might be improved by performing MIBJ as diagnostic and therapeutic approach.

Solid Non Brain Tumours - Rare Tumours and Histiocytosis

PO141 SIOP19-1684 | Upfront versus Delayed Resection of Pleuropulmonary Blastoma

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Background/Objectives: Objectives: Pleuropulmonary blastoma (PPB) is a rare and aggressive lung tumor found in children. The purpose of this study was to evaluate the outcome of diagnosis and treatment of PPB.

Design/Methods: Methods: This is a retrospective analysis of consecutive patients from 2001 to 2017 with a minimum follow-up from 6 months to 11 years.

Results: Four patients were treated with PPB, three girls and one boy, aged from three months to seven years old. Symptoms presented were two with superior vena cava syndrome, and all patients had respiratory difficulties. A biopsy was performed prior to surgery on two. Pathology results after the surgery showed two patients with PPB subtype I and two with PPB subtype II all with a free borderline. Multiagent neoadjuvant chemotherapy was applied in two patients with symptoms of oncology emergency and one patient presented pneumatocele and pneumothorax after chemotherapy. Postoperative chemotherapy was applied in all patients and radiotherapy in one with PPB subtype II. The surgical approach was posterior lateral thoracotomy on three patients and clamp shell thoracotomy on one. The weight of the tumor ranged from 70 to 1500g. All three girls survived. One patient died 15 months after being diagnosed with PPB subtype II because of progression of the disease.

Conclusions: An aggressive surgery and subsequent chemotherapy was curative for all type I tumors. Symptoms of superior vena cava syndrome conditioned the form of treatment as multi-agent neoadjuvant chemotherapy, biopsy prior to surgery followed by post-surgical chemotherapy, and radiotherapy. The pathological outcome on the free-bound tumor in PPB type II was not an impediment to the reoccurrence of the disease.

PO142 SIOP19-1435 | Volumetry with 3D-Slicer Might be Accurate in Measuring Volumes of Pediatric Ovarian Tumours

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Background/Objectives: Assessment of response to chemotherapy is critical in the treatment of pediatric solid tumours. The Response Evaluation Criteria in Solid Tumors (RECIST) using two-dimensional measurements in imaging studies is widely used in the evaluation of treatment effectiveness. However, two-dimensional measurements may not be able to reflect the true volume changes of tumours during disease courses, especially for large tumours with irregular or blurred margins in imaging. 3D-Slicer is an open source software developed for medical imaging processing. Previous reports about its utility on tumour visualization and volumetry have shown its potential in monitoring disease progression. Validation of volumetric measurements by 3D-Slicer with resected tumours in the real world is scarcely reported. This study investigated the accuracy of volumetry with 3D slicer in ovarian cystic tumours as those often

can be wholly resected with no or as little as possible the surrounding tissue.

Design/Methods: A 12-year-old girl came to our hospital because of acute abdominal pain. Pelvic CT scan showed multiple cystic ovarian tumours with delineated boundaries. The girl received emergent operation to remove the tumours. The exact volume of the largest tumour was measured with a 500ml glass filled with saline. 3D-Slicer was used for 3-dimensional reconstruction and volumetric calculation. Two measurements were compared to assess its accuracy.

Results: The exact volume of the tumour was 106ml and the volume from 3D-Slicer was 112.54ml. The absolute error was 6.54ml and the relative error was 6.17%.

Conclusions: In this case, the accuracy of volumetry with 3D-Slicer is high in measuring the tumour volume. More data is needed to validate its accuracy.

PO143 SIOP19-0014 | A Child with Atypical Pneumonia, Later Diagnosed as a Rare Bronchial Carcinoma, Mucoepidermoid Carcinoma (MEC)

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Background/Objectives: The incidence of community acquired pneumonia (CAP) requiring admission to the hospital in children aged 0-16 years is 12.2 per 10,000 children per annum.¹ Around 300 children per million a year are diagnosed with cancer in the UK, less than 5% are diagnosed with lung carcinoma, making it exceedingly rare.²

Design/Methods: In December 2017 an eight year old girl was admitted with history of several days of fever, cough and shortness of breath. Chest x-ray revealed left upper lobe consolidation. She was given IV antibiotics, made a good recovery and was discharged without follow-up.

In August 2018, she represented with similar complaints and oxygen requirements. Chest X-ray revealed left upper lobe consolidation. She was started on IV antibiotics but did not improve as expected.

Results: Bronchoscopy revealed endobronchial mass in left main bronchus. CT chest confirmed this to be 8mm in diameter. Biopsy and cytogenetics confirmed this to be Mucoepidermoid Carcinoma (MEC). She underwent radical surgery.

Conclusions: MEC is the most common type of salivary gland malignancy in adults but can arise from the bronchial gland, glandular tissue identical with salivary glands located in the submucosa of the trachea and bronchus with incidence of 0.1-0.2% of all primary lung cancers. 3-5.8 MEC is a rare in the paediatric population. 7 Radical surgical resection of the

low-grade-type tumour has an excellent prognosis in children. 6, 9 Despite the rare occurrence, our case highlights that follow up chest radiograph in patients should be considered in those with a round pneumonia, collapse or persisting symptoms as per the BTS guidelines.

PO144 SIOP19-0722 | Thoracic High-Grade Sarcoma with CNS Metastases: the Challenges of Histological Diagnosis and Treatment

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Background/Objectives: Ewing-like sarcoma (ELS) are within a subset of small round cell tumors (SRCT). The histological diagnosis of SRCT is difficult due to the primitive character of the cells.

Design/Methods: Case report.

Results: A 5.5-year-old boy was admitted with dyspnea. Chest CT revealed the large tumor mass in the right lung. Soon after percutaneous biopsy, he developed superior vena cava syndrome and underwent right thoracotomy with the reduction of tumor mass. Histopathological analysis at the treating institution showed Type II pleuropulmonary blastoma (PPB). The boy received four cycles of ifosfamide, vincristine, doxorubicin, and dactinomycin and then underwent total resection of tumor rest. After surgery, he received eight cycles of ifosfamide, vincristine, and dactinomycin. Central pathology review provided by the International PPB Registry showed SRCT with ELS features. Genetic analysis of the tumor was negative for mutations in *DICER1*. FISH tests for both *CIC* and *BCOR* rearrangement were negative. After primary treatment, the boy was discharged in complete remission. Three months later, two brain metastases were detected. He underwent gross total resection of the CNS metastases and received second-line treatment with ifosfamide, carboplatin, and etoposide followed by whole brain radiation therapy. After that, the boy was in complete remission for 8 months. Unfortunately, 8 months later, he was found to have a metastatic lesion in the right lung. He underwent total gross resection and he is currently receiving third line chemotherapy with topotecan and cyclophosphamide. Radiation therapy to the site of lung recurrence is planned.

Conclusions: The thoracic location of this rare tumor may have increased the risk of CNS metastases. Despite extensive pathology review, these tumors remain challenging clinically

and histologically. Incorporation of real time next-generation sequencing techniques may facilitate histological classification and clinical management.

PO145 SIOP19-0932 | Pancreatic Tumor in Children: 15 Cases in a Center

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Background/Objectives: to study the clinical feature and surgical treatment of pancreatic tumor in children.

Design/Methods: we conducted a retrospective review of all cases operated in Children's Hospital 1 from July 2009 to July 2014.

Results: there were 15 cases, 2 boys and 13 girls from 4 to 164 months old. One was lymphoma, 3 cases of inflammatory myofibroblastic tumor and 11 cases of Solid Pseudopapillary tumor.

Conclusions: pediatric pancreatic tumor is very rare. The two main kind is solid – pseudopapillary tumor and inflammatory myofibroblastic tumor. Operation is the treatment of choice.

PO146 SIOP19-0534 | Askin Tumor in Child: Case Report and Literature Review

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Background/Objectives: Background: Askin tumor is a rare malignant tumor arising from soft tissues of the chest wall, rarely in the lung. usually occurring in children, it still raises many questions about its individualization and its links with Ewing's sarcoma.

Design/Methods: We report a case of Askin tumor in a 12-year-old girl with reviewing the different data from the literature

Results: Case report: 12-year-old girl presented because of a palpable mass on the right chest wall for 2 months. She complained of vague pain in the chest lasting for 1 month. There was no history of headache, cough or fever. On physical examination, the mass was slightly tender with little movement. The CT scan demonstrated a well-demarcated, homogeneous soft tissue density mass on the right posterior chest wall with a small amount of pleural fluid and no rib involvement. No mediastinal or axillary lymphadenectasis was found. A provisional diagnosis of benign tumor was made. Subsequently,

local mass resection was performed. Histologic examination under the light microscope showed small round cells with scanty cytoplasm growing as rosettes that were immunohistochemically positive for NSE and CD99. The diagnosis of Askin tumor was established. The patient was treated according to Ewing Memphis protocol she is at 6 months of the treatment (maintenance 2) with good response.

Conclusions: Discussion-conclusion: Chest wall tumors in children can be caused by a wide range of benign and malignant diseases. Askin tumors are rare but highly malignant and must treated by aggressive interdisciplinary management. Multimodality therapy has improved local control and overall survival for patients with PNET of the chest wall, but uniform treatment regimens remains undetermined. The prognosis in Askin tumor is very poor despite the combination of chemotherapy, radiotherapy, and surgical removal; with a 2-year survival of 38%

PO147 SIOP19-0550 | BCOR-CCNB3 Fusion Positive Clear Cell Sarcoma of the Kidney

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Background/Objectives: Clear cell sarcoma of the kidney (CCSK) is the second most common pediatric renal malignancy. BCOR Internal Tandem Duplication (ITD) is the most common genetic abnormality described in CCSK. We report two patients with CCSK with BCOR-CCNB3 fusion and intracardiac extension of their tumors.

Design/Methods: Case reports

Results: Case #1: A 10-year old male presented with 3 weeks of abdominal pain and dyspnea. CT scan revealed a right renal mass with tumor thrombus extending through inferior vena cava (IVC) into the right atrium, and a large left pleural effusion. Biopsy of the mass revealed CCSK; BCOR ITD was negative but BCOR-CCNB3 fusion was detected by targeted next-generation RNA sequencing. He was treated according to COG AREN0321 Regimen UH-1 due to stage 4 disease (malignant cells in the pleural fluid). After 12 weeks of chemotherapy, he underwent right nephrectomy with removal of the intracaval and intracardiac tumor thrombus. Pathology revealed no viable tumor. He received radiation therapy to whole lung (1200cGy) and abdomen (1050cGy). He is in remission 10 months from diagnosis.

Case #2: A 14-year-old male presented with one day of severe back and abdominal pain. CT scan revealed a large left renal mass with tumor thrombus extending through the IVC into

the right atrium. He was diagnosed with undifferentiated sarcoma and received one cycle of therapy according to COG AEWS 1221. Further pathologic evaluation at our institution revealed morphology consistent with CCSK. BCOR-ITD was negative, but BCOR-CCNB3 fusion was detected by RT-PCR and direct Sanger sequencing. His therapy was switched to AREN 0321 Regimen I. Tumor resection is planned including removal of the intracardiac portion of the tumor, followed by radiation therapy.

Conclusions: Molecular diagnostic confirmation of CCSK should include BCOR-CCNB3 fusion testing. These patients may have a predisposition to develop tumor thrombi, which needs further investigation.

PO148 SIOP19-0855 | The Clinical Experience of Management in Langerhans Cell Histiocytosis in a Tertiary Center Included Children and Adults

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Background/Objectives: Langerhans cell histiocytosis (LCH) is a rare disease marked by proliferation of Langerhans-type cells and describes a spectrum of clinical presentations ranging from a single systemic lesion to an explosive disseminated disease.

Design/Methods: A retrospective charts of patients diagnosed with LCH proofed by the tissue pathology from January 2005 to December 2018 were reviewed in a tertiary referral medical center in Taiwan. Demographic data, including age, sex, clinical manifestations, management and outcome were collected for analysis.

Results: A total of 28 patients with LCH were enrolled including 25 children (less than 18 year-old) and 3 adults. There were 17 males (60.7%) and 11 females (39.3%). The mean age of the children was 4.68 years and the adults was 29.3 years. A total of 21 (75%) patients suffered from single systemic involvement including 15 cases with bone lesions and 6 cases with soft tissue lesions. The other 7 (25%) cases were multiple systemic lesions. There were 20 (71.4%) patients who received chemotherapy or radiotherapy and 8 (28.6%) patients were kept under observation without chemotherapy. Central diabetes insipidus (5 cases; 18%) and bone fracture (5 cases; 18%) were the most common complications or comorbidity in those patients. The overall recurrent rate was 35.7% (10/28). The recurrent rate of multiple systemic lesions was 57.1% (4/7) and 28.6% (6/21) in those patients with single systemic involvement with statistically significant. One child and one adult died during the period of treatment, both due to complicated sepsis. The overall mortality rate is 7.14% in the study. The mortality rate of adult (33.3%) is higher than children (4%).

Conclusions: The high recurrent rate was noted in patients with multiple systemic LCH in the study. In spite of the low mortality rate of patients with LCH in children, the high recurrent rate and co-morbidity of multifocal LCM remain a challenge.

PO149 SIOP19-1627 | Testicular and Para-Testicular Tumors in Children: 18-Year-Experience

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Background/Objectives: Prepubertal testicular tumors are a rare entity distinguished through epidemiology, histology types and management compared to tumor occurring post-pubertally. The annual incidence of testicular tumor in children is only 0.5-2 per 100.000 boys, accounting for 1-2% of all pediatric tumors. The aim of our study is to analyze the spectrum of testicular tumors in prepubertal children and the therapeutic results in the pediatric surgery department of the Hospital of Fattouma Bourguiba, Monastir, Tunisia.

Design/Methods: We did a retrospective, hospital archive search for children admitted to our pediatric surgery department with the diagnosis of testicular tumor from January 2000 to December 2018. A total of 12 boys were included.

Results: Twelve patients were operated on because of testicular tumors. The mean age was two years. The presenting symptom was a testicular mass gradually increasing in size in all cases. Six lesions were found in the left side and three in the right one. One case presented with bilateral scrotal mass. Alpha-fetoprotein was elevated in six cases. All these children underwent surgery. Inguinal radical orchidectomy was done. The final histological diagnosis was: yolk sac tumor in five cases, teratoma in three cases, para- testicular fibrous pseudotumor (rhabdomyosarcoma) in one case, cystic dysplasia tumor in one case, *endodermal sinus tumor in one case and granulosa cell tumor in the last case*. Adjuvant chemotherapy was indicated in two patients. All these children were under close follow-up ranging from 1 to 15 years. Death occurred in one case who had a rhabdomyosarcoma. None of the other children had recurrence

Conclusions: Prepubertal testicular tumors are uncommon and benign tumors are more common in this age group. Treatment depends on histological type. Classically, radical inguinal orchidectomy is the universally accepted initial surgical management of malignant GCTs followed by chemotherapy, and a radiation if necessary.

PO150 SIOP19-1297 | Our Patients with Extremity Vascular Anomalies

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Background/Objectives: Difficulties are encountered in the diagnosis and treatment of vascular anomalies located in the extremity region. Vascular anomalies most commonly located in the extremities are vascular malformations and hemangiomas. More rarely, Klippel Trenaunay Syndrome (CTS) can be seen. Treatment is variable according to the etiology of the lesion and the severity of symptoms. In this study, we aimed to share the characteristics and follow-up of vascular lesions in the extremity region followed by Cerrahpaşa Pediatric Hematology and Oncology Department.

Design/Methods: The files of 330 patients with vascular anomalies followed by Cerrahpaşa Pediatric Hematology and Oncology Department were retrospectively reviewed. A total of 44 patients were included in the study. The diagnosis age, sex, prematurity, lesion type and location, imaging and biopsy findings, complications, treatment and follow-up were evaluated.

Results: Forty-four patients were included in the study. 25 (56%) of these patients were female and 19 (44%) were male. The female to male ratio was 1.3:1. The lesion of 28 patients (63%) had been present since birth, 3 (6%) occurred in the first 1 month and 6 (13%) after 1 year of age. The median value of the age at admission was 17 months (0.33 days - 180 months). Only 5 patients (11%) had a history of premature birth. The lesions were located in the upper extremity in 19 (43%) of the patients, in the lower extremity in 22 (50%) and in the lower and upper extremities in 3 (7%). Of these, seven were intramuscular and two were intraarticular lesions. 12 of them were hemangioma, 9 of them were lymphangioma, 17 of them were vascular malformations and 5 of them were CTS.

Conclusions: There may be difficulties in the diagnosis and treatment of vascular anomalies located in the extremity region. First, determine the type of lesion and treatment accordingly. The correct diagnosis allows timely and appropriate treatment.

PO151 SIOP19-1593 | Spontaneous Regression of Solitary Eosinophilic Granuloma of the Skull Vault after Minor Trauma

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Background/Objectives: Eosinophilic granuloma (EG) is classified as the mildest form of Langerhans cell histiocytosis. It mostly affects children, adolescents, and young adults. The skull is the most common site of involvement.

Design/Methods: We report a case of a 7-year-old boy who presented to Prince Mansour Military Hospital with a painful scalp swelling over the left parietal bone after minor trauma at school. The boy complained of increasing headache and size of the swelling, but no other symptoms of increased intracranial tension.

Results: Skull X-ray revealed a lytic bony lesion in the left parietal bone. The brain CT showed a soft tissue mass (3.3x2.8x2.3 cm) at the left high parietal zone that causes lytic process of the adjacent skull bone with minimal extension inside the brain at the subdural area and minimal effect on brain parenchyma. Brain MRI demonstrated a well-circumscribed left parietal bone defect with erosion of inner and outer tables by a heterogeneous soft tissue lesion with reactive dural and subgaleal enhancement. A provisional diagnosis of EG was presumed based on the radiological findings. Spiral CT of the neck, chest, abdomen and pelvis revealed no other abnormality. Skeletal survey confirmed absence of other bony lesions. A surgical excision was planned, but the lesion started to regress spontaneously. Almost full regression was confirmed by brain CT after 2 months of the initial presentation.

Conclusions: The development of EG after trauma is doubtful, however trauma could be an aggravating factor. The conservative management and close observation in case of small well-defined solitary EG of the calvaria is a rational approach to avoid unnecessary surgical interventions.

PO152 SIOP19-0265 | Immunological Landscape for Improving Clinical Outcomes in Rare Tumors: A 10-Year Registry in the National Institute of Pediatrics

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Background/Objectives: Rare tumors are a heterogeneous group of malignancies that when appear during childhood show advanced-stage of disease at diagnosis, recurrence is also frequent. Despite the development of multidisciplinary strategies in treatment, immune-based therapies are gaining traction based on its anti-tumor efficacy in adults. Understanding tumor immunogenicity is essential to prescribe newly developed treatments in children. Here, we present a comprehensive overview on current epidemiology, clinical outcomes of rare tumors in order to better understand the clinical impact of immunotherapy in Mexican children.

Design/Methods: According to the Children's Oncology Group Classification, the prevalence of rare tumor diagnosis was assessed among a group of 1,872 patients. Only 67 eligible patients were included from January 01, 2007 through December 31, 2017. A detailed description of clinical features, stage disease, treatment behavior and clinical outcomes were analyzed.

Results: Out of 1,872 patients suffering from cancer registered at the National Institute of Pediatrics, we selected a group of 67 patients who fulfilled criteria for rare tumors as previously stated, representing a 3.5% frequency, median age at diagnosis was 12.2 years. Among the rare tumors, diagnosis were as follows: papillary thyroid carcinoma (38.8%), adrenal carcinoma (9%), pheochromocytoma (9%), paraganglioma (9%), and melanoma (6%). Advanced stage disease frequency was 60% at diagnosis. Complete remission was achieved in 32% of cases, 19% relapsed and 26% showed progression. Overall, 5-year event survival was 50% ($p < 0.01$).

Conclusions: As opposed to adults, children with solid tumors, do not show impressive anti-tumor activity, leading to their classification as tumors of low immunogenicity. Nevertheless, cancers arising from biallelic mismatch repair deficiency, present elevated frequency of nonsynonymous somatic mutations leading to a high response rate to checkpoint inhibition treatment either alone or in combination, resulting in increased mean survival rate.

PO153 SIOP19-0749 | Important Tumour Suppressor Function of Succinate Dehydrogenase Clinical Correlation and Literature Review

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Background/Objectives: Succinate Dehydrogenase Complex (SDH) is a key respiratory enzyme, composed of 4 subunits (A-D). It is involved in coupling the oxidation of succinate to fumarate in the citric acid cycle. Inactivation results in a cellular accumulation of succinate, an onco-metabolite postulated to be a key-driver in tumorigenesis. Germline heterozygous mutations in the SDH genes cause inactivation of the function of the protein. Loss of the remaining wild type allele in the somatic cells creates a neoplastic transformation leading to the complete loss of the enzyme function. SDH mutation has been identified in pheochromocytomas/paragangliomas (PGL)/gastrointestinal stromal (GIST) tumours, and recently identified in renal carcinomas and pituitary adenomas.

Design/Methods: We presented 2 cases of SDH deficient tumours which presented to our institution in the past

year. We review current literature on SDH tumours and highlight the diagnostic and surveillance pitfalls.

Results: We present the clinical cases of two female patients who presented to our service, outlining their history, examination findings and diagnostic work up. 1 was diagnosed with a large localised paediatric-wild type GIST and the other a thoracic paraganglioma. We present the clinical context of their presentation highlighting the types of SDH deficient tumour that present. We explore the role of surveillance and discuss the genetic issues these cases highlighted.

Conclusions: Increased awareness of the significance of SDH mutation tumours is important for correct identification of genetic predisposition syndromes in patients presenting with PGL, GIST, renal carcinomas and pituitary adenomas. Appropriate genetic counselling of patients and their families is important before embarking on a surveillance program.

PO154 SIOP19-0913 | Pleuropulmonary Blastoma, a Rare Pediatric Tumor: Two Case Reports

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Background/Objectives: Pleuropulmonary blastoma is a rare pediatric tumor of dysontogenic origin, and aggressive nature. Histologically containing malignant mesenchymal tissue, blastema undifferentiated cells and differentiated cartilaginous rhabdomyoblastic or fibroblastic areas.

Objective: To describe the clinical, radiological and pathological profile, treatment response and over all outcomes of two cases treated at the Hospital General del Centro Médico Nacional La Raza.

Design/Methods: Case Reports

Results: CASE 1: a 33-month-old female with a consolidation, pneumonia-like imaging, the CT scans describes an heterogeneous tumor in the left hemithorax with well-defined borders and a 60% invasion. She underwent left thoracotomy with a partial resection of the tumor. Histologically it was compatible with a solid and cystic pleuropulmonary blastoma (Type II). After surgery, she was treated with a cyclophosphamide, vincristine and doxorubicin for 12 cycles of chemotherapy, and finally she received 50 Gy of radiation therapy to the site. That patient went into remission for two months and did not survive, due to multifocal pneumonia and pulmonary necrosis. CASE 2: a 23-month-old female, initially with pleural effusion, treated with a chest tube and antibiotics. CT scan revealed round tumor with a complete and total invasion of the left hemithorax. A biopsy was performed; the histologically report was compatible with a solid and cystic pleuropul-

monary blastoma (Type II). She also underwent thoracotomy with a partial resection. She initiated chemotherapy IVADO regimen (ifosfamide, vincristine, doxorubicin and dactinomycin) for 9 courses. She had an unfavorable outcome, with relapse after one month of remission and died from complicated pneumonia.

Conclusions: Pleuropulmonary blastoma is a rare tumor with an aggressive nature due to local recurrence and with dismal outcome. Clinically it can be either asymptomatic or with initial respiratory symptoms. Treatment includes resection and multi agent chemotherapy.

PO155 SIOP19-0101 | Surgical Management of Unicentric Castleman's Disease in the Abdomen: Report of Five Cases

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Background/Objectives: Castleman Disease (CD) is a rare and exact statistical data are missing, not very familiar to surgeons. Unicentric Castleman Disease (UCCD) at one end of the spectrum is a localized disease. The pathogenesis is a subject of debate and the limited number of cases renders the study of the disease difficult.

Design/Methods: Case series

Results: We report five new pediatric observations from November 2017 to February 2019; all cases were unicentric disease. Their age ranged from 10 to 14 years old, with female: male ratio of 3:2. The average duration of symptoms before they came our hospital was 14.8 months. Chief complaint was an abdominal pain for all patients. Four patients came our hospital with vertigo, anorexia, weakness. We found abdominal mass on deep palpation in 3 patients; enlarged liver and spleen was found in one patient who had a mass on mesenteric. All patients presented pallor had microcytic anemia with low MCV; mean size: 63.14fl. We found that platelet count was higher than normal in five patients (mean count: 542x109/L). Significant elevated C-reactive protein was observed in 4 patients (mean level: 112.51mg/dL). Five patients underwent computed tomography scan which displayed only an atypical homogenous soft tissue mass in the abdomen (mesenteric:3 case; retro-peritoneum:2 case). The mean size of involved lymph node was 5.6cm. There were two histological subtypes (hyaline vascular type:2 case; mixed hyaline vascular plasma cell: 3 case). All patients underwent surgery laparotomy for complete resection of the tissue mass. After operation, the average follow-up time was 8.4 months, symptoms disappeared and abnormalities in the diagnostic examinations returned normal.

Conclusions: CD is a rare disorder with a wide spectrum of clinical presentation requiring appropriate management

strategies. UCCD is primarily treated by surgical excision with good outcome.

PO156 SIOP19-1629 | Pediatric Melanoma: An Institutional Series of 17 Patients

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Background/Objectives: Pediatric melanoma is a rare disease, with three molecular subsets: classic melanoma (CM), associated to giant congenital melanocytic nevus (GCN) and spitzoid melanoma (SM).

Design/Methods: A retrospective, observational, single-institution review and report of our institutional experience in pediatric melanoma is presented. Patient demographics, melanoma description, treatment details, and survival data were analyzed.

Results: Seventeen patients at median age of 11.1 years-old (range 1.8-17.2 years) at diagnosis were diagnosed and treated for melanoma between 2004 and 2018. Fourteen (82%) cases were CM, 2 (12%) associated to GCN and 1 (6%) SM. Two patients presented with metastasis were misdiagnosed. Three (18%) cases had confirmed molecular alterations 2 BRAF V600E (CM) and 1 N-RAS (GCN). Six (35%) cases had affected margins in first biopsy. The NCCN stage was I-II in 5 (29%) cases, III in 4 (24%), IV in 3 (18%); not applicable in 5 (in situ melanomas). Fourteen (82%) patients needed a second surgery of wide excision, where 6 (35%) of them also had a lymph node resection. Nine patients (53%) received adjuvant treatment. Three patients were treated with interferon; 3 with ipilimumab: one progressed and switched to nivolumab achieving complete remission of metastatic disease; another patient received nivolumab and consolidation with dabrafenib; 2 were treated with double therapy (dabrafenib and trametinib) of which one progressed and switched to pembrolizumab and then again to double therapy. The majority (65%) are in complete remission, while 3 (18%) died of disease progression. The 10-year OS was 82% (95% confidence interval: 65-100%).

Conclusions: Pediatric melanoma is a disease that requires accurate molecular diagnosis for proper management and responds similar to adult melanoma.

PO157 SIOP19-0399 | Precision Medicine at its Best: Successful Treatment by Crizotinib in a 13-Year-Old Child Presenting an ALK Rearranged, Secondary Mesothelioma

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Background/Objectives: Malignant pleural mesothelioma (MPM) is an aggressive neoplasm, seldom concerning children. Without any accepted standard of treatment for childhood MPM, Precision Medicine becomes extremely valuable.

Design/Methods: A 13-year-old girl was diagnosed with a MPM 7 years after receiving total body irradiation as a conditioning regimen for an allogenic bone marrow transplantation for an Acute Lymphoblastic Leukemia. She first received chemotherapy by Cisplatin and Pemetrexed with partial response. Interestingly, her tumor presented a rearrangement of Anaplastic Lymphoma Kinase (ALK) and an overexpression of tyrosine kinase c-MET. She was successfully treated by Crizotinib, an oral tyrosine kinase inhibitor targeting ALK and c-MET. The treatment was interrupted after the scheduled three years. She relapsed two weeks later, immediate reintroduction of crizotinib was successful. Six months later, she relapsed once more, demonstrating a resistance to crizotinib. She has been treated ever since with Pembrolizumab, an anti-PDL-1 (programmed death 1 ligand) antibody, with prolonged success.

Results: Second cancer is the main cause of treatment-related death in childhood cancer survivor, irradiation being the main provider. MPM can be a second tumor following thoracic radiation. In MPM, there is no actionable driver mutations and its prognosis is dismal. ALK plays crucial roles in the pathogenesis of various neoplasms mainly through genomic rearrangement but none has been described in MPM. C-MET, on the other hand, is often overexpressed. Crizotinib has never been used for MPM in the clinical setting. In vitro studies showed that the use of crizotinib in association with other molecule such as mTOR inhibitors or anti-VEGF is interesting. Mesothelioma is immunogenic but often expresses PD-L1, evading immune destruction. Ongoing clinical trials are studying immunotherapies such as pembrolizumab, with optimistic results.

Conclusions: Exceptional cases warrant thorough molecular analysis in order to give access to innovative drugs in hope for a prolonged survival.

PO158 SIOP19-1612 | Nasopharyngeal Carcinoma: Report of a Series of 16 Children and Adolescents from a Single Institution

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Background/Objectives: Nasopharyngeal carcinoma is a rare malignancy in children. The aim of this study was to provide analysis of children with nasopharyngeal carcinoma treated in a single institution.

Design/Methods: Between 1999 and 2018, sixteen pediatric patients with a diagnosis of undifferentiated nasopharyngeal carcinoma were treated in our institution, and the patients' clinical characteristics, treatment modality, outcome, and toxicity were analyzed.

Results: The median age at diagnosis was 15.5 years. The gender ratio was 1:1. The majority of patients had regionally and/or locally advanced tumors and one had bone metastases at the time of diagnosis. All patients received chemotherapy before radiotherapy, with partial response in fifteen patients and complete response in one. Radiation dose to the primary tumor and involved cervical lymph nodes was 55-65 Gy, uninvolved cervical and supraclavicular regions received prophylactic radiation with dose of 45-50 Gy. Ten patients received adjuvant chemotherapy. Five-year overall survival (OS) rate was 73% respectively, and after ten years remained the same. At the end of follow-up period, twelve patients were alive, and four died. All of the patients that had distant metastases died. Most common late complications were skin fibrosis and xerostomia.

Conclusions: Multimodal therapy of children with nasopharyngeal carcinoma is associated with long-term survival. It is expected that further advances in the management of these patients, with improved radiotherapy and chemotherapy, will reduce acute and late toxicity and improve quality of life of treated children.

PO159 SIOP19-0375 | Askin Tumor. A Rare Neoplasm in Childhood. Report of 9 Cases in the Hospital Civil de Guadalajara. A 24 Years Review

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Background/Objectives: Background: Askin tumor is a primitive neuroectodermal tumor of thoracopulmonary region described for the first time in 1979. With a mean age of presentation of 14.5 months, female preponderance, and median survival of 8 months. There are not specific guidelines of treatment, with the result of very bad survival rates. The

objective is to show our way to treat this tumors and show the behavior and the modalities of treatment used.

Design/Methods: Design: We present our experience, in a lapse of 24 years, since the first case was reported. Unfortunately because of the many years included, some of the information is missing. We made a retrospective revision of the 9 patients medical records, taking the information about the characteristics of the patients (sex, age, date of diagnosis, metastatic disease at diagnosis, localization of the tumor, modality of treatment, chemotherapy used, dose of radiotherapy, date of surgery, actual status of the patient, and date of death). With this information we tried to describe the behavior of the neoplasm. About the patients who are alive, we make the description of the specific treatment.

Results: Of the 9 tumors, 6 (67%) were in males, and 3 (33%) in female, with a mean age of 6.4 years. The youngest patient was of 10 months' age, the oldest of 16 years. About localization there was 3 in the clavicle, 3 at posterior mediastinum and 3 in ribs. Only 33% had metastatic disease at diagnosis. About survival, 3 are still alive, 2 with a free survival over 5 years, 1 still in treatment and 6 are death.

Conclusions: Still there are only 9 patients talk about this tumor is important because the 5 years OS is over 20%, which is better than the reported in previous series, and there are no specific guidelines of treatment.

PO160 SIOP19-0787 | Treatment Outcomes of Infantile Extracutaneous Hemangioma: Single Center Experience

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Background/Objectives: To evaluate the frequency of visceral/extracutaneous infantile hemangioma and the efficacy/toxicity of first-line treatment with propranolol.

Design/Methods: All consecutive patients affected by infantile hemangiomas referred to the Pediatric Oncology Unit in collaboration with the Dermatology Unit have been enrolled. Propranolol was administered at 2 mg/kg/die in 2 daily doses in cases presenting complications such as ulceration, bleeding, visual impairment, suction deficit, acute respiratory failure, potential life-threatening localization, permanent aesthetic damage.

Results: Between January 2017 and February 2019, 20 patients (15F/5M; 30% premature) affected by infantile hemangioma were enrolled; out of these 14 (10 F/ 4M) with cutaneous hemangioma and 3 (3F) with visceral/extracutaneous involvement received oral propranolol due to the associated complications. Case n1: multifocal lesions of the liver, associated with acute respiratory failure and

hypothyroidism. No cutaneous hemangioma was present. Therapy was started at 5 months of age and lasted 24 months with complete resolution of liver lesions and clinical symptoms. Case n2: increasing multifocal lesions of the liver in the neonatal period. No cutaneous hemangioma was present. Therapy was started at 55 days of age and lasted 6 months with complete disappearance of liver lesions. Case n3: parotid involvement with a bulky, painful and ulcerated mass of the right hemiface. No cutaneous hemangioma was present. Therapy was started at 2 months of age and lasted 17 months. The mass presented a re-growth three months after stop therapy and therefore propranolol was administered for further 9 months with complete resolution. No significant side effects were reported.

Conclusions: Visceral/extracutaneous involvement was recognized in 18% of the cases. Propranolol is a valid and safe therapy in visceral/extracutaneous localizations of hemangioma.

PO161 SIOP19-0605 | SMARCA4/BRG1 Mutation Detected by Next-Generation Sequencing in a Patient with Malignant Extrarenal Rhabdoid Tumor

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Background/Objectives: Malignant extrarenal rhabdoid tumor (MERT) is a rare and highly aggressive tumor. MERT mainly occurs in infancy and childhood rather than adults with a 3-year survival rate of only 9%. Despite of high mortality, there is no treatment guideline and only intensive multimodality treatment is recommended. The genetic hallmarks of MERTs are mutations in *SMARCB1* in most cases and mutations in *SMARCA4* in rare cases. Herein, we report a case of MERT in a one-year-old boy who was shown to harbor a mutation in *SMARCA4* by next-generation sequencing (NGS).

Design/Methods: Case report: A 8month-old boy was brought to the emergency department with fever and upper respiratory symptoms. A chest computed tomography showed 8.6 x 5.4 x 4.5 cm sized soft tissue mass involving upper mediastinum with multiple bilateral cervical lymph node enlargement. The patient underwent anterior mediastinum and right cervical lymph node biopsy. On immunohistochemistry, the tumor cells expressed vimentin, EMA and Ki-67 was 80%. INI-1 was intact and MyoD1, CK, CD1a, LCA, Ki-1, CD34, CD56, desmin, S-100, CD138, SMA, cytokeratin, nestin, MUC-4, BCL-2 and CDK-4 turned out to be negative. Initially, microscopic examination and immunohistochemical

staining led to a diagnosis of undifferentiated sarcoma. To identify a pathologic genetic mutation, NGS was done.

Results: NGS revealed a nonsense mutation of *SMARCA4/BRG1*, which led to a diagnosis of MERT. The patient received alternating chemotherapy with ifosfamide, carboplatin, and etoposide and chemotherapy with doxorubicin, vincristine, and etoposide. The size of the tumor decreased gradually through a series of treatment. Positron-emission tomography showed a very good metabolic response. The patient was proceeded to a high-dose chemotherapy and autologous stem cell transplantation.

Conclusions: NGS lead to a molecular diagnosis of MERT in our case. Our case report suggests that NGS can be used as a helpful tool for differential diagnosis of undifferentiated sarcoma.

PO162 SIOP19-0013 | Study of Clinicopathologic Features of Thai Children with Adrenocortical Carcinoma Caused by Germline TP53 Mutation

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Background/Objectives: To determine the clinicopathologic features and frequency of germline *TP53* mutation in children with adrenocortical carcinoma (ACC)

Design/Methods: A retrospective study of children diagnosed with ACC at King Chulalongkorn Memorial hospital between 2009 and 2018. Clinical presentations, hormonal profiles, and pedigrees were recorded. Mutation analysis of the *TP53* gene using targeted next-generation-sequencing (NGS) method was performed on all patients and their parents with a positive germline mutation.

Results: Two males and five females with ACC were included in this study. The median age at diagnosis was 8 months (range 3 to 62 months). All patients had virilization and hypertension. Of seven patients, five had Cushing syndrome. All underwent total tumor removal and three patients received adjuvant chemotherapy consisting of etoposide, doxorubicin, and cyclophosphamide. Of seven, targeted NGS revealed two different mutations in *TP53* (29%). The *de novo* c.1010G>A (p.Arg337His) was identified in patient 1 and the c.916C>T (p.Arg306Ter) was found in patient 2. Both patients with *TP53* mutations had pulmonary metastasis. The others with localized disease harbored the wild-type *TP53*. With the median follow up of 31 months (range 10 to 115 months), six patients survived without tumor recurrence. No second malignancy was found in these patients. The patient with c.916C>T died of pulmonary metastasis at 10 months after diagnosis.

Conclusions: We successfully identified two different germline *TP53* mutations in patients with ACC. With *TP53* mutations, the clinical courses tended to be more progressive with pulmonary metastasis. The outcome for the treatment of childhood ACC was good with the combination of surgery and adjuvant chemotherapy.

PO163 SIOP19-1603 | Efficacy of ANTI-PD1 Immunotherapy for Skin Carcinomas and Malign Melanoma in a Child with Xeroderma Pigmentosum

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Background/Objectives: The hypersensitivity of DNA repair deficient xeroderma pigmentosum (XP) patients to solar irradiation results in the development of high levels of squamous and basal cell carcinomas as well as malignant melanomas in early childhood. XP is an orphan disease of poor prognosis.

Design/Methods: A 13-year-old male patient, who has been diagnosed with XP since 2 years of age, presented with discoloration in the face and a tumor in the scalp with itchy, dryness and exfoliative skin lesions. A large number of nevus, hyperpigmentation, photosensitivity, and hyperemia in conjunctiva, an eyelid tumor on the right side and a large tumor below the jaw.

Results: The tumors were treated with surgical excision. The patient's right eyelid mass lesion revealed of squamous cell carcinoma, lesion below the jaw malignant melanoma and the tumor in the scalp of basal cell carcinoma, respectively. Malign melanoma tumor sample showed PD-1 positivity, BRAF V600 negativity. Anti PD1 inhibitor treatment nivolumab was started at 480 mg /dose every two weeks. Parallel therapeutic efficacy of antiPD1 was observed in melanoma and nonmelanoma skin cancers with a very good response and excellent tolerance.

Conclusions: Melanoma occurs frequently in patients with XP. Presented as a rare condition because of the simultaneous occurrence of three different skin cancers at an early age. Our observation suggests that cancer immunotherapy with antiPD1 treatment may be considered in patients with XP and malignant melanoma and nonmelanoma skin cancer, but warrants further studies.

PO164 SIOP19-0478 | Pheochromocytoma and Paraganglioma in Children, Clinical Features and Genetic Findings, Single Center

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Background/Objectives: Pheochromocytomas and paragangliomas (PCCs/PGLs) are rare neuroendocrine tumors with almost the same clinical manifestation and pathology features while different origins. Discoveries of new hereditary forms of PCCs/PGLs and their associated susceptibility genes were found during these decades.

Design/Methods: 3 cases of PCCs/PGLs in our hospital from March 2017 to March 2019 were retrospectively analyzed. The clinical manifestations, pathological characteristics and genetic testing results were summarized in this study.

Results: 3 patients diagnosed with PCCs/PGLs confirmed by pathology (1 case was multiple endocrine neoplasia 2, MEN 2) underwent resection of their tumors. 2 boys and 1 girl, age from 5 to 12. Hypertension was the main manifestation of patients before operations. All the operations were first-time. Genetic testing was performed after operations for known PCCs/PGLs susceptibility genes (GDNF, KIF1B, MAX, RET, SDHB, SDHD, TMEM127, VHL, NF1) in a clinical laboratory certified by National Health Commission of the People's Republic of China (NHC). A retrospective analysis was performed, including patients characteristics (age, gender, and ethnicity/race), clinical data (operative process, operative duration, the extent of adrenalectomy, tumor size, and pathologic features), and genetic testing results, as well as laboratory data including dopamine, epinephrine etc. Genetic testing showed that: Case 1 did not carry any suspected mutations of the known PCCs/PGLs related pathogenic genes. Case 2 carried a SDHB gene variant, and several family members also carried the same variant (father, grandmother, aunt, brother), while mother and grandfather were negative. Case 3 did not carry any suspected mutations. However, the patient carried a pathogenic mutation of retinitis pigmentosa, MERTK gene c.225delA heterozygous deletion mutation. She also carried a rare variant of polycystic kidney disease, the C. 5122G > A heterozygous missense variant of PKD1 gene. Her mother carried a Heterozygous Missense Variation of PKD1 Gene c.5122G>A.

Conclusions: Surgery is the only effective treatment for PCCs/PGLs. Gene testing in patients and family members is helpful for genetic and reproductive guidance.

Solid Non Brain Tumours - Renal Tumours

PO165 SIOP19-1469 | Unusual Metastases of Wilms Tumour (WT) is not Common, A Case Report

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Background/Objectives: In pediatrics, WT is the most common renal tumor. We report a case of a 3 years and 10 months old boy diagnosed with WT, stage I who developed pulmonary and unusual presentation of right iliac metastases at the end of chemotherapy.

Design/Methods: The patient was healthy and had no significant medical, surgical or social history. He was diagnosed with WT of the right kidney on June 2017. Induction chemotherapy by Vincristine and Actinomycine was started according to the protocol SIOP nephroblastoma 2001. One month later, he underwent a total nephrectomy. The tumor was localized and limited. The histopathology showed a mixed nephroblastoma of intermediary risk associated with epithelial 35%, blastomatous 25% and stromal 40% components without necrosis. The SIOP WT staging was I. There were no nephrogenic rests or lymphadenopathy. At the end of chemotherapy, he developed bilateral pulmonary metastases and a nodular lesion in the right iliac fossa along the path of the right resected ureter. The radiological imaging were inconclusive to know the histological nature of this iliac lesion; whether lymph node or residual nodule. A significant regression of pulmonary and iliac lesions was achieved after a treatment by etoposide, carboplatin, cyclophosphamide and doxorubicin. He was then operated for complete excision of these metastatic lesions. He received bilateral pulmonary and pelvic radiotherapy followed by chemotherapy. Treatment was achieved on August 2018. He is actually in a complete remission.

Results: The surgical removal of these masses, whose nature was uncertain, confirmed the location along the path of the right ureter. The histopathology of these lesions confirmed the residual nature of the primary tumor and was not in favor of lymph node.

Conclusions: This case is unusual for two reasons; a very early relapse at the end of first chemotherapy and the unusual residual iliac metastasis which were not a lymph node.

PO166 SIOP19-1446 | Pediatric Non-Wilms Renal Tumors

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Background/Objectives: Pediatric non-Wilms renal tumors (NWRT) are poorly understood due to their heterogeneity and rarity. This study aimed to determine the outcomes, demographics, clinical and surgical characteristics of NWRT.

Design/Methods: Forty-three children who underwent surgery for NWRT between 1970 and 2016 were included.

Results: The female to male ratio was 15:28. The most common presenting symptoms were abdominal swelling (n = 16) and abdominal pain (n = 10). The most frequent finding upon physical examination was a palpable abdominal mass (n = 32). Mean age at the time of diagnosis was 3.8 years (1–10) in clear cell sarcoma of the kidney (CCSK), 11.5 months (10 days–2 years) in congenital mesoblastic nephroma (CMN), 9.3 years (2.2–16) in renal cell carcinoma (RCC), and 1.2 years (1–1.6) in cystic nephroma (CN). Two patients with angiomyolipoma were aged 6.5 and 10 years. Two patients with malignant rhabdoid tumors (MRT) were aged 15 and 68 months. The remaining four cases (sclerosing nephrogenic rest, renal tubular adenoma, metanephric stromal tumor, and renal adenocarcinoma) were 3, 14, and 3.5 years, and 3 months old, respectively. Hypercalcemia was detected in three patients (2 RCC, 1 CMN) at presentation. Nephroureterectomy was the most frequently used surgical treatment (n = 38) (88%). Four patients underwent only nephron-sparing surgery (NSS). The mean follow up time of 29 patients was 8.1 years (1–30). The mortality rate was 21% in malignant NWRT (3 with CCSK, 2 with MRT) and 10% in benign NWRT (2 CMN) during the five year follow up period.

Conclusions: Non-Wilms renal tumors are rare in childhood and half are malignant. Nephroureterectomy is the treatment of choice in most cases although NSS can be achieved in selected benign cases.

PO167 SIOP19-1637 | Local Recurrence of Wilms Tumor: Single Center Retrospective Study from Tunisian Pediatric Department

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Background/Objectives: Identifying the risk factors for local recurrence of Wilms tumor

Design/Methods: This is a retrospective study including cases of local recurrence of Wilms' tumor, collected in the pediatric surgery department of the Hospital of Fattouma Bourguiba, Monastir, Tunisia, in 1995 until 2018.

Results: Sixteen children had a Wilms' tumor recurrence. The local recurrence had a frequency of 12%. The deadline for local recurrence was 25.5 months on average. It was shorter

in case of more than 3 years of age, greater than 110 mm in tumor size, immediate association with metastasis, difficult tumor resection, no lymph node sampling and resistance to chemotherapy. Also, in stages III and IV, the blastemata type, anaplasia and above 550 g tumor weight. Treatment of recurrence was primarily surgical, with or without adjuvant chemotherapy. The prognosis of recurrence was good in 71.5% of patients (30% of cases was associated with distant metastasis) and poor in 28.5% of cases.

Conclusions: We recommend a special attention and further investigation of the therapeutic alternatives when local recurrence of Wilms tumor occur, in order to improve the prognosis in these children

PO168 SIOP19-1255 | Parents' Roles in Survivorship of Schoolchildren of Childhood Brain Tumor

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Background/Objectives: Purpose: Brain tumor is the second most common childhood cancer. Brain tumor survivors have a variety of symptoms such as paralysis since onset, as well as motor disorders, chronic fatigue, endocrine-related dysfunction, and cognitive dysfunction etc. after the completion of treatment. Combined with these complications, survivors experience school return and learning difficulties, bullying and withdrawal as difficulties in friendship in schoolchildren and adolescents. Previous researches reported importance of parental support as well as parents' effort, conflict, and difficulties in normalization promotion of survivors during survivorship. However, Japanese parental roles on a daily basis have not yet clarified. Therefore, the aim of this study is to describe parental roles in daily life using narrative of parents of brain tumor survivors.

Design/Methods: Methods: Ten mothers of survivors of brain tumor were interviewed. Age of survivors was ranged from 6–14 year old.

Results: Findings: Since there were little information, mothers felt uncertainty about whether their children's conditions were late effects or not, what will happen to their children's conditions in the future, and how far they should keep their children working on daily basis. Under the circumstance, parental recognized roles were advocate for normalcy of their children in school, encourage their children, provide rehabilitations, connect with and/or protect from others and environment such as schools, enhance to gain confidence, and support children's mental and desires. As the children's growth, it became harder for mother to grasp the situation, problems, and feelings of children. Although mothers continued to support, they were aware that their children had to be independent,

but also struggled with the late effects preventing children's independence.

Conclusions: Mothers played various roles during survivorship, and the roles were unstable depend on the state of children's late effects, development, social situations.

PO169 SIOP19-0598 | Wilms' Tumor Arising from Nephrogenic Rests Located Inside a Tubular Colon Duplication Adherent to the Kidney: An Exceptional Case

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Background/Objectives: Colonic duplication is the less common reported congenital duplication of the gastrointestinal tract. The clinical presentation varies from asymptomatic duplications found incidentally, to severe complications. Renal adhesion of a duplication at an early stage may induce the infiltration of the digestive wall by embryonic nephrogenic tissue, that could give rise to neoplastic lesions.

Design/Methods: We report an exceptional case of Wilms' tumor (WT) arising from diffuse nephrogenic rests (NRs) located inside a tubular colon sigmoid duplication adjacent to the upper pole of the left kidney in a 2 years-old child.

Results: This child with no significant medical history was referred to the emergency for mild abdominal bloating and fever. Ultrasound and CT Scan found a tubular communicating sigmoid colon duplication, ending in a retroperitoneal extra-renal and extra-adrenal cystic calcified collection (5cm), thought to be part of the malformation. The surgical removal of this duplication was delayed because of ENT infection, and given the absence of severity criteria. Pre-operative clinical and ultrasound examination 2 months later showed a growing palpable colon duplication (10cm). Surgery found the duplication ending in a large cystic mass, adherent to the kidney. Cyst rupture during surgical manipulation revealed a suspect tissue, compatible with a WT in frozen section. The duplication resection was completed by a left nephrectomy. Final histological examination confirmed the diagnosis of WT. Colonic wall of the duplication end was infiltrated by immature glomeruli associated with islands of blastema evocative of NRs, that were continuous with the malignant tumor.

Conclusions: We report a case of WT deriving from colonic nephrogenic rests located inside a kidney-adherent colon sigmoid duplication. The fusion between the digestive duplication and the kidney may have taken place at an early stage of embryogenesis in this child. This exceptional case demonstrates the potential of heterotopic immature nephrogenic tissues to evolve into primary WT.

PO170 SIOP19-1031 | Renal Tumors Non Nephroblastoma in Children: Single Institution Experience

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Background/Objectives: Renal malignant tumors comprise approximately 4,6% of all childhood tumors. Among these heterogeneous group, the most frequent is nephroblastoma (95%).

In Argentina, between 2000 and 2016, 1033 renal malignant tumors were diagnosed, 34 carcinomas and 11 other kind of tumors non nephroblastoma.

Our objective is to describe the experience in our institution with pediatric patients suffering non Wilms kidney tumors.

Design/Methods: It is a retrospective observational study. From January 2000 to December 2018, 8 pediatric patients with kidney tumors no Wilms, were diagnosed and treated in Hospital Italiano de Buenos Aires.

Results: N= 8 Median Age= 9.9 years (r: 4 months - 16 years) Ratio men/female 2.5:1 Six patients presented local disease, and two, metastatic disease. The anatomopathology informed: two carcinomas of clear cells (CCR), two papillary carcinomas type II, one chromophobe tumor, one rhabdoid tumor, one mesoblastic nephroblastoma and one renal sarcoma. Seven patients underwent radical nephrectomy as initial treatment, and one polar nephrectomy. The patients with local stage 1 only received surgery and now they are in complete remission. Patients with CCR manifested metastatic disease are alive on target therapy at 57 months follow up. Patients with rhabdoid tumor and sarcoma received chemotherapy and died within the year.

Conclusions: Renal tumors non nephroblastoma are infrequent. Renal masses in children older than 5 years old suggests a different etiology than nephroblastoma. Complete resection is the best prognostic factor of survival. Molecular profile is necessary to adapt target therapies to metastatic disease. As the low incidence in pediatrics, it is essential to work in cooperative groups.

Solid Non Brain Tumours - Retinoblastoma

PO171 SIOP19-1585 | Presenting Features and Outcome Analysis Post Enucleation in Pediatric Retinoblastoma

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Background/Objectives: To conduct an outcome analysis and determine the clinical profile of patients with Retinoblastoma (Rb) who underwent unilateral or bilateral enucleation at our institution.

Design/Methods: This is a retrospective review of the records of 58 pediatric (≤ 14 years) patients with Rb who underwent enucleation, and treated at King Faisal Specialist Hospital and Research Centre (KFSHRC), Riyadh, Saudi Arabia between January 2012 – December 2016.

Results: A total of 86 eyes in 58 patients with Rb were retrospectively analyzed. Thirty patients (51.7%) had unilateral, 26 (44.8%) bilateral and trilateral in 2 (3.4%). There were 30 (51.7%) females with a median age at diagnosis of 20.5 months (3-97.8). One (1.7%) had metastatic disease at presentation. 61 enucleations were done in 58 patients; 52 (85.2%) pre-, 5 (8.2%) post- and 4 (6.6%) both pre- and post- neoadjuvant chemotherapy. 5.2% (3) patients had bilateral enucleation. 4 (6.9%) patients received thermotherapy, 1 (1.7%) cryotherapy and 1 (1.7%) trans-pupillary intravenous carboplatin. Post-enucleation International Classification for Intraocular Retinoblastoma was carried out for all eyes; 43 (70.5%) were in Group E, 11 (18%) Group D, and 3 (4.9%) Group C and A each, followed by 1 (1.6%) in Group B. Ten patients (17.2%) received External Beam Orbital Radiotherapy (EBORT). Of 44 evaluable cases, 41 (93.2%) were in CR, 2 (4.5%) had stable disease and remaining 1 (2.3%) (1) had progressive disease. Probability of five-year overall survival for the whole cohort was 93%; 94.5% for Group E and 80% for Group D.

Conclusions: A large number of patients in this study had advanced disease validating the decision of enucleation. Earlier detection of the disease could potentially lead to a higher rate of eye preservation; with the newly introduced Intra – Arterial chemotherapy (Melphalan) program in the country, lasting tumor control and / or eye salvage rates should improve further.

PO172 SIOP19-1436 | Treatment and Outcome of Retinoblastoma in Children of Northern Vietnam

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Background/Objectives: To evaluate the management and outcomes of retinoblastoma treated with the collaboration of two centers over a 3-year period.

Design/Methods: Retrospective cohort study of 69 patients (91 eyes) with retinoblastoma treated at Vinmec Hospital and National Institute of Ophthalmology, Hanoi between May 2016 and April 2019. All patients were treated according to modified French protocol. Indication of adjuvant chemotherapy after enucleation depends on the results of histology. Conservative treatment with cryotherapy and laser photocoagulation +/- systemic chemotherapy +/- intra-arterial chemotherapy +/- intra-vitreous chemotherapy.

Results: Disease and treatment characteristics of sixty nine patients (47 unilateral and 22 bilateral) were recorded over a median 20.17 month follow-up. Five patients (7.25%) had extraocular disease at diagnosis (1 orbit, 3 optic nerve involvement, 1 orbit and optic nerve involvement). There were no treatment-related deaths. The main toxicity was hematological and infectious but manageable. Up to now, one patient died 8 months after enucleation due to involvement of the cut end of optic nerve, one patient primarily enucleated developed leptomeningeal and bone marrow metastatic disease and receives palliative treatment. Sixty-one eyes were primarily enucleated. Thirty eyes were treated conservatively with a median 17 month follow-up. Eight eyes received intra-arterial chemotherapy as part of their treatment (7 eyes of International Classification of Retinoblastoma (ICRB) groups D, 1 of ICRB groups C), and two eyes of ICRB groups C received intra-vitreous chemotherapy. Overall ocular survival was 100% for ICRB groups A-C. 5/10 eyes of ICRB group D-E were secondary enucleation (3/7 eyes received ophthalmic artery chemosurgery).

Conclusions: Outcome of retinoblastoma patient is good. The conservative treatment of larger tumors is evolving with the development of local chemotherapy. Multidisciplinary approach is important for the management of retinoblastoma in the developing countries.

PO173 SIOP19-0525 | Retinoblastoma: Experience of Pediatric Hemato-Oncology Department of Marrakech

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Background/Objectives: INTRODUCTION: Retinoblastoma is a malignant tumor of neuroepithelial origin, occurring in babies and young children. Despite its rarity, Retinoblastoma is the most intraocular malignant tumor frequency of child.

OBJECTIVE: to study the epidemiological, clinical, para-clinical, therapeutic and evolution of retinoblastoma in pediatric hemato-oncology department of Marrakech.

Design/Methods: MATERIALS AND METHODS: retrospective study of all cases of retinoblastoma followed in the unit of Pediatric Hematology-Oncology department of the university hospital Mohamed VI in Marrakech, over a period of 5 years, from January 2014 to January 2019

Results: twenty six cases were collected with an average of 27.9 months and a sex ratio (M/F) of 1.55. 84% of patients had a unilateral form. One child has a family history of retinoblastoma. The consanguinity was present in 15% of cases. The circumstances of discovery were leukocoria (73%), proptosis (13% of cases), strabismus (19% of cases), and orbital mass (7% of cases). Clinically, the merits of eye objectified a whitish mass in 74% of cases, retinal detachment in 10% of cases and a vitreous swarming in 16% of cases. Therapeutically, Neoadjuvant chemotherapy was given in 19% of cases, enucleation was performed in 88% of cases and additional chemotherapy was recommended in 92% of cases. Two cases among those with bilateral retinoblastoma benefit from conservative treatment of the least affected eye. the outcome was favorable in 56% cases, 19% of cases died, 15% of cases were lost, 7% of cases are under treatment, and 3% of patients relapsed.

Conclusions: Retinoblastoma is a rare and serious illness in children that engages the visual and vital prognosis, but it is a curable disease. The improvement of prognosis in our context requires improvements in early diagnosis and multidisciplinary consultation.

PO174 SIOP19-0997 | Orbital Implants in Retinoblastoma Patients: Experience of One Institution

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Background/Objectives: To evaluate complications of orbital implants from polytetrafluoroethylene following enucleation for retinoblastoma.

Design/Methods: From 01.2017 to 12.2018, 62 eyes (59 patients) which was performed enucleation.

Results: 47 (75.8%) out of 62 eyes were enucleated, followed by the installation of an implant of polytetrafluoroethylene. 15 (24.2%) enucleations were performed without implant placement due to the possible need for the use of radiation therapy in the future (according to MRI data). 4 (8.5%) out of 47 patients had their implants removed because of the resulting infectious complications and exposure of the implant in the postoperative period. The average age of the patients was 18 months (min. 1 month, max 7 years). 3 patients underwent bilateral enucleation.

Conclusions: Polytetrafluoroethylene orbital implants can be recommended for implantation in pediatric patients, since they do not require additional tissue cover and have a low complication rate (8.5%).

Solid Non Brain Tumours - Soft Tissue Sarcomas

PO175 SIOP19-1549 | Rhabdomyosarcoma in Children: Clinical and Therapeutic Characteristics in the Tunisian Center About 32 Cases

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Background/Objectives: Rhabdomyosarcoma (RMS) is a heterogeneous disease with variable survival rates depending on the primary site, tumor size and histological type.

The purpose of this work was to study the clinical characteristics of our population and to evaluate our therapeutic results.

Design/Methods: A retrospective study was conducted on 32 RMS patients treated at the medical oncology department of CHU Farhat Hached from January 2002 to December 2017 according to RMS95 and RMS2005. The analysis of the data was carried out according to the Spss 19.0 software and survival curve according to the method of Kaplan Meyer.

Results: The median age at diagnosis was 5 years [1-14 years] with sex ratio of 1.66. The most frequent localization was in the head and neck (31%) followed by the limbs (18.8%) and the retroperitoneal (15.6% cases). Embryonic RMS was the

most common histologic subtype (80%). Five patients (5.6%) were metastatic at the time of diagnosis. Eleven patients had a primary surgery that was of type R0 in 6 cases, R1 in 3 cases and R2 in 2 cases. Eleven received adjuvant radiotherapy and six received adjuvant chemotherapy. Fifty three patients received neoadjuvant chemotherapy with objective response in 76%. The secondary resection rate was 70%. Recurrence was noted in 28% of cases with a median time of 5 months. The 5years overall survival was 41%. Two third of metastatic patient died within a median survival of 6 months.

Conclusions: The multidisciplinary management of RMS, the most common soft tissue sarcoma in children, needs more challenge for metastatic forms in limited resources countries.

PO176 SIOP19-1000 | Single Center Experience of Non-Rhabdomyosarcoma Soft Tissue Tumors

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Background/Objectives: To evaluate patients with non-rhabdomyosarcoma soft tissue tumors (non-RMSSTT) who were diagnosed and treated at our center.

Design/Methods: The medical records of patients with non-RMSSTT were analyzed. The clinical characteristics, treatment details, responses were analyzed retrospectively. Patients with extraosseous ewing sarcoma were excluded from this analysis. Non-RMSSTT categorized as: (1) GR1: intermediate rarely metastasing group, (2) GR2: intermediate local aggressive group, (3) GR3: malignant tumor group. Clinical characteristics, treatments and responses, overall and event-free survival rates were analyzed.

Results: There were 40 patients treated with non-RMSSTT. The median age of diagnosis was 11.5years (1month-18years), M/F:0, 7. Tumor location: extremity 35%, head-neck 25%, the thoracic region 20%. 31% of the cases were metastatic at diagnosis, metastasis as follows: lung (n:7), bone (n:2), kidney (n:1), liver (n:1), spinal (n:1). Although chemotherapy (CT) protocols were changed over the years, treatment schedules included ifosfamide-etoposide-adriamycin-actinomycin. 44-66Gy radiotherapy (RT) applied to the primary site. Patients who underwent primary surgery (n:27): Fifteen patients complete resection and tumor

negative surgical margins. Six of these patients had only surgery, 3 had only RT, 2 had only CT, and 4 had CT+RT. Primary relapse occurred in 5 of patients who had primary surgery with residue and four of them died with progression. Patients undergoing neoadjuvant chemotherapy (n:13): induction CT response was 61% (2CR+6PR). Delayed surgery (n:11) resulted in complete resection in 5.4/11 patients died with progression. One of the two patients with no surgery after neoadjuvant CT was unresponsive to treatment and died of local aggressive tumor progression, the other patient had remission with chemotherapy. Only 1 of 11 patients in group 1 and 2 had relapse/refractoriness. Two patients died due to non-malignant local aggressive disease and complications. Median follow-up time was 4 years (1 months-26 years). OS was 81% in 1 year, 70% in 5 and 15 years. EFS was 62% at 1 year, 52% at 5 and 15 years.

Conclusions: Non-RMSSTT is a heterogeneous tumor group with a large number of histological subtypes. Recurrence, unresponsiveness and progression were observed in patients who had surgery with residual tumor and almost all of the patients who died were in this group. Overall and event-free survival rates were acceptable. Local treatment (surgery and radiotherapy) is the most important factor affecting survival in these patients with low chemotherapy sensitivity.

PO177 SIOP19-1388 | Outcome of Treatment for Rhabdomyosarcoma at Vietnam National Children's Hospital from 2013 to 2018

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Background/Objectives: Overall survival (OS) of rhabdomyosarcoma (RMS) at developed countries was 64 to 81%. The aim of this study to evaluate the outcome of treatment for RMS in children at the Vietnam National Children's Hospital (VNCH).

Design/Methods: 43 patients with RMS, excluding stage IV enrolled the research from January 2013 to May 2018 and followed up until March, 2019. All patients were treated according to the EpSSG – RMS protocol. The outcome, which included progressive disease, recurrence, death, OS and event free survival (EFS) at 5 years, were analyzed.

Results: Median of the following time was 31.4 months (10 to 64 months). The percentage of patients under 5, from 5 to under 10, over 10 years old was 60.4%, 34.9%, and 4.7%, respectively. Unfavourable site was 86%. Tumor with size of 5 cm or more accounted 60.5%. IRS III staging was 93%. Embryonal RMS was 76.7%. Low risk, standard risk, high risk, very high risk was 2.3%, 20.9%, 74.4% and 2.3%, respectively. Completed remission was 55.8% and partial remission was 16.3% at completed treatment. 76.7% of the patients

had been resected tumor. Only 62.5% among 40 patients who needs radiation had received radiation. 51.1% patients are alive and free disease. Nine patients (20.9%) are alive with events: 2 patient with progressive disease, 2 patients abandoned during treatment, 1 patient had kidney failure and ceased chemotherapy soon, 4 patients with recurrence. Mortality rate was 27.9% (12 patients). The causes of death of 12 patient included: septicemia (4), liver failure (1), recurrence and/ or progressive disease (7). OS and EFS at 5 years were 53.2% and 38.4%, respectively. There were no statistical differences in either OS or EFS between age, site, pathology, and risk groups.

Conclusions: Outcome of treatment for RMS in children, excluding stage IV at VNCH was lower at developed countries.

PO178 SIOP19-0215 | The Experience of Diagnosis and Treatment for Non-Rhabdomyosarcoma Soft Tissue Sarcomas—A Retrospective Study in a Single Institution in 11 Years

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Background/Objectives: The purpose of the study is to summarize the experience of diagnosis and treatment for the non-rhabdomyosarcoma soft tissue sarcomas in our single institute.

Design/Methods: We performed a retrospective analysis of all the data of non-rhabdomyosarcoma soft tissue sarcomas in our hospital in 2009-2018. Clinical basic data (gender; age, location, etc), pathological type and therapeutic strategy (radical operation; chemotherapy; radiotherapy) were reviewed.

Results: There were 56 cases in total. There were 8 pathological types: synovial sarcoma (15, <26.8%), fibrosarcoma (15 <26.8%), PNET (10 <17.8%), hyalocyte sarcoma (5 <8.9%), acinous soft tissue sarcoma (4 <7.1%), embryonal sarcoma (3 <5.4%), malignant small cell sarcoma (3 <5.4%) and extraosseous Ewing's sarcoma (1 <1.8%). There was a difference about tumor location among the eight sarcomas. (P<0.01) SS usually occurred in trunk and limbs but the common sites for fibrosarcoma and PNET were trunk. The most common treat strategy was radical operation plus chemotherapy (and/ or radiotherapy). The rate of operation was 89.3%. In the 56 cases, the 2-year survival rate and 5-year survival rate was 35.7%(20/56) and 8.9%(5/56), respectively.

Conclusions: Radical operation was the primary treatment for pediatric NRSTS, and chemotherapy was the important adjuvant therapy. Those cases that had received radical operation plus chemotherapy had better survival rate.

PO179 SIOP19-0362 | Successfully Treated Synchronous Double Malignancy of Rhabdomyosarcoma and Wilms' Tumor in Infant

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Background/Objectives: The majority of RMS cases arise as sporadic non inheritable tumors with small fraction of tumors are associated with heritable genetic syndromes. Rhabdomyosarcoma constitute 3% of childhood cancers and pediatric renal tumors account for approximately 5% of pediatric malignancies

Design/Methods: Patient initially presented to our hospital 20/11/2011 with a synchronous tongue embryonal rhabdomyosarcoma and wilms tumor. patient had initial investigation local and metastatic work. study management of the case

Results: Patient was presented at the age of 3 months at 2011. She was initially presented tongue Rhabdomyosarcoma During investigating the tongue lesion accidental discovery of renal swelling. renal swelling was proved to be Wilms' tumor. Patient started rhabdomyosarcoma protocol based on COG (ARST-0331) at 12-2011 She was scheduled for biopsy from right renal mass pathology was Rt. renal mass wilm's tumor patient had radical nephrectomy and followed by radiotherapy at renal bed RMS protocol ended 13-12-2012 she continued on IR-RMS protocol with replacing Actinomycin-D with Adriamycin every other cycle. Radiotherapy to tongue was omitted because of age and the initial complete resection of lesion (in spite that margin was not confirmed to be clear) patient was put under follow up. At 4-2014 patient developed tongue mass recurrence, Pathology was Recurrent Embryonal Rhabdomyosarcoma. She received salvage chemotherapy (CCE) with local radiotherapy to tongue ended 1-2015 Patient is under follow up with last visit was December, 2018. She was clinically well and both tongue and renal bed were free radiologically.

Conclusions: Neonatal cancer is rare and comprises a heterogeneous group of neoplasms with substantial histological diversity. Almost all types of pediatric cancer can occur in fetuses and neonates; however, the presentation and behavior of neonatal tumors often differs from that in older children, leading to differences in diagnosis and management

PO180 SIOP19-1080 | Soft Tissue Swelling in Children

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Background/Objectives: When a child presents with a soft tissue swelling, it may be clinically difficult to distinguish between benign and malignant tumors. These tumors cover a heterogeneous group of cancers originating from the bone or the extra skeletal nonepithelial tissues of the body. The purpose of this study is to establish a baseline of the epidemiologic and clinical features of pediatric soft tissue masses, to investigate the survival rate and to study pronostic factors which influence survival.

Design/Methods: All cases of histological proven cancers revealed by swelling in soft tissues between 2006 and 2018 were retrospectively collected and analysed. Clinical presentation, radiological investigation, histology, management, recurrence, and mortality were recorded.

Results: Among the 58 patients, we collected 26 soft tissue tumors (19 rhabdomyosarcoma, 1 infantile fibrosarcoma, 1 rhabdoid tumor 4 undifferentiated sarcoma, 1 granulocytosis sarcoma), 16 Ewing's sarcoma, 8 osteosarcoma and 8 others tumors (1 malignant fibrous histiocytoma, 3 langherans cell histiocytosis, 4 neuroblastoma). The male to female ratio was 1.3. The median age was 6.2 years (2 months-15 years). The median tumor size was 6.2 cm (ranges 2 - 31cm). The commun location of swelling was the limbs (53%), however head and neck locations were less frequent (20%). 5-years overall survival (5-y OS) was 70%. Among all tumors, osteosarcoma had the worst prognosis (5-y OS=45%) compared to Ewing's sarcoma (5-y OS=92%) and soft tissue sarcoma (5-y OS=66%) (p=0.028). Similarly, the presence of lung metastases influence negatively the 5-y OS (50%, p=0.011). Other pronostic factors were studied but didn't influence survival: tumor size (p=0,2) and the delay (p=0,5).

Conclusions: In paediatric cases of swelling masses, imaging exams are frequently indicated to allow the correct diagnosis to be made. Any child with a soft tissue mass increasing in size, whether or not painful, should be referred to a specialized center for specific investigation.

PO181 SIOP19-0834 | Ewing Sarcoma Family of Tumors: Single Center Experience

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Background/Objectives: To evaluate clinical features and treatment results of the children with the diagnosis of Ewing sarcoma family of tumors (ESFTs) in our center.

Design/Methods: Medical records of children with ESFTs treated between 1988–2018 were analyzed retrospectively. Clinical characteristics, treatments and survival rates were analyzed.

Results: 43/51 cases were eligible and analyzed. Median age at diagnosis was 141 mos (0-17yrs), M/F ratio was 0.8. Primary tumor site: extremity 30.2%(n:13), paravertebral 11.6%(n:5), pelvic 23.3%(n:10), extrapulmonary intrathoracic 23.3%(n:10), skull bones 9.3%(n:4), neck 2.3%(n:1). Histopathologic examination revealed Ewing sarcoma in 72%(extraosseous 15, osseous 16) and PNET in 28%(n:12) of cases. The rate of metastatic cases was 39.5%(lung 12, bone 5, bone marrow 3, distant lymphnode 2, liver 1) at diagnosis. In the median 23 mos follow-up time (2 mos-18 years), 5-10-15 years EFS 27%; 5 yrs OS 43%, 10-15 yrs 32%. Primary surgery performed in 8 cases: These cases were admitted to our center after they had been operated at another center. Different chemotherapy (CT) regimens were given to these patients, and radiotherapy (RT) to the primary tumor site was applied to 7 cases. Of these 2 have been alive without disease, 2 have been alive with disease, 4/8 cases died. Neoadjuvant chemotherapy was given in 35 cases after biopsy: Primary chemotherapy was ICESS 92 protocol in 8 cases, POG8850 and 9354 protocols based regimens in 19 cases, AEWS0031 in 8 cases. Induction chemotherapy response was 82%(1CR+28PR). Surgery performed after neoadjuvant CT in 12/15 cases. Relapse occurred in 2 cases (at 6 and 16th months), refractory disease in 4, 4 of them died. Surgery wasn't performed after neoadjuvant CT in 10/20 cases. RT had performed to primary site in these cases. 10/20 patients were metastatic at diagnosis. 13 cases died, 2 went to different center and other 2 lost to follow-up. Only 3 cases were alive without disease. Among cases, no treatment related death, secondary malignancy occurred in one case, 2 cases were alive after mutilation surgery.

Conclusions: Although CT and RT to primary region, half of the cases had died, event-free and overall survival rates were low. This results can be associated with the advanced and metastatic disease at diagnosis, also low primary surgery rates.

PO182 SIOP19-0841 | Rhabdomyosarcoma Experience: A Single Center Results

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Background/Objectives: We reported clinical features and treatment results of children diagnosed with rhabdomyosarcoma (RMS) in our center.

Design/Methods: Medical records of patients with RMS between 1988-2018 were analyzed retrospectively. Demographic features, clinical characteristics, treatment results and survival rates were analyzed.

Results: There were 48 patients with a median age of 65 mos (4 mos-17 yrs), M/F ratio was 1.18. The median duration of complaints was 5 weeks (1 week-7 mos). The primary tumor site was head and neck in 42%; genito-urinary in 19%; extremity in 14%; trunk in 17%; pelvic in 4% and intraabdominal in 4% patient. 23% of cases were metastatic at diagnosis. Biopsy was performed 56% and primary surgery 44% patient at diagnosis. The tumor histology was embryonal in 67% and alveolar in 33% cases. Clinical group (CG) distribution of patients: CG 1: 3 (6%), CG 2:7 (15%), CG 3: 27 (56%), CG 4:11 (23%). Primary surgery was resulted with total resection in only 7 patients. "The Intergroup Rhabdomyosarcoma Study-IRS"-based treatment regimens were used in 28 patients, SIOP MMT89 in 13, COG ARST0431 protocol was used for other 7 patients. Nineteen patients received conventional radiotherapy to the primary tumor site, one patients to metastatic site. RT performed for 2 patients to primary site after relapse. Delayed surgery was performed in 8 patients and complete resection was achieved in 7 of them. The median follow up time was 30 months (1 mos-19 yrs), EFS was 36% at 5 and 10-years; overall survival was 34% at 5 and 10-years. Six patients had died related to sepsis or tumor related complications in first six months, 2 patients stopped treatment. Relapse/progression was developed in 22 patients, 17 of them died from progressive disease. There was no relationship between tumor site and histopathology-treatment results. Median relapse/progression time was 10 months (2- 30 months).

Conclusions: Our event-free and overall survival rates were lower than literature and it was thought that 79% of the cases could be due to clinical stage 3-4 advanced stage disease. Also surgical intervention in different centers and different experience teams.

PO183 SIOP19-0734 | Neonatal and Adolescent Paratesticular Rhabdomyosarcoma

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Background/Objectives: Paratesticular rhabdomyosarcoma (PTRMS) accounts for only 12% of childhood scrotal tumours. We report an exceedingly rare presentation in a neonate and evaluate the disease free survival and overall survival in patients with PTRMS.

Design/Methods: We retrospectively reviewed all paediatric surgical patients with PTRMS in our centre from 2000 to 2019.

Results: Two patients (aged 0 day and 17 years at presentation) with non-metastatic PTRMS were identified. Both underwent unilateral inguinal orchidectomy revealing

embryonal histology. In the neonate, local invasion to the paratesticular fat was found requiring left hemiscrotectomy. Surgical resection was complete in both patients. None underwent lymph node sampling, retroperitoneal lymph node dissection or radiotherapy. No complications from chemotherapy were reported. Disease free survival and overall survival were 100%. Follow up duration was 3 years and 19 years respectively.

Conclusions: Paratesticular rhabdomyosarcoma can arise in neonates and are completely asymptomatic. Prompt recognition, referral to a specialized centre and adequate surgery is essential. The long term disease free and survival outcome are excellent in non-metastatic PTRMS.

PO184 SIOP19-0593 | Clinical Characteristics and Treatment Outcome of Pediatric Non-Rhabdomyosarcoma Soft Tissue Sarcoma – Experience from a Tertiary Care Cancer Centre from South India

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Background/Objectives: Soft tissue sarcoma (STS) comprises 7% of all pediatric malignancies. Non-rhabdomyosarcoma soft tissue sarcoma (NRSTS) accounts for 50-60% of STS in children. There is limited data regarding outcome in resource limited countries.

Design/Methods: Children, ≤14 years of age, diagnosed as NRSTS from January 2007 to December 2017, were retrospectively analyzed. 3 year event free survival (EFS) and overall survival (OS) were noted and outcomes were correlated with stage, and post-surgery margin status.

Results: Fifty nine children were diagnosed as NRSTS, including 15 (25%) synovial sarcoma, 11 (18.5%) undifferentiated sarcoma, 6 (10%) alveolar soft part sarcoma, 10 (16%) lipoblastoma, 6 (10%) malignant peripheral nerve sheath tumor, 3 (5%) dermatofibrosarcoma protuberance, 3 (5%) inflammatory myofibroblastic tumor, 1 (1.5%) each clear cell sarcoma, pleomorphic sarcoma, embryonal sarcoma of liver, fibromyxoma, chondrosarcoma, infantile fibrosarcoma, and fibromatosis. Mean age at the time of presentation was 100 months (Range 1 - 168). All children underwent surgery; 23 (41%) and 16 (28%) children received chemotherapy and radiation, respectively. Twenty (34%), seventeen (29%), twenty (34%) and two (3%) children had group I, II, III and IV disease, respectively. There were 5 (9%), 23 (39%), 29 (49%) and 2 (3%) children with stage I, II, III and IV disease, respectively. Four patients were lost to follow up. Out of 55 children who received treatment, 10 died, due to relapse or progres-

sive disease. At median follow up of 46 months (Range 0-143) 3 year EFS and OS were 72.9% and 84.6%, respectively. 3 year EFS for stage I, II, III and IV disease was 100%, 84%, 63.4%, 50%, respectively (P=0.146). 3 year OS for stage I, II, III and IV disease was 100%, 94.4%, 74.2%, 100%, respectively (P=0.2). 3 year OS with post-operative margin positive and negative status was 71.3% and 91.3%, respectively (P=0.004).

Conclusions: Pediatric NRSTS in India have good outcomes. Children with post-operative margin positivity had inferior survival.

PO185 SIOP19-1703 | Congenital Infantile Fibrosarcoma Mimicking a Vascular Lesion

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Background/Objectives: Infantile fibrosarcoma accounts for approximately 25-30% of soft tissue malignancies in children younger than 1 year, and mostly located in extremities. We present a newborn with a rapidly growing mass on her hand.

Design/Methods: A 20-day-old girl was admitted to our unit for a mass surrounded by a colored area from pink to purple with fluctuation and warm to touch on the dorsum of the right hand. This mass had been detected at the birth, the lesion had grown to a mass (37x42 mm), and she was referred to our unit as a vascular lesion.

Results: Ultrasonography was compatible with a vascular lesion as well. She had not got extra lesion, and all laboratory evaluation (CBC, PT, aPTT, fibrinogen, AFP, beta-HCG, cranial, abdominal USG) was normal except abnormal thyroid function tests (FT4:0.37 pg/ml, TSH:49 mU/L). After the cardiac evaluation, propranolol and levothyroxine was started at the 3rd day of admission, and MRI of the hand was planned at the same time. However, the lesion did not show clinical improvement, and the first signs of compartment syndrome developed in one week of the therapy. There was a solid component and hemorrhage in the invasive soft tissue mass at the MRI, and the urgent surgery was done. However, partial excision was possible, and the congenital infantile fibrosarcoma was diagnosed. Initial metastatic workup was negative, Vincristine and actinomycin-D (VA) was started, however, she had residual lesion after the five courses, and the surgery was impossible. The cyclophosphamide therapy was added (VAC therapy), but, the surgery was not possible, again due to the last MRI findings (minimal residual invasive appearance without a mass) at the 6th VAC. She is currently on

VAC therapy, she will be re-evaluated after the next three courses.

Conclusions: In conclusion, congenital infantile fibrosarcoma may sometimes resemble vascular lesions. However, the onset, morphology, and growth pattern are different and they must be evaluated histologically for an exact diagnosis.

PO186 SIOP19-0190 | The Clinical Characteristics and Prognosis of Pediatric Non-Rhabdomyosarcoma Soft Tissue Sarcomas-A Study of Single Institutional Series

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Background/Objectives: Objective: Analyzing the clinical features and prognosis of non rhabdomyosarcoma (NRSTS) in children, to her understand these tumors.

Design/Methods: Methods: From June 2011 to May 2018, 29 children with NRSTS were admitted to our hospital. The clinical and pathological data of the children were collected, and the relationship between clinical characteristics, IRS-surgical pathologic group system (IPGS), COG risk group and prognosis was analyzed. The follow-up ended on 31 October 2018. The survival analysis was performed by Kaplan-Meier method.

Results: There were 14 males and 15 females, aged from 7 to 169 months, with a median age of 59.5 months. There were 10 pathological types. There IPGS stage I and II in 12 cases, stage III and IV in 17 cases.

9 cases received preoperative chemotherapy, 17 cases received postoperative chemotherapy, 3 cases could not be resected surgically, and 9 cases had not been completely resected surgically. The follow-up period ranged from 4 to 89 months, with a median of 16 months. Six of 29 children died, including 3 cases of malignant rhabdomyoid sarcoma. The 2-year OS was 77.6% and the 2-year EFS was 53.2%. By analyzing the factors influencing survival, it was found that the IPGS, COG risk group, primary site were related to prognosis. The 2-year EFS of children with IPGS I-II and III-IV were 75.0% and 35.9%, respectively ($P=0.007$), the 2-year OS was 100% and 61.8% ($P=0.028$); The 2-year EFS in COG low and median/high-risk was 66.7% and 44.7% respectively ($P=0.042$), the 2-year OS in COG low and median/high-risk was 100% and 66.3% respectively ($P=0.066$); The 2-year OS in visceral and non-visceral sites was 59.3% and 92.9% respectively ($P=0.04$).

Conclusions: NRSTS in children is heterogeneous. The 2-year OS was 77.6% and the 2-year EFS was 53.2%. Location of visceral sites, IPSGIII-IV were associate with poorer outcomes.

Survivorship

PO187 SIOP19-1337 | Adolescents and School Teachers Conceptions About the Adolescent Body After Cancer Treatment: An Education Dialogue in the School

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Background/Objectives: The progressive increase of cure of child-youth cancer opens strand for studies related to the post-cancer treatment moment, including full reintegration into school. to describe the conceptions of adolescents and teachers about school inclusion of an adolescent after cancer treatment; to implement a group and participatory approach, as a strategy to problematize adolescents' school inclusion after cancer treatment; to analyze the implications of this approach in the promotion of health mediated by the practices of coexistence among.

Design/Methods: Participatory research with qualitative approach and creative and sensitive method with 10 participants, being 4 teachers, 5 students/adolescents and an index case. To produce data, we used creativity and sensitivity dynamics talking map, ethnographic encounters and description of the index case. Data analysis was with Bardin's thematic content. Respecting ethical aspects, there was ethical committees approval from the proposing institution and the hospital institution of the index case. Awareness process, as well as the sociohistorical theory were theoretical lenses.

Results: The index case was an adolescent with altered body image derived from oncological diagnosis and treatment; the conceptions of adolescents and teachers revealed the expectation of the adolescent index to be "made fun of" on arrival at the new school, the initiatives of reception and diswelcoming by peers; the application of participative educational action generated expectations in the index adolescent of being accepted and attitudes compatible with the concreteness of apprehension of the reality in the pairs.

Conclusions: The participative educational action collaborated in the process of transition from hospital to school, mediating development with instrument and signs, leading adolescents through the proximal zone of development to the critical transitivity of consciousness in the promotion of the socio-scholar inclusion of an adolescent in post-treatment of cancer.

PO188 SIOP19-0052 | Challenges Childhood Cancer Patients and Survivors Face Pursuing Post-Secondary Education

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Background/Objectives: As a childhood cancer survivor myself, I am interested in determining the challenges other patients and survivors face in pursuing a post-secondary education and how these could be addressed and supported. The treatment of childhood cancer greatly affects the quality of life of childhood cancer survivors, and as a result, survivors are faced with significant late effects. As the childhood cancer survivorship population grows, I want to assist in enhancing the support and reduce the challenges this population encounters in the pursuit of their post-secondary education.

Design/Methods: A study was conducted of families who patient/survivor was 17 year of age or older within the Candlelighters' member database. An explanation letter and survey invitation was sent out to 150 families which consisted of 18 questions regarding the patient/survivor of childhood cancer and their pursuit of a post-secondary education.

Results: The 40 survey respondents were comprised of 77.50% parents and 22.50% patients/survivors. Respondents reported the average age at diagnosis was 10.85 years of age and 20.95 years of age currently. The 87.50% majority of respondents are planning on attending, currently attending or have already attended post-secondary education. Of the 55.00% currently or having previously attended a post-secondary institution, 81.82% of these students needed financial assistance. Candlelighters offers a financial support bursary of which 82.50% of surveyed members were aware. Other needs highlighted were 39.47% said providing equipment, technology and toolkits as well as 34.21% said providing workshops and educational fairs would assist in the pursuit.

Conclusions: As a childhood cancer survivor, I know firsthand that childhood cancer patients/survivors experience various challenges and require different forms of support in their pursuit of a post-secondary education. Candlelighters support of continuing education through a bursary is a valuable assistance and Candlelighters could expand support by providing workshops, equipment and assistance with applications as well as continued financial assistance.

PO189 SIOP19-1322 | Evaluation of Quality of Life and Sociodemographic Characteristics of Patients Between the Ages of 5-18 Following with Childhood Sarcoma

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Background/Objectives: In this study, we aimed to identify and compare the physical and psychosocial quality of life of childhood sarcoma patients by using the data obtained from them and their parents.

Design/Methods: A total of 155 children (64 patients with sarcomas, 91 healthy control) have been included in the study. Data were collected between June 2017 and September 2018. The patient group consisted of the pediatric patients diagnosed with sarcoma between the ages of 5 and 18 and their parents. The control group consisted of the healthy children aged 5-18 years and their parents. PedsQL form, which is appropriate for children's age, was applied to children and their parents.

Results: According to PedsQL scores, the patients reported the lowest quality of life in Physical Health subdimension, while their parents reported the lowest quality of life in School Functioning subdimension. When the patient and the healthy group were compared, the patients had lower quality score than the healthy children for the Physical Health, School Functioning and Total PedsQL. In parental form, only Physical Health scores was significantly lower for the patient group. According to comparison for the scores between sub groups of the treatment status variable, the quality of life of the patients whose on treatment process was lower than the patients whose treatment were ended.

Conclusions: We found that pediatric sarcoma patients had lower Physical Health, School Functioning, and Total PedsQL scores than the healthy children. Additionally, we observed that continuation of the treatment may be a reason of difference in quality of life. Although we have some limitations due to sample size, we believe that our study provides a preliminary data for the larger studies should be carried out in this area.

PO190 SIOP19-0233 | The Influence of Different Intensity of Treatment on Hormonal Markers of Gonadal Function In Survivors of Acute Lymphoblastic Leukemia

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Background/Objectives: Gonads are susceptible to the deleterious effect of anticancer therapy, which essentially can lead to oligospermia in males and in females can induce ovarian insufficiency due to depletion in the number of oocytes. The treatment for acute lymphoblastic leukemia (ALL) represents a low risk of gonadotoxicity and the probability of infertility is less than 20%.

We analysed hormonal markers of gonadal function in adolescents - leukemia survivors, treated during childhood with the protocols of different aggressiveness.

Design/Methods: In sixty nine adolescents and young adults, leukemia survivors (44 males) treated with BFM protocols, stratified into standard (SR), intermediate (IR) and high (HR) risk groups and 80 healthy controls (38 men) at a similar age we analyzed hormone levels: in whole group - FSH, LH, inhibin B; in males - testosterone; in females- E2 and anti-Müllerian hormone (AMH). Fifteen males and six females had received cranial radiotherapy (12 or 18 Gy).

Results: Males classified into HR group presented, in comparison to control, higher FSH values ($p=0.001$), LH ($p=0.001$), lower inhibin B ($p=0.015$) and normal testosterone, whereas in SR and IR group the hormonal values were comparable to control. In females, in all risk groups, the levels of FSH, LH, E2 and inhibin B were comparable with the control but the mean AMH levels were lowered ($p=0.016$). We did not observe the effect of prophylactic cranial irradiation, the time of treatment (before vs. during puberty) on hormone levels. In females, a positive correlation was found between the time interval after the end of treatment and AMH levels.

Conclusions: Male leukemia survivors having undergone more intensive chemotherapy present the symptoms of disturbed spermatogenesis and need a follow-up in the future. Women, irrespective of the risk groups, can develop the signs of preterm ovarian insufficiency. They should be informed about the impact of the treatment on gonadal function.

PO191 SIOP19-0954 | Late Effects in Survivors of Childhood Cancer in a Tertiary Hospital in Veracruz, Mexico

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Background/Objectives: Cancer is a leading cause of death in children globally. Its impact on morbidity among survivors is now also better established, in high-income-countries (HIC). However, little is known about long-term morbidity in low-and-middle-income countries (LMIC). Mexico is not

an exception; a study in 2018 showed that only 13% out of 74 hospitals had records of clinical late effects. This study aimed to describe adverse late effects in survivors of childhood cancer in a tertiary hospital in Veracruz, Mexico.

Design/Methods: This cross-sectional retrospective study evaluated the medical records of 133 consecutive survivors of childhood cancer (all pathologies) who transitioned to survivorship care between 2005 and 2010. Survivors included were 1-19 years old. Data was collected using a standardized case form. Patients with incomplete records, deaths unrelated to cancer, or relapse were excluded.

Results: Of 133 records identified, 108 were included. Survivors transitioned at an average age of 10 years (SD 5.1 years). Survivors were predominantly male (59.3%), 5.2 years (1.4-10.8 years) out from treatment completion, and treated for ALL (29.6%), germ cell tumors (15.7%) and Hodgkin lymphoma (11.1%). Most survivors (82.4%) experienced at least one physical adverse late effect, including all solid tumor (100%), lymphoma (71.8%) and acute leukemia (60%) survivors. The most frequent late effects noted were endocrine-metabolic (obesity, 33.7%), stomatological (dental cavities, 25.8%) and reproductive (phimosis and ovarian cysts, 20.2%). The most immediate late effects were respiratory and cardiovascular, with average onset of 6 and 8 months, respectively.

Conclusions: This study documents a high frequency of adverse late effects among childhood cancer survivors at a single institution in Mexico. This, despite age and follow-up being considerably shorter than in large cohort studies from HIC. It also serves as evidence that this information can be collected in LMIC and can help understand the burden of childhood cancer.

PO192 SIOP19-0468 | Effectiveness of Acupuncture in the Management of Chemotherapy-Induced Tinnitus in Pediatric Patients and Survivors: A Case Series

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Background/Objectives: The last several decades have seen a growing interest and steady increase in the use of complementary and alternative medicine (CAM) in the United States. The use of acupuncture as a complementary therapy for patients undergoing treatment for cancer has been demonstrated. Certain chemotherapeutic agents may damage the inner ear structures, specifically the cochlea. Patients receiving ototoxic chemotherapeutic drugs may experience hearing loss, vestibular dysfunction and tinnitus, which may decrease quality of life and hinder workplace performance.

Several studies have shown that acupuncture may be effective in reducing the intensity and severity of tinnitus.

We examined the effectiveness of acupuncture as a supportive care option during and after chemotherapy to lessen the severity of chemotherapy-related tinnitus.

Design/Methods: Three long-term pediatric cancer survivors who were identified to have chemotherapy-related tinnitus and one adolescent/young adult patient currently receiving ototoxic chemotherapy completed the Tinnitus Handicap Inventory (THI) prior to each acupuncture visit. Patients received acupuncture weekly for at least four weeks.

Results: A course of acupuncture treatments was shown to improve and/or prevent tinnitus in all patients. Patient-perceived benefit did not correlate with THI score. Followup suggests that tinnitus symptoms may return without ongoing acupuncture maintenance therapy.

Conclusions: Acupuncture may be an effective tool for the treatment of chemotherapy-related tinnitus. However, continued acupuncture may be necessary for sustained symptom management. Further study is warranted.

PO193 SIOP19-1230 | Xerostomia in Children and Adolescents Treated of Malignant Neoplasms

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Background/Objectives: The fight against xerostomia-related diseases is a priority because it has a considerable impact on the state of hard dental tissues, and this, in turn, affects the psycho-emotional state and social adaptation.

Objective: To analyze the prevalence, intensity and nature of damage to the salivary glands after chemotherapy and radiation therapy during the rehabilitation period of convalescents of malignant tumors.

Design/Methods: During the period from January 2018 to February 2019 in the Clinical Rehabilitation Research Center "Russkoye polle" a routine examination was performed in 27 patients who had undergone treatment for malignant neoplasms in remission for 2 or more years. The duration of remission is 4.9 ± 1.95 . The median age of patients at the time of the research ranged from 3 to 17 years, $M 8 \pm 2.3$. In the examined group, 23 patients received radiation therapy, as in combination with chemotherapy and / or surgery: acute lymphoblastic leukemia 12 Gray; CNS tumors and soft tissue head-neck tumors 35 - 90 gray; total irradiation before bone marrow transplantation of 12 Gray to the site. 4 patients received treatment without radiation therapy.

Results: The dentist from Clinical Rehabilitation Research Center in patients revealed changes in the function of the salivary glands. Xerostomia, focal demineralization (white spots), and carious lesions of the teeth were detected in 85% of patients. So complicated condition depends on deficiency saliva due to its composition and physicochemical properties is necessary to preserve the health of the oral cavity and teeth.

Conclusions: Xerostomia caused by radiation or chemotherapy or combine in cancer patients is difficult to treat. This is due to the fact that the treatment induces the necrosis of acinar parenchyma - an actively secreting organ. Therefore, it is necessary to conduct a more detailed study in the period of the follow-up and rehabilitation of patients.

PO194 SIOP19-0047 | Experiences and Opinions on Breaking Bad News; A Survey on Childhood Cancer Survivors and Their Parents

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Background/Objectives: PURPOSE: The purpose of this study is that childhood cancer survivors and their parents who had diagnosed cancer in relation to awareness of how to know about the cancer diagnosis, and the preference for cancer diagnosis disclosure is intended to identify.

Design/Methods: METHODS: A survey was conducted of patients and their family members who were diagnosed with childhood cancer by pathologic diagnosis at 10 cancer institutes from July of 2011 to January of 2012. Patients with multiple original carcinogenesis of tumor and a history of psychiatric illness were excluded. All patients experienced one or more treatments of chemotherapy, radiation therapy, or surgery.

Results: We survey 283 dyads of pediatric cancer survivors aged 10 to 24 years and their parents answered multiple choice questions, respectively. Two hundred five parents (76%) knew about their child's diagnosis, cancer survivors were 99 survivors (35%) knew about their diagnosis. One hundred thirty-four parents (45.7%) wanted physicians to explain the treatment plan and prognosis, and also to inform the survivors. In contrast, 106 parents (36.2%) wanted to hear the diagnosis first and to explain their children Department of Pediatrics, Cancer Research Institute by themselves. Fifty parents (17.1%) wanted physicians to explain directly to their children, and the other 3 parents (0.01%) didn't want to inform about the diagnosis to the children. Among the 193 survivors,

112 survivors (39.5%) was informed the cancer diagnosis by the parents, and 35 survivors (12.4%) was informed by the physician, respectively.

Conclusions: Health care providers should effectively convey information that is tailored to the emotional needs of patients and their families who have experienced a never before experience of being diagnosed with cancer. The role of being able to motivate their active participation for treatment is important.

PO195 SIOP19-0548 | Thirteen Years' Experience of Pediatric Abdominal Mass and Analysis of Associated Factors Affecting Repeated Operation

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Background/Objectives: To investigate the clinical characteristics of abdominal tumor and to analyze the associated factors affecting repeated operation for abdominal malignancies in pediatric population.

Design/Methods: Retrospective chart review was performed from January 2005 to December 2017 for patients who underwent surgery for abdominal tumor at Seoul National University Children's Hospital. Patients' characteristics, tumor location, tumor size, method of operation, intent of operation, total number of operation, pathologic result, secondary tumor, and follow-up data were investigated. Survival curves were obtained with Kaplan-Meier estimator. *P*-values < 0.05 were considered statistically significant.

Results: Among 16,719 operations, 15,648 operations irrelevant to abdominal tumor were excluded. After detailed review of pathologic results and operation note, 792 operations in 662 patients were identified for abdominal tumor. Median age was 4 years old. The number of male was 252 (38.1%). The number of malignancy was 340 (51.4%). The number of patients who underwent surgery at least 2 times was 119 (18.0%). Mature teratoma and ovarian cyst were common benign tumor. Neuroblastoma and hepatoblastoma were common malignant tumor. The number of patients who occurred secondary tumor was 23. Tumor location was significantly different, more in ovary and pancreas for non-repeated group and more in retroperitoneum in repeated group (*p*=0.014). Diagnosis was not different significantly (*p*=0.183). Secondary tumors were more in repeated group than in non-repeated group (15.6% vs 3.3%, *p*<0.001). The 5-year survival rate for patients with malignant tumor was 80.3%. Survival rate was significantly different according to age, diagnosis, location, intent of operation, and reoperation. In multivariate

analysis, reoperation and liver location were significant factors affecting survival.

Conclusions: Various tumors were occurred in pediatric population. Repeated operation for abdominal malignancies was associated with tumor location and development of secondary tumor, and poor survival. Long term surveillance for detecting secondary tumor is needed in patients who underwent repeated operation for abdominal malignancies.

Treatment and Care - New Drugs - Experimental Therapeutics

PO196 SIOP19-0675 | Trametinib Use in Pediatric Patients in a Single Institution

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Background/Objectives: MAPK pathway mutations are described in Plexiform Neurofibromas (PN), histiocytosis (LCH), low grade gliomas (LGG), glioblastomas and melanomas among others in pediatrics patients (pts.)

Objective: to report our experience with trametinib (single agent or associated with dabrafenib) in patients with PN, LCH and LGG.

Design/Methods: We reviewed the reports of patients with known alteration of mapk pathway tumors, and treated with inhibitors after standard treatments due to several relapses, refractoriness or progression.

Results: Six patients, 4 with NP associated with type 1 neurofibromatosis (all with compromised head and neck), 1 with LCH, 1 with LGG (BRAF V600+, optical pathway).

The median age of the patients at the start of treatment was 7 yrs. old (range 6-18 yrs.), 3 were women.

In 5 patients it was used as single drug, 1 associated with dabrafenib. Median of Previous treatment lines: 2 (range 1-6). The median time the drug was used was 7 Months (range 4-16 mo).

Response: complete remission 1 pt. (LCH), 4 partial responses (in PN) 1 stable disease (LGG) with clinical improvement. In 2 pts. with PN the treatment allowed the surgical resection and improve the Life Quality.

Toxicities: dermatological GRADE 1-2 in 3 patients.

Currently all patients continue in treatment.

Conclusions: Trametinib was useful drug in this group of patients, with diverse pathologies with known alterations of the MAPK pathway, when standard treatment failure and with acceptable toxicity. Its role in standard of first lines treatments, should be defined in future investigations.

PO197 SIOP19-1395 | How Children's Cancer Center in Gothenburg have Implemented Early Research Studies (Phase I and Phase II) in the Regular Care

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Background/Objectives: In 2017, we were accredited to ITCC (Innovative Therapies for Children with Cancer). Decisions were made that we would receiving research studies in an early phase (phase I / II) and that this would be part of regular cancer care for children. All staff in the ward and day care department was trained to understand GCP (Good Clinical Practices) / the Helsinki Declaration, study procedures, research ethics and basic principles. Research coordinators' work changed to more teaching and participating.

Design/Methods: First we did a survey of what was needed to change and improve in order to start phase I / II studies.

Results: Our start was to revise the SOPs (Standard Operation Procedure). We monitored our action regarding clinical trials flow and changed how we receive study inquiry. We started training of the staff in a three-step training. Step 1: Why research studies and study ethics (one hour). Step 2: Basic research principles (one hour). Step 3: Good Clinical Practices (GCP) / Helsinki Declaration, study procedure (one full day). Affected personnel are invited to start up meetings before the start of study. Expansion from 3 up to 6 research coordinators. Research coordinators prepare everything in the studies and supervise the staff responsible for nursing and responsible for patients. Research coordinators are not closest to the patient but are available at the department to help with all study related work.

Conclusions: Research studies are now a part of the everyday work with the patient in childhood cancer care in Gothenburg. The nursing staff feel safer and more knowledgeable in participation of studies and positive to the fact that the research coordinators are involved with support and preparation in the department.

PO198 SIOP19-0590 | Institutional Review Boards (IRBS)/Ethics Committees (ECS) are not Prepared to Correctly Assess the Scientific and Clinical Value of Pediatric Studies Demanded by Regulatory Authorities

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Background/Objectives: In 2016, two "pediatric" studies in adolescents with metastasized melanoma had to be terminated because recruitment waned. One study (ipilimumab)

was FDA-rewarded, both (ipilimumab; vemurafenib) were EU pediatric investigation plan (PIP)-demanded. Both offered monotherapy when combination treatment had become standard-of-care. Both recruited worldwide. Both should never have started. Why were they not rejected by IRBs/ECs?

Design/Methods: FDA documents, the academic ipilimumab study publication, and the www.clinicaltrials.gov documentation of both studies were analyzed on the background of the history of drug development, US/EU pediatric legislation, and current discussion of "pediatric drug development".

Results: Despite contrary FDA/EMA claims, the terminated studies were neither "pediatric", nor is conventional melanoma in adolescents "pediatric", nor offered the studies standard-of-care treatment. Bodily, the patients were mature humans, but they were administratively FDA/EMA-classified as "children". Increasing off-label prescription of standard-of-care combination treatment was the reason that finally recruitment waned. The ipilimumab academic study publication avoids to admit that the study was questionable from the beginning, but recommends for the future inclusion of adolescents with melanoma into adult pivotal studies. Meanwhile, the FDA recommends in general inclusion of adolescents with malignancies into adult studies. The EMA continues to adamantly demand separate "pediatric" studies; many PIP-triggered questionable studies recruit currently worldwide.

Conclusions: Chronological definition of "children" (FDA <17y, EU <18y) and separate drug approval in "children" deny young patients standard-of-care treatment, the precise opposite of FDA/EMA justifications for "pediatric" activism. IRBs/ECs are not aware of this challenge and continue to approve questionable "pediatric" studies in the illusion that FDA/EMA study demands guarantee their medical sense. IRBs/ECs need urgently training in US/EU pediatric legislation, should be alerted to questionable "pediatric" studies, should suspend ongoing questionable studies and reject new ones. Researchers should refuse to participate in questionable EMA/FDA-demanded "pediatric" studies. US/EU pediatric laws need to be revised.

PO199 SIOP19-0702 | "Druggable" Events or Alterations in Pediatric Cancers are Clinically Empty Promises. They Prepare Research Grants and Questionable "Pediatric" Cancer Studies Demanded by Regulatory Authorities

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Background/Objectives: A recent "Nature" publication on the "landscape of genomic alterations across childhood cancers" claims half of pediatric neoplasms harbour "potentially druggable events". Other publications speak of

“druggable genetic alterations”. Clinically, few cancers are truly “druggable”.

What is the potential intention of such statements?

Design/Methods: The use of the word “druggable” in pediatric cancer publications was investigated for scientific substance and proposed consequences in the light of medical breakthroughs like tisagenlecleucel for acute lymphoblastic leukemia (ALL).

Results: Most publications on childhood cancers fail to define “pediatric”. Cancer in patients <25-years-old are described as “pediatric”. But cancer in a 16-years-old patient is not automatically “pediatric”. Blurring legal, administrative and physiological meanings of “pediatric” allows circular argumentation: pediatric cancer is what pediatric oncologists define as pediatric cancer. The Food and Drug Administration (FDA) now recommends including adolescent ALL or melanoma patients into adult studies. Tisagenlecleucel was not a “pediatric”, but a medical breakthrough.

Pediatric oncology evolved as a societal effort, facilitated by chemotherapeutics working both in adults and children. Its early successes did not result in pediatric labels. Today, true innovation needs regulatory approval. But FDA/ European Medicines Agency (EMA) approve drugs separately in adults and “children”, defined as <17y (FDA)/ <18y (EMA). Today, regulatory approval is needed for medical breakthroughs.

The EMA demands separate “pediatric” studies, often in cancer types different from targeted adult cancers. Such studies copy crudely early pediatric oncology, assuming precision medicines will help in biologically different “pediatric” cancers. From 2020 on, also the FDA will make such demands.

Conclusions: “Druggable” events in “pediatric” cancer fail to address the administrative definition of “pediatric”. These wordings are used to endorse FDA/EMA-demanded “pediatric” studies that guarantee industry funds, but will not advance treatment. Researchers should refuse to participate in questionable “pediatric” studies. Ethics committees should suspend questionable studies, reject new ones.

Treatment and Care - Nursing

PO200 SIOP19-0337 | Evaluation of Transfusional Practices in Pediatric Hematology and Oncology Department of Marrakesh

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Background/Objectives: Blood transfusion is a routine practice in the pediatric hematology & oncology department; this requires a perfect knowledge of the staff with its daily practice given the risk of serious accident.

Design/Methods: Study conducted from September 1st to October 1st 2018, using questionnaire dedicated to all nurses and residents in our center, to identify how they deal with blood transfusion.

Results: Study population made up of medical specialists (9%), resident physicians (31%), nurses (50%). Sixty one per cent of persons interviewed did not receive training on blood transfusion, which means that knowledge of blood transfusion was inadequate in 42.6% and poorly understood in 35.3% of cases. Absence of systematic and rigorous verification of the identity registered on the recipient (23% of cases). No continuous monitoring for the first 15 minutes founded in only 50% of cases. Pretransfusional control in patient room registered in 80% of cases. Misapprehension of purpose and rules of interpretation of Pretransfusional control in 17% of cases. But, the management of transfusion accident was good and mastered for almost 99 percent of staff

Conclusions: According to our study, we found that there was a weakness management of blood transfusion practices, with an insufficient training on this field.

PO201 SIOP19-0709 | Parents' Attitude to the "Tranquil Turtle", as a Remedy, Against Post-Operative Fatigue in Young Brain Tumour Surgery Patients

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Background/Objectives: After neurosurgical surgery, most patients suffer from postoperative fatigue. Previous studies show that mindfulness can help against this problem. At the Children's Cancer Centre in Gothenburg, a "rehab toy", Tranquil Turtle, has been distributed to children who have been operated for brain tumours for the past 1.5 years. The hard shell of the Turtle gives off a bluish light, which gives the impression of being under water. Moreover, the Turtle can play a soothing wave noise or a quiet relaxation sound. The toy has then been given to the families as a gift to take home for continued use after hospitalization. The intention has been to bring opportunities to talk about fatigue and the need for a long rest after a neurosurgical operation, but the turtle has also, with its special features, been meant to aid in the actual rehabilitation of the patients. The aim of this study was to evaluate whether the "Tranquil Turtle" was appreciated by the children's parents.

Design/Methods: We asked 14 parents about how much each child had used the "Tranquil Turtle", and whether the parents would recommend it to others.

Results: We found that the toy was used and appreciated by 13 of the patients, although the time of using the Turtle varied from only the first week after operation to still using it one year later. All 14 parents said that they would recommend this rehab toy to others in the same situation.

Conclusions: The Tranquil Turtle was appreciated by the parents of the post-operative patients, and they would recommend it to others in the same situation. The Turtle may thus be a helpful tool for caregivers in discussing fatigue with young patients and their parents.

PO202 SIOP19-0741 | Evaluation of New Bio-Clean Rooms in a Children's Hospital in Japan

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Background/Objectives: Patients receiving hematopoietic cell transplantation spend many hours in bioclean rooms to protect them from infection. The psychosomatic distress experienced by children during the stay in bio-clean rooms is immeasurable. The recuperative environment of a bio-clean room might relieve stress and improve the quality of life, which might result in increased treatment adherence. It also might increase the success rates of hematopoietic cell transplantation.

Design/Methods: We have recently added two bio-clean rooms to its two existing rooms, and this paper reports the opinions of nurses regarding the comfort provided by the new bio-clean rooms, which was compared to pre-existing bio-clean rooms.

Results: Compared to the pre-existing bio-clean rooms, the new bio-clean rooms have different design aspects, equipment, comfort, and so on that support effective nursing care. Moreover, the patients and their families as well as the nurses benefitted from the friendly environment of the new bio-clean rooms. By installing HEPA filters in the ceilings, the sizes of the rooms were slightly expanded. Toilets that automatically measured urine volumes were installed to facilitate accurate volume monitoring at specified times. This implementation decreased the nursing burden. Installation of a door directly to the corridor enabled prompt transportation of patients during emergencies. Installation of glass windows along the corridor wall lessened the sense of confinement and increased communications with other patients. The feeling of isolation decreased for patients and their families. A 43-inch televisions were installed that increased the entertainment and satisfaction of patients and their families.

Conclusions: Adding new bio-clean rooms is not common because of the effort, time, and cost involved. Further, basic renovations and repairs after they are in use tend to be diffi-

cult. Therefore, widespread sharing of information, nationally and internationally, about high-quality bio-clean rooms can offer suggestions for guidelines to improve the environments of pediatric hematopoietic cell transplantation.

PO203 SIOP19-1203 | To Assess the Compliance to Sample Collection Protocol Among Nurses Working in Pediatric Ward

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Background/Objectives: **Background:** Tata Memorial hospital is a tertiary care oncology hospital where turnover of patients is very high. One of the major and common activities in caring for immune-compromised patient care is frequent venous blood collection (VBC) which is vital component for further and continued treatment. This is also a potential source for errors in healthcare which compromises patient safety.

Objective: To find out the compliance to sample collection protocol among nurses working in pediatric ward.

Design/Methods: **Methods:** Quantitative research with survey to assess the compliance to sample collection practices among 30 nurses working in pediatric ward in Government Hospital. Nurses were selected using convenient sampling. Observation checklist was used to collect data regarding compliance to sample collection protocol.

Results: The major factor for non-compliance were; bypassing the steps of protocol, inappropriate skill mix of nursing professionals, lack of practicing two patient identifiers, specimen transferring from syringes to test tubes. The common time when sample collection error seen was during early morning hours and shift changing time.

Conclusions: Adherence to patient safety practices could be better with better education and training of nursing personnel. Focused sample collection by phlebotomy nurse will improve the sample collection practices

PO204 SIOP19-0993 | How we Implemented Immunotherapy in Nursing Care in Bratislava 2018

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Background/Objectives: Annually in Slovakia there are 150 children diagnosed with cancer, and about 30 ALL and 8-10 neuroblastoma cases. There are three center dedicated to pediatric oncology in Slovakia. Due to new innovation in cancer treatment as is immunotherapy in ALL or in neuroblastoma, during the year 2018 we have introduced immunotherapy also in treatment of our patients.

Design/Methods: Retrospective analyse of implementation immunotherapy in nursing care during the year 2018 in Slovakia, Bratislava.

Results: There were six patients with neuroblastoma treated with Dinutuximab beta, two patients with ALL cured with CARs T-cells, three patients cured by Blinatumomab, two patients cured with Inotuzumab. These four implemented types of immunotherapies were started in Bratislava in 2018.

Conclusions: There are still, however, situations in which children need new therapy. In some countries, like we are, there is not easy to have every possibility which our world is providing to children with cancer. Even we have informations, the process of establishment for new therapy is hard to succeed in the health care system, also from financial side. Educational system for nurses is not focused on oncological therapy. There is lack of nurses speaking English or other language and paediatric oncology is educated in the hospitals during the practice. Without cooperation with other clinics and experts abroad using these therapies there were no possibility to start to use these therapies. We started and now there are still 11 children alive with their families and happy. We can say these children profits not only from the therapy, but also from the cooperation all over the world.

PO205 SIOP19-0973 | When Resources are Limited: Assessment of Sleep Disturbance in Children and Adolescents Undergoing Treatment for Childhood Cancer

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Background/Objectives: Sleep disturbance has been described as one of the most distressing symptoms experienced during cancer therapy and into survivorship. Prevalence of disrupted sleep and fatigue have been reported to be higher among patients treated for CNS tumors, those treated with radiation therapy, solid tumors and Hodgkin Lymphoma; however, changes in sleep patterns have been reported across all cancer diagnoses.

Design/Methods: This presentation will review cancer populations known to be at greatest risk for sleep disturbances, sleep hygiene practices and assessments for sleep disturbances in clinics with limited resources. The nurse will be able to describe the cancer populations most affected with sleep disturbances, common sleep hygiene practices that may be initiated within the hospital and home, and assessments that may be completed in the clinic setting.

Results: The nurse will have a better understanding of nurse-led interventions that may improve sleep and ultimately health-related quality of life (HRQoL)

Conclusions: Sleep disturbances including difficulty maintaining sleep and daytime sleepiness are described as distressing symptoms, significantly impacting the patient's HRQoL. Many patients are never assessed for sleep disturbances due to the lack of resources or available interventions. This presentation will increase the nurses' knowledge of patient populations at greatest risk, sleep hygiene practices for the hospital and home setting, and methods of assessment that may be conducted by the nurse.

PO206 SIOP19-0695 | The Six Aspect Meal Model as a Conceptual Framework in Nursing Research - Childhood Cancer/Stem Cell Transplantation and the Mealtime Situation with a Gastrostomy Tube

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Background/Objectives: Children with cancer undergo an intensive and demanding course of treatment, which can consist of chemotherapy, radiation, surgery or stem cell transplantation, separately or in combinations. The cancer treatment may induce side effects, which negatively affect the child's appetite and ability to eat and drink, thus causing eating problems. Therefore, a gastrostomy tube may be required in order to maintain and optimise the child's nutritional needs. There is limited knowledge and experience of the environment and the mealtime situation for children with cancer who have undergone a stem cell transplantation and required a gastrostomy tube.

Design/Methods: Interviews were developed from semistructured questions and were performed with the aim of investigating the experience of living with a gastrostomy tube, focusing on the mealtime situation. The Six Aspect Meal Model (SAMM) was used as a base in the interview guide. The transcripts were analysed using a qualitative directed content analysis approach.

Results: It emerged that all the different aspects were represented in the interviews, but there were also many experiences related to the gastrostomy tube that did not fit under any of the six predetermined categories. Experiences that were associated with psychosocial dimensions emerged as an important factor with regard to the gastrostomy tube and the mealtime situation. As a result, SAMM needs to be supplemented with one more aspect.

Conclusions: The psychosocial aspect seems to affect the mealtime situation, and it is important to include this in nursing practice. According to the result, SAMM have to be added

with one more aspect in order to meet the children's needs in an optimal way. It seems to be a model which can be transferred and used in clinical nursing practice in order to chart and improve the mealtime situation for those children with cancer who has required a gastrostomy tube.

PO207 SIOP19-0332 | BIL, An Educational Doll to Help Children Understand That They Have Cancer

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Background/Objectives: Announcing the diagnosis is a key part of pediatric oncology because of the enormous effect the cancer will have on the life of the child and family.

Talking about the disease and future treatments can be a huge emotional strain on the child. These topics therefore need to be handled carefully.

Design/Methods: Since the ministerial circular of March 29, 2004 on the organization of care in pediatric oncology, a nurse now spends time with the child discussing the information they received when the diagnosis was given to see how much they have understood.

Results: At the Oscar Lambret Center, in the hope that children will get more out of this consultation, and to help identify the different fears that illness and medical procedures bring out, we introduced an educational doll, BIL. The doll is used with children aged 4 to 7 or more by a nurse and a psychologist, with the parents present, a few days after the diagnosis is announced. One is the "puppeteer", giving the medical information, while the other is a non-silent observer who pays attention to non-verbal language. Their role is to build trust and encourage the child to speak and play.

Conclusions: With this tool, children show what they are feeling through play, and can stage how they see the medical world to explore it, better understand it and make it less frightening. In other words, it protects the child from a direct immediate connection with reality. This is what makes this tool so useful in pediatric oncology.

PO208 SIOP19-1606 | Patients' and Families' Experiences of Care Between Primary Treatment Centres and Paediatric Oncology Shared Care Units

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Background/Objectives: The objective of this exercise was to ascertain what, if any, differences in the perception of care offered by Primary Treatment Centres (PTCs) and Paediatric Oncology Shared Care Units (POSCUs).

Design/Methods: Informal discussions were held with patients and their families at their POSCU during oncology outpatient clinics for patients receiving chemotherapy as part of their treatment protocols.

Results: It was anticipated that the busy nature of the PTC would mean that patients and families would be given less time and that continuity of care by the same health professional might be an issue. What was not expected was the strength and universal nature of negative feeling expressed by both patients and families and particularly the fact that all complained of a feeling of lack of welcome. In contrast there was overwhelming positive feedback for all aspects of the care provided by the POSCU save, inevitably for the occasional time delay.

Conclusions: In conclusion, the PTC must strive to offer a more personalised service whilst at the same time accommodating the far greater number of patients that are seen. It also highlights that the POSCU offers an invaluable service to its patients and families.

PO209 SIOP19-0264 | Factors for Grief Support to Hospitalized School-Aged Children in Japan

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Background/Objectives: To identify factors for grief support to hospitalized school-aged children.

Design/Methods: Semi-structured interviews were conducted with four nurses who provided care to school-aged children when a peer died from illness; all nurses consented to participate in the interview. A verbatim record of obtained data was created, and Data were classified in terms of grief support to school-aged children. In effort to prevent bias, the study was conducted by three pediatric nursing researchers. The study protocol was approved by the Ethical Review Board of the researchers' affiliated institution.

Results: The following 10 categories of grief support to hospitalized school-aged children were identified: (1) Consulting with the family and medical staff to decide whether to inform the children; (2) Deciding whether to inform the children depending on their stage of development and condition; (3) The family and medical staff are in a calm state while informing the children; (4) All individuals involved with the child provide support; (5) All individuals involved with the child keep check on the child and act when necessary; (6) Providing support while respecting the intentions of the child and their family; (7) Staying by the child's side when a peer dies; (8) Sharing the same thoughts as the child; (9) Creating an

environment in which children can easily express themselves; and (10) Paying attention to the response of children when informed of a peer's death.

Conclusions: From the ten categories, We identified three factors of grief support to school-aged children when a peer dies, including "grief support policy," "premise for providing grief support," and "specific care in grief support."

PO210 SIOP19-0113 | The Experience of Adolescents with Cancer Involve Their Cancer Treatments: Let Love Make Decisions

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Background/Objectives: adolescents have their rights to be involved their treatment decision making. However, health teams and parents desire to shield them from distressing information.

Design/Methods: Adolescent participants between 15 and 18 years of age receiving cancer treatment at medical centers in Taiwan were interviewed. Their interview data was analyzed qualitatively to identify meaning with regard to participation in medical communication and/or decision-making.

Results: Two major themes emerged: 1) Be healthy again, which included fully corporation, active inquiry, and be responsible; 2) Gain control, which included negotiation, and involvement. Participants highlighted how their roles in health care discussions varied from direct participation to indirect involvement. Overall, doctors and parents decided their level of involvement communication and/or decision-making. Challenges with regard to the minority and parents' concerns were identified. Love and trust were key components during cancer treatments.

Conclusions: The preferred level of involvement oscillated between participants as well as within one and the same child across time. Participants generally valued their participation but some may choose to shy from distressing information. Future research need to develop the best clinical care model based on the level of participants needs.

Treatment and Care - Palliative Care

PO212 SIOP19-0437 | Integrating Palliative Care in a Pediatric Oncology Approach. A Project of the Franco-African Group of Pediatric Oncology (GFAOP) Supported by the my Child Matters Program

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Background/Objectives: The GFAOP has supported the development of pediatric oncology units (UP) throughout french speaking africa. Despite steady improvements, cure rate remains far below those reported in High Income Countries (HIC), and symptomatic treatment and family centered care are often neglected. To adress this situation a three-year training program aims to integrate palliative care in clinical approach of all UP was launched. As it goes to its end, are lessons to be learned and which ones?

Design/Methods: This program targeting healthcare professionals was designed by a core group of French and African teachers. It consisted of 3 steps: 5-day initial training in 3 different cities, evaluation of implementation, and deepening of selected topics. To access this program, each volunteer unit delegated a team of multidisciplinary trainees to carry out a project for improving care in the field of pain and / or palliative care and for ensuring its implementation.

Results: The initial sessions brought together 65 caregivers representing 18 UPs from 15 different countries. The interim assessment performed in all units by questionnaire and/or in situ visits revealed that half units had started to implement their project. Those active teams were invited to deepen their knowledge during a group session. For the other teams, we found they would benefit more from practical on-site training to enable them to identify the specific barriers to implementation and find ways of overcoming them.

Conclusions: In HIC, it has been slowly admitted that palliative care skills should be primary skills in oncology. Our mitigated results remind us that the transferability of knowledge acquired in HIC to other economic and socio-cultural contexts requires a wide range of skills, rooted in diverse or unknown realities, organized in a pragmatic way. But it also provides an opportunity for a bilateral reflexive practice without which we can never hope to provide good care.

PO213 SIOP19-0035 | Referral Practices of Oncologists and Hematologists to Pediatric Palliative Care

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Background/Objectives: Pediatric palliative care (PPC) is an active holistic care that promotes the quality of life and the alleviation of suffering, regardless of the stage of the disease and comprehensively addresses the physical, psychosocial and spiritual needs of the child and the family. Our objective was to describe the referral practices and attitudes of pediatric oncologists and hematologists to the palliative care service.

Design/Methods: Survey-type study that included the anonymous participation of Pediatric Hematologists members of the Mexican Association for the Study of Hematology (AMEH) and Pediatric Oncologists members of the Mexican Association of Oncology and Pediatric Hematology (AMOHP)

Results: The response rate was 29.5%, participants were between 40 to 59 years old (62%). The results showed that 84% during their residency in hematology or pediatric oncology, did not have a rotation in PPC. 62% of the respondents had a PPC unit in their hospital, 51% responded to have an exclusively pediatric pain and palliative clinic, 26% of respondents always refer to patients, 49% do so when there is a life expectancy between 1 and 6 months. 84% of respondents feel more comfortable changing the term PPC as quality of life team, 42% of respondents believe that their patients have negative perceptions about PPC, 48% feel comfortable treating their patients at the end of life.

Conclusions: Socializing and raising awareness among the population about the patient's early referral to PPC is important in order to timely refer the patient to PPC regardless of whether there is a curative intent or not, to send the message to relatives and patients of the service as quality of life can exercise greater acceptance among health personnel, as well as increasing sympathy, both in the family and in the patient, with which it is likely to increase therapeutic adherence.

PO214 SIOP19-0311 | Are we Achieving the Last Wishes of Dying Children: An Audit of End of Life and Palliative Support

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Background/Objectives: Cancer is the leading cause of childhood non-accidental deaths in the UK, with 4 children dying weekly. Place of death is regarded as an essential goal of end of life care and achieving a preferred place of death contributes to achieving a "good death." Home death is preferred allowing families to retain some control and sense of

normality, which may reduce the long-term effects of bereavement and provide a higher quality of death. We performed a retrospective audit of final wishes of children and their parents, where the child died between 1st July 2016 and 1st July 2018 in a single tertiary oncology centre to assess whether final wishes were fulfilled.

Design/Methods: Data was collected through retrospective chart review and staff interview. All children (n=14) aged <18 at time of death, living within Bristol area and with a diagnosis of cancer were included. Data collected included age, gender, end of life wishes and place of death.

Results: Thirteen children had documented preferred location of death, choosing either home or a local children's hospice. Eight achieved their preferred place of death. Six children preferred to die at home, only 2 achieved this, (3 hospital; 1 hospice). Six out of seven children preferring to die in a hospice achieved their wish, (1 hospital). Reasons for not achieving preferred place of death included: lack of service provision for 24/7 home palliative care and need for specific medication requiring hospital admission.

Conclusions: Our audit shows that families choose for their child to die at home or in a children's hospice and we should be offering support for this choice. Currently, in the UK dying at home for a child with cancer is difficult due to the restricted funding and specific medication that allows a child to die comfortably; these dynamics will vary internationally.

PO215 SIOP19-1373 | The Uninvited Guest: Fear at the Bedside. Are You Managing or Contributing to Anxiety Around the Child? A Parent's Perspective on Palliative Care

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Background/Objectives: To understand how approaches from medical, non-medical staff and families in Paediatric Palliative Care may contribute to or alleviate heightened fear and anxiety in the child. Increased emotional distress can delay or lengthen procedures, and require additional staff resources to calm the child and administer medication or perform simple protocols.

Design/Methods: Oral presentation, drawing on Simon's experience as a parent and on examples from the three year terminal cancer journey of his four year old son with Neuroblastoma, in both hospital and home environments. Also draws on his experience as a consumer volunteer within The Royal Childrens Hospital, Melbourne; and on his experience as a national Palliative Care advocate.

Results: Reflecting on his son's three-year cancer journey with five months under Palliative Care, the presentation

explores how different approaches from medical and non-medical staff in both hospital and home environments brought out vastly different responses in the child. Certain approaches increased fear and anxiety in the child. Such increased anxiety could lead to greater physical rigidity, emotional tension and distress and then longer procedures which inevitably ensued. Some professional approaches might be deemed efficient for the individual doctor or nurse, but had a detrimental effect on the child and carers. Alternatively a calm, considered, and measured approach that invests time in assessing and communicating with both carers and child can alleviate anxiety, build trust and rapport and generate positive outcomes resulting in shorter and less traumatic procedures.

Conclusions: Palliative Care professionals can bring fear to the bedside, through their demeanour, approach and communication skills. This can be detrimental to the emotional welfare of child and the carer, and increase the resources needed for simple protocols. Yet a balanced, calm approach employing clear communication and patience, that assesses both child and environment carefully, can deliver important care while maintaining emotional comfort and security.

Treatment and Care - Psychosocial (PPO)

PO216 SIOP19-0743 | Analysis of the Relationship of Adolescent Oncopatients and Their Parents in Child Oncology Tertiary Center in Kazakhsan

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Background/Objectives: The relationship between adolescent oncopatients and their parents in inpatient department becomes complicated because ties become stronger; the sense of parental commitment to a teenager get sharper due to long-term traumatic treatment. The aim of this study is to identify the impact of relationship optimization on mental health of parents and adolescents through cognitive-behavioral psychotherapy (CBR) training.

Design/Methods: Sixty patients and their parents were interviewed during 9 month period. There were 48 girls and 12 boys aged between 12-17 years old. Used psychodiagnostic methods were for adolescents "Parents assessed by children (PAC)" (I. Furmanov, A. Aladin) and for parents «Analysis of family relationships (AFR)" (E. Eidemiller, V. Justickis).

Results: According to the results of the PAC offense of upbringing were revealed: hyper-protection 40%, indulgence 60%, ignoring needs 20%, inadequate requirements-prohibitions 40%, excessiveness/severe punishments 20%, unstable education 60%, educational uncertainty of the parent 60%, loss of phobia 20%. AFR figures: hyper-protection 20%, excessiveness of requirements-prohibitions 20%, minimal punishments 40%, expansion of parental feelings 60%, preference in adolescents children's qualities 60%. As a result in the relationship of adolescents with parents following deviations revealed: unstable upbringing - fluctuated upbringing techniques from strict to liberal style, heightened attention to adolescent and his emotional rejection; educational uncertainty: indulging hyper-protection or reduced requirements. While parents express over-parenting-increased protection (indulging or dominating) due to destructive reasons (death, divorce and emotional coldness), preferring children's qualities in a teenager - conniving hyper-protection, ignoring adolescent maturation; the preference of feminine qualities, expressed by the unconscious rejection of the adolescent boy by the mother, the father sees a lot of shortcomings in the son, thus they show emotional rejection.

Conclusions: The study revealed a high percentage of emotional rejection of adolescents by parents and parents' hyper-protection, which led to developing the training to reduce parents' emotional rejection and hyper-protection.

PO217 SIOP19-0318 | Overcoming Inequalities in Paediatric Cancer Care at Kumasi, Ghana: Both Care Givers and Patients Perspective

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Background/Objectives: Paediatric cancer continue to be in an increase and about 200 000 children and adolescent are diagnosed every year worldwide with most of them coming from Low-Middle Income Country. Moreover, 90% of these die of the disease due to limited recourses. Despite the new medical technologies and advances in the global fight against cancer, inequalities in cancer care between the developed and the developing countries remains the same. However, these patients suffer in pain with no access to complete treatment and pain medications and these disparities cannot be ignored.

Objectives: To determine the inequalities in paediatric cancer care between developed and developing Countries

Design/Methods: A cross sectional survey was employed using a semi-structured questionnaire and field notes to interview one hundred patients who access care at the paediatric oncology of Komfo Anokye Teaching Hospital and originated from various social and ethnic groups as well as

geographically distinct areas of Ghana and fifty nurses. The-matic analysis was employed

Results: 65% revealed that proper collaboration to learn from each other, improving employment and working condition, fostering public engagement and solidarity, increase personal engagement, development of commitment of the public health community and obtain a commitment from the community could overcome the inequalities in paediatric oncology care. However, 35% also think there is the need to intensified paediatric cancer awareness campaigns, educating health care providers and general public on early diagnosis and early referrals for appropriate treatment and also data based availability and research

Conclusions: Inequalities in cancer care are issue and should be dealt with. Organization should establish partnership for research, funding provision of equipment's. These steps can achieve success and make some impact on the live of patients from the developing countries

PO218 SIOP19-1344 | Anxiety Disorders in Pediatric Oncology

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Background/Objectives: Immense progress is being made in pediatric oncology with a clear improvement in the vital prognosis of children but, the therapeutic means are very aggressive requiring periods of separation of the child from his usual environment. The objective is to describe the frequency of anxiety disorders in children followed in pediatric oncology and their correlation with some criteria for these patients.

Design/Methods: This descriptive study focused on 35 children followed in the medical oncology department of FarhetHached Hospital during the period January-March 2019. The Screening Child's Anxiety Related Disorders (SCARED) was used to screen the anxiety disorders in school-aged children. Biographic and clinical data were collected using a pre-established form.

Results: The mean age of the population is 10 years (7-15 years), sex ratio of 4. The family structure was nuclear, single-parent and large respectively in 77%, 11% and 11%. The parents are in couples in 85.7%, separated in 11.4%. School enrollment is regular in 82.9%, irregular in 8.6%, absent in 8.6%. All children were treated for their cancers for more than 6 months. The primitive tumor was localized at Abdominopelvic space, head and neck and members respectively in 59.3, 29.6% and 11%. Complete remission was reported in 77%. The total score of SCARED was pathological in 71.4%. The sub-scores are pathological for panic disorder

in 48.6%, generalized anxiety 31.4%, separation anxiety 57.1%, social anxiety 54.3% and school anxiety 22.9%. The statistical analysis shows a significant correlation between separation anxiety and the parental marital status ($p=0.03$); between the panic disorder and the quality of school insertion ($p=0.05$), the localization of the cancer ($p<0.01$). Generalized anxiety has a significant statistical relationship with child age ($p=0.008$)

Conclusions: Medical team in pediatric oncology and family have new challenges for long-term care transdisciplinary management of the disease

PO219 SIOP19-1350 | Parental Coping in Pediatric Oncology

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Background/Objectives: Coping, a new concept that concerns what the individual thinks and do facing a problem, is a specific process particularly in oncology with different steps from diagnosis announcement to treatment modalities and outcomes. This study will describe parental coping strategies and its correlation with some patients' characteristics in pediatric oncology.

Design/Methods: It's a descriptive study of 31parents of 31patients followed in the medical oncology department at the farhetHached hospital using the Toulousaine coping scale during the period January-March 2019. The biographical and clinical data were collected using a pre-established form. The statistical analysis was made by SPSS19.0.

Results: The mean age of the children group was 9.16 years (3-15 years) with sex ratio 2.87. The schooling of the children is regular in 64%, irregular 16%, absent 19.4%. All children were followed clinically for their cancer for more than 6 months. A complete remission was reported in 71%. The parental group has a mean age 37.3 years, sex ratio 0.14. Families are with both parents in 71%, single parent in 16.1% and large in 12.9%. The parents are in couples in 80.6%, separated 16%, father died in 3.2%. The coping strategy is focused only on information, action or emotion respectively in 45.2%, 29% and 16% and combination of action with information or action with emotion respectively in 6.5% and 3.2%. Significant statistical correlation is reported between parental coping strategy centered on emotions and parental marital status ($p=0.01$), family type ($p=0.003$), children schooling ($p=0.001$), child age ($p=0.02$).

Conclusions: The parental couple is a corner stone in the management of children diseases especially when it is chronic and serious, highlighting the importance of multiaxial intervention in pediatric oncology.

PO220 SIOP19-1361 | Parental Attachment Style in Pediatric Oncology

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Background/Objectives: A child cancer disease is a real physical and psycho-social challenge for the whole family. Parents will adopt social behavior and feelings searching security in the existing relational. This study aims to describe the parental attachment style in pediatric oncology and their correlation with their childrens.

Design/Methods: It is a descriptive study of 31 parents of 31 patients followed in medical oncology department at the farhetHachedhospital during the period January-March 2019. Attachment style of the parents was estimated by the Adult Attachment Scale AAS. The biographical and clinical data were collected using a pre-established form. The statistical analysis was made by SPSS19.0.

Results: The mean age of the parents was 37.3years with a sex ratio 0.14. Families are nuclear type with both parents in 71%, single parent16.1% and wide12.9%. The parents were in couple80.6%, separated16% and father died3.2%. The Parents' social attachment style was close in58.1%, anxious in32.3% and dependent in9.7%. The mean age of children was 9.16 years (3-15years), sex ratio2.87. Their School enrollment was regular in 82.9%, irregular8.6% and absent8.6%. All children were medically followed for their cancer diseases for more than 6 months and a complete remission was reported in 71% of cases. The cancer type is nephroblastoma26.7%, neuroblastoma 26.7%, Ewing sarcoma 10%, Burkitt lymphoma 10%, carcinoma 10%. The statistical analysis shows a correlation between the closed type of parental attachment and the quality of children schooling ($p=0.01$); parental attachment style dependent and complete remission of cancer, marital status of parents, type of family, children schooling respectively with ($p=0.001$), ($p=0.01$), ($p=0.003$) and ($p=0.001$). Anxiety attachment style is statistically correlated with the cancer type ($p=0.03$), children schooling ($p=0.005$), child age ($p=0.05$).

Conclusions: Parents are the fixe partners in medical care in pediatric oncology. The relational profiles of these partners should always be taken into consideration by the medical team.

PO221 SIOP19-1680 | Impact of Children Cancer on Life Quality in the Center of Tunisia

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Background/Objectives: The pediatric cancer is a rare but very grave disease which commits the survival. The multimodal treatment is heavy: surgery, chemotherapy and/or radiotherapy according to the type of cancer which improves the outcome of OS up to 70%.

These treatments affect the quality of life and induce physical and psychosocial deficits.

Design/Methods: This study was designed to emphasis the impact of cancer and its treatment on the quality of life of the child and his parents and its psychosocial consequences.

We led a transverse descriptive study with 66 children from 2 to 18 years old affected by cancer and their parents. We used a validated scale, PedsQL cancer module (Arabic version).

Results: The median age was 7 years [2-18 years]. There was a slight male predominance with a sex ratio 1,27. Revealed cancers were: rhabdomyosarcoma (19,7%), bone tumors (13.6%), neuroblastoma (9.1%), and brain tumors (9,1%). Of all patients, 82% didn't know their diagnosis. 41,5% of children stopped, temporary, going to school. According to the scale PedsQL, the major consequences were: pain (44.87%), nausea (36.4%) and the physical appearance (49.82%).

Conclusions: Cancers and their treatments have negative effects on the physical, psychological well-being and the quality of life of the young patients. Improving the multimodal treatment by the experts to reduce side effects, physical activities and regular psychological are expected to improve the quality of life of this population with pediatric cancer.

PO222 SIOP19-1429 | The Countertransference of the Health Team in a Paediatric Oncology Unit of a Tertiary Hospital

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Background/Objectives: The daily exposure to situations of high tension and emotional load faced by the professionals of the Paediatric Oncology Units entails a suffering that is evident in the daily work that is carried out. The emotional reaction of the staff is referred to here as countertransference. It is essential to know and analyse how, when and why such countertransference occurs in order to prevent it from becoming an obstacle in the work procedure, both in dealing with patients and their families and in the internal functioning of health teams.

Design/Methods: The approach to the behavioural part of the countertransference is done through daily clinical observation by two psychologists, who have been observing and accompanying the different areas of health intervention of the Unit. At the same time, the analysis of the emotions that affect the

different professionals of the Unit when performing hospital work, are evaluated through semi-structured interviews with them.

Results: Most health professionals working in Hospital Units of these characteristics are moved by many emotional aspects that include the appearance of unconscious defensive mechanisms to protect themselves from such suffering. If this phenomenon is not taken into account and analysed it can lead them to unwelcome behaviours towards patients, their families, and the rest of the co-workers. In addition, over time it can negatively affect the emotional state of these professionals.

Conclusions: Countertransference is evident in the health teams of the Paediatric Oncology Units. They need self-care spaces where think about and acquire the tools to handle it in an appropriate manner.

PO223 SIOP19-1441 | Parent's Support Programme in a Paediatric Oncology Unit of a Tertiary Hospital: "Coffee with Parents"

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Background/Objectives: A cancer disease for a child carries a high emotional impact on parents and their relatives. We consider important to provide these family members with a solid and adequate support network within the hospital, where they can support themselves and acquire appropriate tools for handling the condition. This will work as a protective psychological support system that will promote support and beneficial care in order to cope with this situation.

Design/Methods: A psycho-educational group program for families of children diagnosed with cancer, led by the psychologist and the nursing supervisor of the Unit. It consists of a monthly one and a half hour session about a specific topic that is decided jointly by parents and professionals. If needed other hospital professionals may provide information on the chosen subject as invited participants. Some of the topics have been: feeding during the illness (digestive paediatrician invited), school during the disease (hospital's teacher), fears associated with the disease (oncologist paediatrician), communication with children, the siblings. After each session the parents fill in a satisfaction survey. The number of attendees is also registered, and both aspects allow for an evaluation of the program's functioning.

Results: The results obtained have been very satisfactory, as can be deduced from the analysis of the surveys filled in by the parents, the number of attendees to each session, and the prizes awarded (two Start-Up Awards). Parents report an

improvement in their emotional state thanks to their participation in this program, better training to handle the situation that befalls them, a broader support network and an improvement in effective communication with other parents as well as with professionals.

Conclusions: The creation of a space for reflection and group support helps improve the emotional state of the relatives of children diagnosed with cancer and facilitates a constructive relationship with the hospital treatment team.

PO224 SIOP19-1455 | The Symbolization of the Experience of Illness in Children Diagnosed with Cancer

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Background/Objectives: Children who are diagnosed with cancer are exposed to a sudden life change so they need emotional support to adapt and cope with the situation that befalls them. Children need communication with adults to be adapted to their psycho-development state, which is often a complicated aspect for hospital health personnel. In the Paediatric Oncology Units we have the responsibility to listen to all of these messages, which include the subtle and metaphorical communication modes that children usually use.

Design/Methods: Analysis of three clinical cases of 4 and 5 year old patients who undergo Paediatric Palliative Care due to the incurable character of their oncological diseases. During the final stage of their lives, these patients received psychological support from the psychologist, who is part of the health team. Results of these psychological treatments are conclusions about how each of these children talk about death. It also allow us to analyse the different metaphors that they use to explain and understand their end-of-life experience, as well as their communication and listening's needs from adults.

Results: The children usually use a metaphorical communicative mode about their end-of-life situation, through which they express their feelings, their needs and their questions. The most used themes are shown through the Disney stories: death through the story of Peter Pan, loneliness and lies through the story of Pinocchio, physical changes through The Beauty and the Beast, among others, which allows them to talk about their feelings and detect their needs to prepare to say farewell.

Conclusions: A willingness to listen and respect the different ways that children have to communicate permits professionals to detect and maintain the communicative style that

the child chooses and needs to use, and help them to understand and tolerate the complex feelings that occur at the end of life.

PO225 SIOP19-1021 | The Plea for Counselling in Childhood Cancer: What Do Parents Want?

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Background/Objectives: This study arose from a felt-need among parents in the Irish paediatric cancer service, and specifically investigated the social-support needs of parents journeying through childhood cancer. This abstract reports on one key finding: the plea for counselling.

Design/Methods: Action research informed every methodological detail of this study.

The qualitative field research consisted of semi-structured interviews with 17 parents and semi-structured interviews/focus groups with 18 staff members representing 8 different professions. A directed content analysis was utilized in the analysis of data with a four-tier definition of social support providing an initial framework for categorizing data.

The resultant themes guided the creation of a survey which was formed by a team over a number of months. Surveys were distributed to 580 families. 232 surveys were returned from parents of children in treatment and remission and 9 from bereaved parents.

Results: The volume of requests for counselling rendered it one of the most compelling findings of this research. Parental requests for counselling and emotional support can be classified within the following four categories:

- 1) Parent Support: a) Talk therapy to process distress, b) Equipping and guiding the parent, c) Couple counselling to ease strain, d) Peer support.
- 2) Support for the Child with Cancer: a) Psychological intervention at critical points, b) Talk therapy to process distress, c) Play therapy, d) Peer support and role models, e) Resources.
- 3) Sibling Support: a) Sibling workshops and peer support, b) Talk therapy to process distress, c) Play Therapy, d) Inclusion.
- 4) Family-Focused Support: a) Family focused talk therapy at critical points b) Family-to-family peer support.

Conclusions: These findings closely correspond with the Standards for the Psychosocial Care of Children with Cancer and Their Families (Wiener et al. 2015). In particular, standards 4, 6, 7, 8, 9 and 10, strongly resonate with this data.

PO226 SIOP19-0726 | Maternal Representations of Traumatic Experience and Supportive Sources During the Treatment of Adolescents with Oncological/Hematological Diseases in Russia: Retrospective Study at the Survival Stage

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Background/Objectives: The specifics of traumatic experience in conjunction with supporting resources are the most important information for developing psycho-social programs for families during and after the treatment (Rodriguez E. M. et al, 2012). The aim of this pilot study was to analyze the maternal representations of traumatic and supportive factors during the children's diseases and treatment at the survival stage.

Design/Methods: 20 Russian mothers of survived adolescents (mean=15.95) with lymphomas (n=9) and leukemias (n=11) were retrospectively interviewed about significant traumatic and supportive sources during the previous treatment. Median of surviving time was 2 years, mean of treatment duration was 2.5 years. We performed content and correlation analysis, estimation of statistical significance.

Results: The mean value of maternal traumatic factors was 3.5; of supportive factors – 4. *Severe emotional experience* (75%); *Difficulties of disease acceptance* (45%); *Impossibility to support the child*, *Treatment aggressiveness*, *Children's emotion problems* (25%) were the most common traumatic factors. *Positive thinking* (60%), *Actual medical treatment* (55%), *Family* (45%) and *Friends support* (35%), *Self-confidence* (35%), *Supportive environment* (35%), *Psychological help* (30%) were the most encouraged sources. Mothers of adolescents with Lymphomas used *Positive thinking* as a supportive resource more frequently ($p=0.012$, t-test). Psychological, family and religious resources were more important for mothers of adolescents with ALL. *Treatment duration* correlated with *Difficulties to protect children*, luck of *Psychological support*, numbers of supportive resources (Pearson's $r=0.4$). *Time after the treatment* was negatively correlated with the number of traumatic factors (Pearson's $r=-0.519$) and *Psychological/Friends support* (Pearson's $r=-0.42$); positively correlated with *Self-confidence* and *Appreciation of life* (Pearson's $r=0.34$).

Conclusions: The coping with own difficult emotions and the acceptance of disease and treatment-related situations should be the main targets for psycho-social support for Russian mothers. The differences according to diagnosis, treatment duration and time after the treatment should be also considered in such programs.

PO227 SIOP19-1749 | Identifying the Psychosocial Support Needs of AYA Transplant Patients

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Background/Objectives: Existing evidence suggests that Adolescent and Young Adult (AYA) patients use more psychosocial support services and have greater levels of distress than do older cancer patients (Mor et. al, 1994). Transplant is challenging for most patients; but the AYA population comes to transplant with exceptional and unique psychosocial needs. The purpose of this study is to explore the psychosocial support needs of AYA patients before, during and after transplant.

Design/Methods: A retrospective chart review of transplant patients referred for psychiatric evaluation within 100 days of transplant, either pre-transplant for screening/evaluation or post-transplant through inpatient hospitalization was conducted. Of the twenty-two total patients, thirteen fell into the AYA group and are described here. Data on sociodemographic, disease, treatment, and personal characteristics of AYA patients who receive psychiatric evaluations were collected using a retrospective chart review tool. Analysis included simple frequencies and descriptive statistics.

Results: Thirteen young adult transplant patients were seen for psychiatric consultation (53.8% female; 46.2% male). Primary reason for referral was anxiety (23.1%), and depression (30.8%). Of those seen, 46.2% had a previous psychiatric history and 46.2% experienced pre transplant distress. High rates of substance abuse were identified with history of alcohol use 69.2%, and alcohol use within 6 months of transplant 23.1%. Prior history of marijuana use 38.5%, use within 6 months of transplant 15.4%. Psychosocial issues included: 15.4% current conflict with support systems or family members; 23.1% had caregiver issues affecting continuity of care post-transplant.

Conclusions: Higher rates of mortality, substance abuse, pre-transplant distress and psychiatric concerns prior to transplant were found in this cancer population subset. Expected prevalence among adults in the community with regard to anxiety and substance abuse were found in similar rates. These findings further highlight the special needs of this population.

PO228 SIOP19-1201 | Peer2Me – A Peer-Support Program for Adolescent and Young Adult Cancer Patients

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Background/Objectives: Past studies have shown that social support during cancer in young adulthood is of central impor-

tance. The exchange with other young patients who have already survived the disease is particularly desirable. A pilot study in pre-post design was developed to meet this need for support.

Design/Methods: In the intervention study "Peer2Me", started in January 2019, AYA cancer survivors (18-39 years) will act as peer mentors and support young adults with acute cancer for a period of three months in a personal one-to-one contact. The mentors are prepared for their task in a 2-day training course which includes among others the teaching of suitable conversation techniques, identification as a mentor as well as basics of Motivational Interviewing. The participation in monthly group supervisions is obligatory for the mentors. Using standardized questionnaires and qualitative interviews, first results on feasibility, satisfaction and psychosocial outcomes (fear of recurrence, depression, self-efficacy, coping) will be derived.

Results: So far, 22 potential mentors have contacted us, 13 of whom are participating in the training in April. Preliminary talks with the mentors have already taken place. These discussions focused on the aims and expectations of Peer2Me and a first clinical impression. The first meetings between mentors and patients are scheduled at the University Cancer Center Leipzig for May, so no results are available at this time. The mentoring activity ends in October, so that first results can be presented.

Conclusions: This study will provide initial results on the feasibility and implementation of a manualized peer mentoring program for AYAs and serve as a basis for future clinically randomized studies on the effectiveness of peer support. Furthermore, results of the intervention on the impact on psychosocial outcomes will be expected.

PO229 SIOP19-0178 | Understanding the Wishes of Pediatrics with Cancer: an Examination of Altruism and Prosocial Thought

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Background/Objectives: Research highlights that children frequently want to help others, without regard for external rewards, reciprocity, or reputation (Warneken & Tomasello, 2009). Researchers found that chronically ill children make more altruistic decisions than their healthy counterparts, with hospitalized children even more altruistic (Seagle et al., 2010). For pediatric cancer patients facing end-of-life, more than half identified an interest in helping others who they did not know (Hinds et al., 2005). Our study aims to further explore

altruism in children who have been diagnosed with cancer, thus adding to this growing body of literature.

Design/Methods: Retrospective chart review was conducted to extract the answer to the question “if you could wish for anything, what three things would you wish” for each pediatric oncology patient who was seen for a psychological evaluation. Demographic and disease-related information was also collected. Study sites include two large, urban pediatric hospitals.

Results: Preliminary results highlight that children’s wishes vary greatly, but often center on helping others. In our ethnically diverse sample, 25% wished to help someone other than themselves; many patients indicated a desire to help others with cancer (i.e., “for all the kids with cancer to be cured”, to donate money to a cancer charity) as well as society as a whole (i.e., ending poverty, world peace). Thematically, other frequent responses included wishes for their own cancer to be cured, for side effects (e.g., pain, nausea) to be eliminated, for family members’ quality of life to improve, and for material goods (e.g., pets, cars).

Conclusions: As one might expect, the wishes of pediatric cancer patients vary and likely are influenced by patients’ age and developmental level, disease status, and past experiences. Despite the physical and emotional burdens of cancer treatment, our study highlights that pediatric oncology patients nonetheless are mindful of the value of helping others.

PO230 SIOP19-1614 | F. I. T for School – Reintegration to School for Children and Adolescents with Brain Tumors and Other Cancer Diseases – A Teachers Guide

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Background/Objectives: Research projects have pointed out considerable effects of diagnosis and treatment of a brain tumor on learning and developmental aspects of children and adolescents. Long term effects like cognitive and social emotional impairment are especially relevant to school integration and quality of life. The need for detailed information for teachers and parents has shown up continually. Interviews with teachers emphasize the need for information about medical treatment and special issues of the disease as well as strategies to cope with resultant problems.

Design/Methods: Fairness, integration and transparency (F.I.T) are the particular characteristics of the booklet to encourage successful school-integration as a milestone in the

process of adaptation to the illness, rehabilitation and regaining normal life after a brain tumor treatment.

The aim is to improve knowledge, understanding and communication about the consequences of brain tumors and to show practical ways, how to support the child in general and concerning specialized issues to balance the disadvantages of the pupil. It refers to the German and Austrian school system and describes the legal basis of school integration, as well as educational training conditions for adolescents.

Results: The main problems are outlined and practical information is provided in detail how to recognize i.e. reduced attention, concentration, memory, planning and organization skills as well as emotional difficulties and fatigue. Strategies and arrangements to assist and support the child will be depicted. Examples of educational development of pupils with different ages and stages of disease show opportunities to support patients at high risk for school-problems and in this way prevent long term limitations in quality of life.

Conclusions: The booklet contributes to improve communication between hospitals, schools and families and fosters children’s experience of school, psychosocial development and participation.

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PO231 SIOP19-0270 | Improving Quality of Sexual Life Among Paediatric Cancer Survivors in Developing Countries: Living Beyond the Disease!

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Background/Objectives: Cancer treatment is one of paediatric medicine’s biggest success stories, chemotherapy, radiation and other therapies can do lasting damage to a child’s developing body. It is incumbent upon oncologists to conceive of Paediatric malignancies as more than just a disease that begins with diagnosis and ends when the treatment protocol ends instead, it initiates a life-long trajectory of survival having long-term implications for quality of life.

Design/Methods: Emotional needs are deeply frustrated in children, due to long hospitalization, strong parental bonds that jeopardize the normal development of autonomy and independence, friends, painful tests, anxiety and anguish, hours of loneliness without tenderness, this critical suspension from normal life and shift to emergency survival further complicates attainment of satisfying sexual identity and disrupts basic psychosexual maturity process.

Results: Adolescent sexuality is very complex, and even more when serious adverse event like cancer affects the individual well-being - sexual and non-sexual—in all its

dimensions. Young survivors are significantly different in specific domains, they are less feminine in sexual identity have more restrictive and submissive images of sexuality, lower confidence with masturbation. They have less experience of intercourse. These effects can be better understood if put in perspectives with many changes and challenges young cancer survivors have to face and cope with in different emotional, affective, relational, cultural and existential domains. Cultural issues in our sexually polite Asian society, such as the myth that children are too young to be interested in sexuality and presumption that issues of survival overshadow sexuality, provide barriers to open communication about sexuality

Conclusions: Sexual function and fertility should no longer be regarded by oncologists as frivolous or irrelevant issues, the very privileged relationship that oncologist have with their patients should permit them to assist children in their journey of cancer management.

PO232 SIOP19-1330 | Applying the Psychodynamic Approach to Working Through the Death Anxiety and Fear of Cancer Recurrence in a Childhood Cancer Survivor on the Follow up Period

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Background/Objectives: A recent review has shown a large body of research aimed at studying death anxiety and fear of cancer recurrence (FCR) in cancer survivors. However, it is still being discussed which methods are most effective for the diagnosis and correction of these psychological problems (Sharpe L. et al., 2018). The aim of this study is to demonstrate the relevance of applying the psychodynamic approach to diagnosing and working through the death anxiety and FCR in a cancer patient.

Design/Methods: The patient was a 15-year-old adolescent (female), 11 months after undergoing treatment for ALL, including HSCT. Eating disorders, hypochondriacal anxieties and nightmares were verbally presented by the patient as the main complaints. Psychological assistance within the framework of the psychodynamic approach was provided in the form of online consultations once a week for two and a half months. Content analysis of 10 sessions was conducted.

Results: The psychodynamic-based case analysis provided an opportunity to find out that the patient did not consciously link her complaints with the presence of death anxiety and FCR. As a result of psychological defence mechanism activity (repression, suppression, and displacement), death anxiety and FCR were repressed into the Unconscious. Then they were displaced to other objects (e.g. dream images, fear of

appearance of another life-threatening disease). Interpreting the manifest content of these psychopathological symptoms as FCR and death anxiety helped to reduce the psychopathological symptoms.

Conclusions: The case analysis confirmed the interrelation of death anxiety and FCR for the patient, as well as the relevance of applying the psychodynamic approach to working through unconscious death anxiety and/or FCR expressed through the manifestation of psychopathological symptoms. It is promising to further study the possibility of applying psychodynamic counseling methods to the diagnosis and correction of psychological symptoms associated with death anxiety and FCR.

PO233 SIOP19-1563 | Supporting Points and Limiting Factors for the Patient and Parents for Long-Term Monitoring in Pediatric Oncology in the Middle-Term Period

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Background/Objectives: The survival rate of children and adolescents treated for cancer reveals a risk of late effects of the disease and treatments. Our study, conducted by the GOCE (western interregional hospital organisation for pediatric oncology) with the group of Psychologists, aims to identify, during the medium-term follow-up, the psycho-socio-medical determinants perceived by the pediatric oncology patients and their families. These determinants will include the support points and limiting factors for long-term monitoring. This study will prepare patient commitment and adherence to a harmonious long-term follow-up and factors for the implementation of a long term (LT) program adapted to their needs.

Design/Methods: A first qualitative step is based on a series of semi-structured interviews, developed with the psychology laboratory and conducted by psychologists from the pediatric units of oncohematology in the GOCE with children and their parents. This first stage of data collection and qualitative analysis will allow the development of child and parent questionnaires. This will be completed by a quality of life scale.

Results: The analysis of the semi-directive interviews demonstrates that psychological suffering is very present in the medium-term period, difficulties and a certain ambivalence, for the children and their parents to project themselves in the

long-term follow-up, without being able to ask for support. We observe that the time of the proposal of the consultation to LT and the professional who initiates it are determining to the adhesion of the patients and their parents.

Conclusions: The analysis of future questionnaires will be used to clarify and expand these initial findings. These suggest the interest for creating a multidisciplinary plan between the hospital and the city.

PO234 SIOP19-1271 | Exploring the Dynamic of Posttraumatic Growth And Delimiting Coping Competencies of Children and Adolescents with Cancer in a Cross-Sectional Study

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Background/Objectives: The study examines posttraumatic growth (PTG) and rumination as a result of struggling with trauma among children and adolescents with cancer. Firstly, the aim is to describe PTG in German children within the different phases of disease, and elucidates predictors relevant to the PTG process. Secondly, to explore if the PTG construct is definable from coping competencies with due regard to potential changes within the two waves.

Design/Methods: The survey consists of three measurements at defined survey points within a six months follow up. Enrolment started in September 2018 at Hannover Medical School and Münster University Hospital. Eligibility criteria include (1) age 11 to 19, (2) diagnosis of cancer without constraints, (3) ≥ 2 weeks from diagnosis at T1, (4) German-speaking, (5) no significant cognitive or sensory deficits. At this stage N=20 children and N=25 parents participate in the survey.

Medical variables, coping competencies, self-reported depressive and anxiety symptoms, perception of well-being and functioning in physical, emotional, mental, social and everyday life areas are assessed with multiple questionnaires. A full spectrum of PTSD might be relatively rare, therefore the focus is set on a confining a more subclinical level. PTG is measured by using a redeveloped version of the posttraumatic growth inventory for children and adolescents (PTGI-CA) to assess five areas of PTG related to the questionnaires (PTGI) by Kilmer et al. (2009) and Maercker & Langner (2001).

Results: First analyses indicate conceptually-relevant variables associated with the five areas of the PTG concept. Results of the first and second wave will be presented at the conference.

Conclusions: Childhood cancer remains a significant and challenging event and the findings will provide initial suggestions of posttraumatic growth with regard to coping competencies.

PO235 SIOP19-0350 | The Potential Impact of Protontherapy in the Radiotherapeutical Management of a Highly Challenging Case of Craniopharyngioma

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Background/Objectives: Comparing, in silico, sparing of relevant organs at risks (OARs) in a ballistically challenging craniopharyngioma (Cr), respective to optic pathway and brain stem, by advanced radiotherapeutical strategies.

Design/Methods: A 28 year-old gentleman with a mixed solid-kystic Cr encasing optic chiasm, anteriorly, and abutting brain stem, posteriorly, was eligible for intercomparison between pencil-beam scanning protons (PBP), tomotherapy® (TO), and cyberknife® (CY). Target volume included GTV on the residue, plus 5 mm margins for CTV, and 3 mm for PTV. Prescribed dose to CTV was 52 Gy[EBR] (Gy[EBR] = physical Gy X estimated 1.1 RBE). Prescribed mean/Maximum dose-constraints to OARs were: right/left hippocampus (RHI/LHI): 7.3/18 Gy, optic chiasm (OC): 52/54 Gy, and right/left optic nerves (RON, LON): 54/54 Gy. Dose-fractionation consisted in 5 weekly sessions of 2 Gy[EBR] each. 3D Dose-distribution was generated by Research TPS® with cumulative dose-volume histograms (DVH) displayed for inter-comparisons. CY hypofractionation regimen was converted in 2Gy/fraction dose-equivalent (EQD2) for inter-comparison purposes

Results: Target coverage for the PBP/TO/CY approaches relative to 95% isodose was (in Gy[EBR]), respectively: 49.8/51.1/54.1. As far as mean dose to OARs: chiasm: 49.9/50.7/52.3; RON: 18.6/25.7/24.7; LON: 17.1/25.1/22.1; RHI: 12.2/30.3/11.3; LHI: 12.5/30.9/9.7 Brain: 6/10.7/9.3, respectively. As far as Maximum dose: chiasm: 51.1/51/52.5; RON: 50.6/51.1/55; LON: 50.6/51.2/52.8; RHI: 46.8/51.3/40.1; LHI: 46.4/51.6/36.3; Brain: 45.9/47.2/44, respectively. Furthermore, only PBP and CY achieved V8 Gy < 50% for LHI and RHI

Conclusions: Target coverage was similar for the 3 approaches. Dose to the optic pathway and brain was close, although slightly lower with PBP; Doses to both LHI and RHI was clearly superior with TO compared with both other technics that predicted further risks of memory deterioration. Since CY presents with multiple technical limitations, which make it appropriate only in small targets, and hypofractionation of the dose, PBP should be recommended in ballistically

challenging Cr, where conventionally fractionated radiotherapy is indicated

PO236 SIOP19-0271 | Role of Radiotherapy in Paediatric Population: An Institutional Experience

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Background/Objectives: To evaluate the role of radiotherapy in paediatric patients at a single tertiary care centre.

Design/Methods: The present retrospective study was carried at department of Radiotherapy, SMS Medical College, Jaipur, India; over pediatric patients less than 20 years who were treated with radiotherapy during 2013 to 2017.

Results: A total of 127 pediatric patients were treated. The median age was 12 (range, 1-19) years; 79 (62.2%) were boys and 48 (37.8%) were girls. 77.2% children belonged to rural background. The most common malignancy seen in pediatric patients were acute lymphoblastic leukemia (ALL, 52.8%) followed by central nervous system (CNS) tumors (21.3%), bone tumors (12.6%), nasopharyngeal tumors (6.3%), and others (7%). The most common cause for prescribing pediatric radiotherapy was prophylactic (52.8%) followed by curative (37%) and palliative (10.2%). The most common RT prescription was (Gy/fraction) 18/10 (43.3%) followed by 50/25 (17.3%), 54/27 and 12/8 (both 15.7%), and others (8%). Among the children who received curative RT, 8.5% had complete response, 44.7% had partial response, 40.4% had stable disease and 6.4% had progressive disease; and among those who received palliative RT, more than 50% symptomatic relief was noted in 77%.

Conclusions: There is scarcity of data regarding RT in pediatric patients. Such patients present with different symptomatology and site of disease, requiring different dose fractionations.

Treatment and Care - Surgery (IPSO)

PO237 SIOP19-0484 | Surgical Approach to an Adrenocortical Carcinoma with Right Atrial Extension in a Nine-Year Old Male: Our Experience

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Background/Objectives: INTRODUCTION: Adrenocortical carcinoma with intracaval and intra atrial extension is an extremely rare occurrence in the pediatric population.

We present the case of a pediatric adrenocortical carcinoma (ACC) with extension into the inferior vena cava (IVC) up to the right atrium.

Design/Methods: DISCUSSION: Adrenocortical carcinomas are rare in the pediatric population. Even rarer is their extension into the inferior vena cava and the right atrium. To the best of our knowledge, ours is the first case reported from Pakistan and the eighth case reported worldwide.

Results: CASE PRESENTATION: A nine-year-old boy presented to our outpatient department with facial swelling, weight gain, and premature pubarche. He was found to be hypertensive with a buffalo hump and Tanner III external genitalia. Biochemical markers revealed primary hypercortisolism. A right adrenocortical mass was discovered on computed tomography (CT) with extension up till the right atrium indicated intracaval and intra atrial tumor extension. An exploratory laparotomy with median sternotomy and excision of supra renal mass along with excision of IVC thrombus and right atrial thrombus was performed. Final histopathology report confirmed the diagnosis of high-grade adrenocortical carcinoma. Through our surgical experience we recommend en-bloc surgical resection as the first line treatment.

Conclusions: Adrenocortical carcinoma with intracaval and intra atrial extension is an extremely rare occurrence in the pediatric population. We advised complete en-bloc surgical resection, where possible, to minimize tumor seeding facilitated by cardiopulmonary bypass. Efficacy of current chemotherapy trials are still largely experimental and inconclusive, however mitotane based protocols seem to predominate. We advise genetic testing of index cases and the establishment of an international tumor registry for such a challenging disease.

PO238 SIOP19-1406 | Laparostomy in Management of Patient with Neuroblastoma and Diffuse Liver Metastases

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Background/Objectives: Abdominal compartment syndrome is considered as one of the possible complications of stage 4S neuroblastoma. Complex therapy including urgent laparostomy could help patients to achieve complete remission.

Design/Methods: A case report of a patient with abdominal compartment syndrome resulting from neuroblastoma of right adrenal gland and diffuse liver metastases.

Results: We report the case of a 6-week-old male who presented with extensive abdominal distension, lower limbs swelling and respiratory insufficiency. Initial examination revealed tumor of right adrenal gland and diffuse metastatic infiltration of the liver. Urgent biopsy and laparostomy was performed, followed by multiple surgical procedures, chemotherapy and radiotherapy. During the 84-day-lasting period of laparostomy multiple complications occurred, such as a new episode of abdominal compartment syndrome, wound infection, radiation dermatitis, multiple fractures (femur, humerus, ribs, metatarsal bones), thrombosis of vena cava inferior, hepatic fibrosis and hemosiderosis. Laparostomy closure was accomplished at the same time as complete remission of neuroblastoma achievement (3 months after diagnosis).

Conclusions: Urgent biopsy and laparostomy is recommended in the initial surgical management of patients with clinical symptoms of abdominal compartment syndrome resulting from neuroblastoma and diffuse liver metastases. Following surgical management depends on the course of the disease.

PO239 SIOP19-1668 | Complications Related to Hypersplenism and Laparoscopy, Could It Be Avoided?

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Background/Objectives: Describe clinical aspects, treatment, complications and evolution of 2 patients with hereditary spherocytosis after laparoscopic splenectomy needs conversion. Laparoscopic splenectomy is accepted as the gold standard approach. There are some technical limitations related to size, more than 15 cms is considered high risk to manage.

Design/Methods: Revision of the medical chart of patients affected of hypersplenism who need splenectomy in the last two years, with serious complications after laparoscopic approach in order to try to avoid them.

Results: Only two patients suffer from serious complications after laparoscopic splenectomy and conversion to open surgery.

Allodinia related to compression of ciatic nerve that requires rehabilitation for a year, psychological support and a variety of drugs to control pain, and the lesion of the spleen artery where the most relevant. In order to avoid them we embolized the main artery 24 hours previous to surgery in the interventional radiologist department. After embolization of the main artery and some collaterals, the size of the spleen was reduced considerably from 20 to 15 cm and allowed a better laparoscopy approach, less risky and better mobilization in the

abdominal cavity. Position of the patient in laparoscopy ready for conversion is essential and embolization of main artery and collaterals previous to surgery in hypersplenism in children has to be considered.

Conclusions: Allodinia is a rare complication related to position or compression and extremely difficult to manage.

Embolization of the splenic artery previous to laparoscopic approach could be useful and also give us idea of the collaterals in huge spleens, reducing size and facilitating mobilization in the abdominal cavity

Encourage to hematologist to contact with surgeons early before hypersplenism became a technical problem

Surgeons need to keep in main complications in laparoscopy, and learn from our mistakes in order to try to avoid them.

PO240 SIOP19-1752 | Invasive Surgical Manipulations in Cytopenic Patients of Pediatric High-Dose Chemotherapy and Bone Marrow Transplant Center

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Background/Objectives: Estimate the safety and short-term complications rate of surgical manipulations performed in pediatric patients with varying degrees of bone marrow failure.

Design/Methods: A total of 801 invasive procedures (surgical manipulation in 73.2%, and endoscopy in 26.8% of cases) were performed in 411 pediatric patients (aged 0 to 18 years) receiving chemotherapy or HSCT due to primary hematological or inherited condition, leukemia or solid tumor. The most common manipulations were long-term vascular access devices (VAD) implantation (n=315) and open biopsies (n=64), drainage in soft tissue infections (n=12), and tracheotomies (n=12). Also, a total of 215 endoscopies (gastrosopies, bronchoscopies, and colonoscopies) were

performed in 110 patients to obtain biopsy samples or stop bleeding. In many cases (44.7% of endoscopies and 23% of surgical manipulations) the patients had thrombocytopenia and received platelets transfusion prior to manipulation (in 65 cases). Also, 25.9% of endoscopies and 17.9% of manipulations were performed in neutropenic patients (ANC <1,0x10⁹ / l). In these patients most common manipulations were soft tissue infections drainage and long-term VAD removal (n = 129), or soft tissue biopsies (n = 80). A significant proportion (60.6%, n = 131) of endoscopies with mucosa biopsies (n = 85) was performed in platelets levels of <80x10⁹/l. In 25.9% endoscopies were performed in patients with ANC of <1.0x10⁹/l.

Results: Among 411 patients only in one case the manipulation (endoscopic biopsy) was associated with severe bleeding. No other cases of post-surgical complications arising in 14-day period after surgical intervention were registered. Therefore, there was no evident association with platelets level or neutropenia severity.

Conclusions: Most minor surgical manipulations and diagnostic endoscopies performed by dedicated surgical team are feasible and safe in cytopenic patients receiving adequate transfusion support.

Treatment and Care - Transdisciplinary Tumor Genomics and Biology and Cancer Predisposition

PO241 SIOP19-0964 | Childhood Cancer and Syndromic Associations – A Single Centre Experience

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Background/Objectives: Hereditary cancer syndromes serve as a predisposition to cancer at an early age and development of synchronous and metachronous cancer. We hereby report a case series of children with cancer and syndromic association.

Design/Methods: We retrospectively analysed data of 7 children with cancer and syndromic associations. Age of presentation, type of malignancy, presence of synchronous cancers, molecular studies, karyotyping, family history of cancer and outcomes were analysed.

Results: A 10-year-old girl with osteosarcoma, family history of sarcoma and ovarian cancer was investigated for Li-Fraumeni syndrome (LFS). Genetic analysis demonstrated p53 mutation, suggestive of LFS. She was treated as per EURAMOS protocol and limb salvage surgery, presently well 1 year post treatment.

A rare case of a 15-year-old girl with situs inversus totalis presented with pre-B cell acute lymphoblastic leukemia (ALL)

with CD10. Karyotyping showed unbalanced t (1, 19). She is in complete remission and doing well.

Four-year-old with Down syndrome presented with Acute Myeloid Leukemia-M7 and achieved remission after 2 cycles of chemotherapy but succumbed to sepsis after cycle 4.

A 2-year-old with Dandy Walker Malformation with operated encephalocele presented with Acute Promyelocytic Myeloid Leukemia, karyotyping showed t (15; 17). He was treated with Arsenic based protocol, presently well 18 months post therapy.

A 16-year-old boy with metastatic germ cell tumor and tall stature was investigated. Karyotyping revealed 47XXY suggestive of Klinefelter syndrome. He remained refractory to therapy and died.

Another 16-year-old boy with refractory B cell lymphoblastic lymphoma and metastatic colonic adenocarcinoma with loss of MSH6 was confirmed to have Lynch syndrome.

A 9-year-old girl with Emberger Syndrome (sensorineural deafness, lymphedema and warts presented with myelodysplastic syndrome) was confirmed to have GATA2 mutation. She underwent successful matched related donor HSCT and is doing well.

Conclusions: It is worthwhile to suspect clinico-biologic association with syndromes where evident, for overall management and future monitoring.

PO242 SIOP19-1496 | The Diagnostic, Therapeutic and Counselling Challenges of Synchronous Rhabdoid Tumors

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Background/Objectives: The diagnosis of synchronous rhabdoid tumors in an infant is almost invariably associated with a germline mutation in SMARCB1 or SMARCA4.

Design/Methods: A previously healthy 12 month old girl presented with an abdominal mass, early morning vomiting and restlessness. A 14 x 19 cm renal tumor and a large posterior fossa tumor with hydrocephalus was found. Synchronous rhabdoid tumors were suspected, and tumor biopsy from the abdominal tumor was consistent with malignant rhabdoid tumor of the kidney. Further work-up revealed no additional tumors. Treatment was started according to the EU-RHAB protocol, and consisted of chemotherapy, stepwise nephrectomy and gross total resection of the brain tumor, high dose chemotherapy with stem cell reinfusion and proton beam irradiation to both tumor locations. The girl tolerated chemotherapy well, and both tumors responded. Before stem cell

re-infusion, a new abdominal wall rhabdoid tumor was found and resected. After finishing treatment she was well and thriving for 9 months until she relapsed with another abdominal wall tumor. Further treatment efforts were futile. The girl expired 18 months after initial presentation.

Results: Analysis of *SMARCB1* and *SMARCA4* from exome sequencing of DNA extracted from blood (germline) and brain tumor did not reveal any abnormal variants. Manual inspection of the data gave no suspicion of mosaicism or copy number variants (CNVs). Promoter and deep intronic variants could not be ruled out. Neither MLPA-*SMARCB1* nor high resolution SNP-array confirmed any CNVs in blood or brain tumor, but FISH-analysis showed 54% mosaicism for a *SMARCB1*-deletion in the brain tumor. No evidence of genetic predisposition was found in 68 solid tumor genes or whole exome filtered for autosomal recessive inheritance.

Conclusions: The absence of a germline mutation in a patient with clinically evident rhabdoid tumor predisposition syndrome leads to major diagnostic and therapeutic difficulties as well as challenges in genetic counselling.

PO243 SIOP19-1400 | The Hypodiploid Acute Lymphoblastic Leukaemia, a New Entity of the Tumour Spectrum in Li-Fraumeni Syndrome?

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Background/Objectives: We describe the case of a patient with a Li-Fraumeni Syndrome (LFS) and diagnosed with a secondary myelodysplastic syndrome (MDS).

A 5 years-old boy was treated for a hypodiploid acute lymphoblastic leukaemia. At diagnosis, leukaemia showed no high leukocyte count and no central nervous system invasion. The medullary karyotype was triploid with a duplicated hypodiploidy and deletion on 17p chromosome. He was treated according to the FRALLE 2000 protocol, group B2. He was steroid-responsive, chemo-responsive and the minimal residual disease was negative at the end of induction.

Design/Methods: The end-of-treatment bone marrow aspiration accidentally found dysgranulopoiesis and dyserythropoiesis with sideroblastic anaemia without blast excess. The bone marrow karyotype was complex with 5q, 7p, 17p deletions and 8 trisomy. It was in favour of a secondary myelodysplastic syndrome with unfavorable cytogenetic. Before this early secondary MDS after the treatment of a leukaemia, a cancer predisposition syndrome was sought.

Results: In the bone marrow a *TP53* mutation was found and confirmed on fibroblast culture. This missense mutation was

in the exon 10, c.1009C>T, p.(Arg337Cys) and has already been described in the LFS. After discussion about the intensity and toxicity of conditioning for this patient, allogeneic stem cell transplant was performed with a myeloablative conditioning.

Conclusions: The LFS is one of the most dramatic cancer predisposition syndromes due to germline mutation of *TP53*. The LFS is characterized by an early onset of cancer and a broad spectrum of tumours including adrenocortical carcinoma, osteosarcoma, soft tissues sarcoma, pre-menopausal breast cancer and, brain tumour. Leukaemia is uncommon in LFS. However, many recent reports have also implicated germline *TP53* variation in the pathogenesis of hypodiploid acute lymphoblastic leukaemia in children. Increased genotoxic effects of radiotherapy are described in LFS patients, and chemotherapy-induced toxicity seems to be majored too. LFS must be searched in children with hypodiploid acute lymphoblastic leukaemia.

PO244 SIOP19-0477 | Application the Genetic Profiles by ACGH Technique in Treatment Tailoring in Vietnamese Low-Risk Neuroblastoma

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Background/Objectives: Neuroblastoma (NBL) is the most common solid tumor diagnosed in the first year of life. While the high-risk NBL is still a big challenge with the clinical, the low-risk group have a excellent prognosis and outcome. At Vietnam National Children's Hospital, the decision of treatment for this group (follow-up or symptomatic treatment) depends on the genetic profiles.

Design/Methods: There are 13 low-risk patients from 2016 to 2018 who was selected for aCGH test. They was under 18 months old, at L2 stage (9 patients), Ms stage (3 patients) and M stage (1 patient). The aCGH technique is performed on SurePrint G3 Human Genome CGH+SNP 2x400K Microarray slide by Human Genome CGH+SNP Microarrays system (Agilent).

Results: In 13 cases, 9 NCA cases, 3 SCA cases and 1 non-contribute case were found. The SCA profiles were found in the M stage patient and 2 other L2 stage ones, while the flat profile was found in the L2 stage, 15.3 months old patient. All those genomic profiles had taken part in the treatment

tailoring in unresectable patients. The two SCA cases in L2 stage had been treated 2 additional courses of chemotherapy. The M stage patient, who had the SCA profile, had continued the palliative chemotherapy. Otherwise, the NCA profiles had helped the young NBL patients avoid overtreatment. A new case had been just followed up and no chemotherapy, one case had been abandoned the 4th course of chemotherapy and the others (seven L2 cases), who were unresectable after 2 course of Carbo-VP16, had continued follow-up.

Conclusions: The genetic profiles by aCGH technique is truly an important step in developing the personalized medicine, resulting in high therapeutic effect as well as minimizing the complications of treatment for Vietnamese NBL patients.

Treatment and Care - Treatment Toxicity and Supportive Care

PO245 SIOP19-0074 | Treatment-Related Toxicities Among Chemotherapy Recipients from a Paediatric Oncology Service in a Rural Ghanaian Setting

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Background/Objectives: The Agogo Presbyterian Hospital (APH) is the oldest mission hospital located in the middle-belt of Ghana. The Paediatrics Department of APH is providing more paediatric oncology services since May 2018 with the appointment of a paediatric oncologist as the departmental head. Chemotherapy is administered at the children's ward by supporting staff with no formal training in paediatric oncology. Supportive care services available includes whole blood support; third and fourth generation cephalosporins and metoclopramide and dexamethasone for anti-emesis. To describe treatment-related toxicities and outcomes associated with chemotherapy from May to November 2018.

Design/Methods: Retrospective review of clinical notes from May to November 2018. The data extracted was analysed using frequency distribution tables. Toxicity was graded using the National Cancer Institute Common Toxicity Criteria version 1.

Results: Overall, 30 cycles of cytotoxic chemotherapy were administered to 8 children for burkitt lymphoma (2), rhabdomyosarcoma (2), hodgkin lymphoma (1) and neuroblastoma (1). Two children with Wilms tumour and leukaemia who are being treated at tertiary centres, presented for chemotherapy-related shared care. There were 157

episodes of treatment-related toxicities as follows: fever (15, 9.6%), myelosuppression (99, 63.1%), vomiting (22, 14.0%), diarrhoea (10, 6.4%), mucositis (3, 1.9%) and alopecia (all the 8 children with grade 2). Among 35 (22%) instances of severe (grades 3 and 4) toxicity, there were 15 (9.6%) anaemia episodes and 4 (2.5%) of thrombocytopenia with 3 requiring blood transfusion; 11 (7.0%) episodes of neutropoenia, with 4 (2.5%) cases of febrile neutropoenia; 3 (1.9%) instances of severe vomiting and 2 (1.3%) episodes of severe mucositis. All children are alive except the child with neuroblastoma who was being palliated and died from her advanced disease. No treatment related mortalities were recorded over the period.

Conclusions: Majority of the treatment-related toxicities were mild or moderate in this new paediatric oncology service in resource-limited settings. Efforts needed to train staff and improve access to supportive care.

PO246 SIOP19-1014 | Protective Diets In Hematologyoncology: Insights from a 4-Hospital Survey

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Background/Objectives: This work emerged from a wish to examine protective diets in children in hematologyoncology from a cross-disciplinary perspective in an area with scant scientific literature. When treated for cancer, children go through different stages for which the level of exposure to bacteria, viruses and germs in general must be kept as low as possible. External germs, especially in food, pose a particular risk.

However, cancer treatment is a long-term therapy and protective diets as implemented today imply a number of restrictions the family must deal with. Protective diets are currently applied more or less strictly depending on particular hospital. This leads to significant differences in support, follow-up, and even compliance to the diet from the children and their families.

Design/Methods: We designed a survey to measure both the practical consequences of the diet in a day-to-day basis and the emotional state of the entire family. We analysed answers from 41 families attended at 4 hospitals in the Auvergne-Rhône-Alpes region using a correlation analysis.

Results: Our analysis showed first that the impact of protective diets on children was dependent upon their ages. Besides, the extent of the differences between the pre-disease family cooking customs and the protected diet impacted the fact that the diet was followed more or less strictly by the child. Finally the major constraint (cost) to the strict observance of the protective diet was the availability of cheap small food packaging.

Conclusions: In order to facilitate the compliance of the protective diet by families and children, hospitals should follow the same practical rules in protective diets and further try to share their own attempts.

PO247 SIOP19-0542 | Secondary Mitochondrial Dysfunction During Chemotherapy for Pediatric Malignancies; Review in Three Pediatric Hematology Oncology Units in Lebanon

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Background/Objectives: Pediatric malignancies are the second cause of death in children. Treatment consists of combination of chemotherapy drugs. Most of these agents target primarily the mitochondrial core in order to achieve remission. While targeting the cancerous cells, healthy cells are also affected, and patients can present with mitochondrial dysfunction. These findings remain rare but when present can deeply affect the well being of the already sick child.

Design/Methods: Between 2010 and 2018, 15 patients (13 leukemia, 1 Rhabdomyosarcoma, 1 Ewing Sarcoma) were identified in 3 pediatric oncology centers in Lebanon;(St George Hospital UMC, Lebanese Hospital Geitaoui UMC and Notre Dame de Secours Hospital UMC). Clinical manifestations varied between myopathy, hypoglycemia, hyperammonemia, lactic acidosis and encephalopathy. There was no evidence of liver failure. These patients had marked improvement after initiation of L-carnitine, Coenzyme Q10 and sodium benzoate, except one patient with ALL who died during induction chemotherapy due to high level of hyperammonemia and encephalopathy with no response to treatment.

Results: Discussion: The exact mechanism remains to be thoroughly investigated. However, incriminated chemotherapy agents include asparaginase and vincristin which are known to interfere with adequate mitochondrial replication. Furthermore, these patients come from a highly consanguineous population where mitochondrial diseases are highly prevalent.

Conclusions: Mitochondrial dysfunction should be suspected in every child receiving chemotherapy with unexplained lactic acidosis, hypoglycemia, hyperammonemia and encephalopathy. Further studies are needed to identify patients at risk

while rapid diagnosis and treatment are crucial to prevent further damage.

PO248 SIOP19-0447 | Inflammatory Myofibroblastic Tumor Following Haploidentical HCT: Case Report and Review of the Literature

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Background/Objectives: Inflammatory myofibroblastic tumor (IMT) is a rare mesenchymal neoplasm of intermediate biologic potential. There are 150-200 new cases of IMT diagnosed annually in the United States, mostly in children and young adults. There are no known biologic or environmental risk factors for the development of IMT. Approximately 50% of IMTs harbor mutations in the *ALK* gene. While cases of IMT have been reported after hematopoietic cell transplant (HCT), there is no known association between haploidentical HCT and IMT. We present the case of a nineteen-year-old male who developed an *ATIC-ALK* fusion positive IMT after haploidentical HCT for acute myelogenous leukemia and review the relevant literature.

Design/Methods: Case report information was obtained from the institutional electronic health record. Literature review was conducted through MEDLINE using search terms including "inflammatory myofibroblastic tumor," "inflammatory pseudotumor," and "plasma cell granuloma" linked with the Boolean operator "AND" to the term "transplant."

Results: Literature review revealed eight cases of IMT following HCT. Seven cases occurred in patients who received non-haploidentical allogeneic transplants for hematologic malignancies. One case occurred following autologous transplant for the treatment of neuroblastoma. No case of IMT following haploidentical HCT has been reported. Proposed risk factors for IMT development after HCT include chemotherapy, immunosuppression, total body irradiation, graft vs. host disease, sepsis/inflammation, and instrumentation. Our case suggests that total lymphoid irradiation may also increase the risk for IMT following transplant.

Conclusions: Patients who receive HCT, including haploidentical transplants, may have an increased risk of developing IMT. Identification of a mass lesion in the post-transplant setting should prompt consideration of IMT. Early recognition and intervention with surgery, ALK inhibitors, and/or other pharmacologic management may improve outcomes. Routine screening is not recommended given the rarity of IMT in the transplant population.

PO249 SIOP19-1634 | Improving Standards for Infection Care and Prevention in Pediatric Oncology Units in Three Hospitals on The Island of Hispaniola

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Background/Objectives: Interventions to improve access to care for pediatric cancer must go hand-in-hand with improving standards in infection care and prevention (ICP). The Hispaniola Island project aims to improve quality of care and survival for children with cancer in 3 pediatric cancer units by collaboratively implementing programs that will be incorporated into the larger structure of the hospital care delivery process. We report results after one year of collaboration with St. Jude.

Design/Methods: We followed the general steps for health promotion when engaging with the new sites, which are: 1) planning the process; 2) conducting a situational assessment; 3) identifying objectives; 4) identifying strategies; 5) developing indicators; and, 6) tracking progress.

Results: We began discussions with local leadership and developed a timeline and working plan for ICP engagement. Three healthcare providers were identified and trained through our educational programs as local ICP champions. Through site visits and focus group discussions, each unit developed a team comprising an infection preventionist and the trained ICP champion. Situational analysis revealed sub-optimal practices in indicators critical for cancer care, such as hand hygiene, central-line management, and mechanical ventilation. Strategies for improving care included implementing prospective monitoring and surveillance of ICP indicators, such as infection rates, with monthly reporting to and mentoring by the St. Jude team. Early results demonstrate feasibility for implementing standardized ICP reporting and focused improvement of care delivery.

Conclusions: Improving ICP standards is essential for any intervention which aims to improve survival of children with cancer. A step-wise procedure in building local teams, engaging hospital leaders, evaluating on-site resources and introducing methods to collect infection rates will effectively enhance the understanding of the local context and improve the safety of cancer care delivery. We developed and used a

model that could introduce sustainability at St Jude Global engaged sites.

PO250 SIOP19-0439 | Home Care in Pediatric Onco-Hematology: How to Work with Liberals?

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Background/Objectives: Since 2008, our home care unit (HCU) has developed the management of children and adolescents with cancer. Working only with liberal nurses close to the child's place of residence allows use to cover the entire region and supports an average of 140 children/year.

Design/Methods: This is a purely descriptive study on the functioning of the HCU.

Results: The multidisciplinary team coordinates care and connects stakeholders. This interface allows a great responsiveness with even complex outputs organized in 24 hours. HCU is offered to children and their families for treatment as a continuation care or as an alternative to hospitalization (IV chemotherapy, home palliative care). In 2007, our HCU was able to take care of 22 children in palliative care, half of whom died at home.

Conclusions: The HCU tends to maintain the intimacy and comfort of the home with the competence and safety of the hospital. Our 11 years of expertise allow us to develop more and more complex management methods with antifungals, immunotherapies and more recently therapeutic trials at home.

PO251 SIOP19-0446 | Investigating Potential Drug-Drug Interactions in Children Receiving Chemotherapy

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Background/Objectives: **Background:** Pediatric oncology patients receive numerous medications during chemotherapy admissions, increasing the risk of potential drug-drug interactions.

Objective: To evaluate the incidence of potential drug-drug interactions among pediatric oncology patients admitted for chemotherapy.

Design/Methods: **Design/Methods:** One hundred admissions for chemotherapy at Texas Children's Hospital from November 2016 to May of 2017 were reviewed. All medications causing QT prolongation were counted. EKGs for all patients were reviewed in the medical record. Twenty-eight

of the admissions were further analyzed using lexi-com with significant interactions being defined as either a risk rating of D or X.

Results: Results: Of the 100 patients evaluated, nearly half (n=44) received chemotherapy for leukemia or lymphoma. Only 4 of the 100 patients received an interacting combination of an antifungal and an antineoplastic medication. The most commonly seen interaction was Etoposide with either Fluconazole or Voriconazole. Ninety-eight of the 100 patients received between 1 and 8 (mean of 3) QTc prolonging medications. One third (n=33) of patients received 4 or more QTc prolonging medications. Of those children, one-fourth (n=8) did not have a documented EKG prior to or during admission. Twenty-eight of the 100 admissions were further evaluated with lexi-com. Over one-fifth (n=6) of those admissions were flagged as having a “D” risk rating interaction. The majority of those interactions (n=4) were flagged for use of numerous CNS depressants. One admission received an “X” rating for the use of both a beta agonist and beta antagonist. The beta antagonist additionally had a “D” rating for reaction with doxorubicin in the same patient, potentially increasing the concentration of doxorubicin with concomitant use.

Conclusions: Conclusion: Pediatric patients admitted to the hospital for antineoplastic therapy are at high risk for drug-drug interactions. The additive effects of multiple agents that cause QTc prolonging or respiratory depression should be carefully monitored.

PO252 SIOP19-0202 | Survey on Satisfaction with the Service of a Clinical Pharmacist on a Pediatric Hematology and Oncology Unit

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Background/Objectives: Pharmacotherapy in pediatric hematology and oncology (PHO) patients is complex. To improve the quality of treatment and care, a team of clinical pharmacists is involved in the PHO unit of the University Hospitals Leuven (UHL) since October 2014. This service can be optimized based on feedback of parents and other healthcare professionals (HCPs).

Design/Methods: An anonymous e-questionnaire on the satisfaction with this service was sent to parents, nurses and doctors on the PHO unit of UHL. Six items were questioned: overall satisfaction (parents and HCPs); patient-friendly medication list, the counseling conversation, the handling of potentially toxic medication (parents); the added value of the pharmacists' advice and the time saving component of the pharmacists' service (HCP).

Results: The response rate was 39% (14/36), 27% (21/77) and 38% (22/58) for parents, nurses and doctors respectively. Eighty-six percent of parents and 95% of nurses and doctors were satisfied to very satisfied with the overall service. For all the parents the counseling is given in an understandable language and 86% receive enough counseling. The patient-friendly medication list is clear (100%) and understandable (86%), although some parents advise some minor changes. Fourteen percent of the parents don't know how to handle potentially toxic medication. The pharmacotherapeutic advice given by the pharmacist to HCPs has added value for 98% of the HCPs, mainly due to the improvement of care for the patient, the obtainment of relevant information, the support that the advice gives to HCPs and the time saving component of this advice. HCP also save time because the pharmacist takes over the counseling.

Conclusions: Overall, most parents, nurses and doctors are (very) satisfied with the clinical pharmacist service on the PHO unit at UHL. However, the pharmacist should focus more on counseling the parents about potentially toxic drugs and on handing over a more patient-tailored medication list.

PO253 SIOP19-0341 | Oral Hygiene Protocol for Children with Cancer: Setting up and Evaluation of Acceptability with Children and Their Parents in Marrakesh

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Background/Objectives: Chemotherapy and radiotherapy are the main ways of treating childhood malignancies. The immediate effect of those therapies is on oral structures such as mucositis, xerostomia, oral fungal infections and gingival sculptures. The management of those complications is a priority in our practice.

OBJECTIVE: to establish an easy and applicable oral protocol and evaluating its feasibility and acceptability for children and their parents at the pediatric hemato-oncology department in Marrakesh.

Design/Methods: Prospective, descriptive and transversal study from December 2016 to February 2017 in the pediatric hemato-oncology department of Marrakesh. The buccal hygiene education was done using educational session for children and their parents, brochure and the evaluation was done after by using questionnaire.

Results: 50 patients were admitted to this study and had education for buccal hygiene. All patients had no information on value of oral hygiene before study, 88% had tooth decay before the protocol and only 22% brush their tooth once a day. 90% declared that the protocol was easy to understand, 52% of the patient applied the protocol once a day, 36% of children

needed their parents help. 80% of them had improved their practice through this study.

Conclusions: The choice of the protocol in this study was made based on several criteria, starting with the latest recommendations from the American Academy of pediatric dentistry, socioeconomic level of patients and the simplicity. The acceptability rate of the protocol was interesting; however, a number of difficulties were encountered, mainly difficulty of applying certain protocol gestures (brushing) and the young age of certain patients. Measures may be considered to improve the oral care of children with cancer beginning with the education of the patient and also medical staff but only parental support and the involvement of the child are the key elements in success of the protocol

PO254 SIOP19-0068 | Pseudo-Tumoral Form of Tuberculosis in Children: A Diagnosis Challenge

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Background/Objectives: To analyze the clinical and radiological features of pseudotumoral forms of tuberculosis hospitalized in pediatric oncology and to evaluate the consequences for immunocompromised patients.

Design/Methods: All pediatric patients <18 years old hospitalized between 1996 and 2016 in 2 pediatric oncology center in Ile de France for suspected cancer and eventually diagnosed with tuberculosis. Aim is to analysis of clinical and radiological presentation with centralized re-reading and epidemiology.

Results: 17 patients were included. Median age: 14 years (range:1-16). 80% vaccinated with BCG. These were pulmonary (1 patient), lymphadenitis (9 patients), visceral (2 patients) or skeletal (5 patients) presentation. Radiological readings showed lymph nodes in 92% (75% necrotic), an apical location of pulmonary nodules (75%) and the presence of collections around bone lesions (100%). 13 biopsies were performed. All TST and 2 BK induced sputum were positive. 1 secondary case had been identified in the nurse staff.

Conclusions: Imaging signs would make it possible to evoke the diagnosis of tuberculosis as a differential diagnosis of cancer and lead to performing a TST in order to avoid unnecessary hospitalization patients with potential contagious tuberculosis in pediatric oncology department.

PO255 SIOP19-0918 | Mid-Upper Arm Circumference: A Reliable and Accurate Anthropometric Measure to Assess Nutritional Status in Children Suffering from Cancer

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Background/Objectives: Currently, there is no accepted method for assessing nutritional status and no consensual criteria for identifying denutrition, in particular in children suffering from cancer in which traditional anthropometric measures such as weight may be insufficient. Because it is convenient, accessible and independent of sodium and water retention, mid-upper arm circumference (MUAC) could be an interesting measure to assess nutritional status for these patients.

In this study, we aimed to determine the intra- and interobserver reproducibility of MUAC measurement in children.

Design/Methods: We prospectively included 30 patients treated at Lille University Hospital in pediatric hematology. For each patient, three independent observers (2 trained observers and 1 observer with no prior experience) undertook three consecutive MUAC measures. The difference between both inter- and intraobserver measurements were calculated. Reproducibility was assessed using three error estimates: the technical error of measurement (TEM), the coefficient of reliability (R) and the intra-class correlation coefficient (ICC).

Results: In our population, median age was 10.2 years [7.6-13.6]. Half patients were treated for acute lymphoid leukemia, 30% for lymphoma, 13% for acute myeloid leukemia and 3% for aplastic anemia. For intra-observer reproducibility, errors estimates were between 0.25 and 0.4cm for TEM and above 98% for coefficient of reliability and ICC. For inter-observer reproducibility, TEM were between 0.39 and 0.65cm and above 96% for coefficient of reliability and ICC.

Conclusions: MUAC is a very simple, affordable and reproducible method. The first step of validation for a measurement method being the evaluation of reproducibility, MUAC measurement appears to be a reliable tool to assess the nutritional status in children. Its convenience and accessibility would make it a great tool to the early detection of acute denutrition in children suffering from cancer worldwide.

PO256 SIOP19-0922 | Food is Medicine: Implementing a Comprehensive Nutrition Program on the Hematology Oncology Unit at Yangon Children's Hospital

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Background/Objectives: Children undergoing cancer treatment who are malnourished demonstrate significant

reductions in two-year survival rates. In low- and mid-income countries (LMIC), malnutrition and treatment abandonment are strongly correlated.[i]

Yangon Children's Hospital (YCH) is a public pediatric hospital in Myanmar. Approximately 50% of children on the inpatient Hematology/ Oncology Unit (HOU) demonstrate mild to severe malnutrition on admission. Lack of trained personnel, absence of nutrition screening tools and inconsistent access to nutritional products, are barriers that limit the provision of nutrition support. This program aims to implement sustainable, evidence-based strategies to improve the nutritional status of children at YCH/HOU.

[i] Ladas, E., Arora, B., Howard, S., Rogers, P., Mosby, T., Barr, R. (2016). A Framework for Adapted Nutrition Therapy for Children with Cancer in Low and Middle Income Countries: A Report from the SIOP PODC Nutrition Working Group. *Pediatric Blood & Cancer*; 63, 1339-1348.

Design/Methods: A Nutrition Support Program was launched at YCH in February 2019. A local nutritionist was hired to lead the program. An adapted malnutrition screening tool was developed to identify underweight children on admission. Children identified as malnourished receive oral nutrition packages that include local high-protein, high-calorie foods and beverages. The nutritionist is responsible for monitoring feeding tolerance and adjusting interventions appropriately.

Results: From February 6th, 2019 to March 17th, 2019, 61% (n=147) of 240 admissions were identified as "underweight" using the malnutrition screening tool; these children received formal evaluation and intervention from the nutritionist.

Conclusions: Nutrition is a critical aspect of childhood cancer treatment. The implementation of a nutrition program which includes targeted education for clinicians, implementation of assessment tools, and food interventions adaptable to local culture is a strategy to improve outcomes for children with cancer. Further data will determine the efficacy and sustainability of the YCH nutrition program and its impact on patient outcomes.

PO258 SIOP19-1331 | The Toxicity of Chemotherapy in Childhood Cancer: The Interest of Supportive Care

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Background/Objectives: The toxicity induced by chemotherapy is associated with significant morbidity, mortality and treatment cost. **OBJECTIVES** Evaluating the prevalence of side effects of cancer chemotherapy, Determine

the main side effects their frequency and their time of appearance

Design/Methods: Analytical prospective study over 2 years from 2017 to 2019

Results: 158 cases of children with cancer aged an average of 7 years (1 year, 15 years) showed side effects to chemotherapy during this period. The sex ratio is 1.1. Cancer pathologies in descending order Leukemia represents the most common pathology 59%. The injectable galenic forms were the most used. The side effects of the anticancer drugs occurred within a period of less than 7 days in 70% of the cases. Febrile neutropenia was the most common with 88%, It is most often severe, complicated by documented sepsis in rare cases Mucositis comes second in 64.4% followed by Vomiting in 48%, of which 58.33% are WHO grade III. hepatic cytotoxicity 47%. Diarrhea and abdominal pain are found in 42%, Other side effects are less common: neurological toxicity (21 cases), induced diabetes (5 cases), drug allergy (12 cases), hemorrhagic cystitis (5 cases) cardiac toxicity (4 cases), psychiatric involvement (3 cases) toxiderma (3 cases) hypoglycemia (1 case) Hospitalization was prolonged for an average of 7 days following side effects in 90% of cases. The clinical signs of toxicity decreased in 60% of cases thanks to measures of supportive care. Death due to toxicity occurred in 16% of cases

Conclusions: The side effects of chemotherapy are numerous and common. Thanks to a better knowledge of these effects, prevention and treatment protocols exist for an anticipatory attitude, a better management and a lower cost for health.

PO259 SIOP19-1729 | Designing and Implementation the Use of Educational Videos to Facilitate Learning in Clinical Guidelines

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Background/Objectives: Treatment and care for children with cancer requires various of clinical procedures performed by the nurses. In order to consistently secure the patients, the best treatment and care clinical practice guidelines for the nurses was developed. Clinical practice guidelines are systematically developed and evidence based, made to assist nurses in specific clinical procedures aiming to improve the quality of patient care and to reduce unnecessary variation in practice. Nevertheless, the families reported that the procedures were performed in several ways by different health care professionals.

Therefore, we followed nurses performing the procedures. The data showed that despite the guidelines, the procedures still were performed differently.

Some of the nurses found, that the guidelines were too complex and hard to understand and as a result they didn't use them.

Design/Methods: To ensure consistent care of the children, and to facilitate that nurses use and understand the guidelines, different thoughts about mutual learning and good ideas by the nurses was used.

In collaboration with the nurses a new supplement to the written guidelines was developed – the educational video guideline.

Results: The nurses are very pleased by the video sequenced guidelines. Using them supports the nurses in carrying the procedures consistently, based on available evidence. The videos support the nurses in differentiated learning and opens up for discussions among the nursing group related to evidence/best practice. The families experience that the procedures are now performed more consistent, and based on evidence for the safety of the child.

Conclusions: An educational video guideline is a way to create overview of a complex procedure and get used to the procedures for the nurses. It assists nurses to understand and perform the procedures correct, consistent and evidence based. Therefore also helps to secure the safety of the child, and make the families feel more secure.

PO260 SIOP19-1420 | Non Tuberculous Mycobacterial Infections in Children with Cancer: A Single Centre Experience Over 2 Years

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Background/Objectives: Nontuberculous mycobacteria (NTM) have been associated with various clinical manifestations in both immunocompetent and immunocompromised children. However relatively few cases of these infections in Paediatric oncology patients have been documented.

Design/Methods: A retrospective review was undertaken for all paediatric patients with cancer at Great North Children Hospital with a culture positive for atypical mycobacteria spp from 1997 until 2018. Clinical details of patients with positive isolates were taken from their medical records and the spectrum of atypical mycobacterial infections was reviewed in these patients.

Results: During the 22-year period, four paediatric oncology patients at our hospital had cultures positive for atypical mycobacterial infection and were treated for symptomatic infection. Three cases occurred in patients with solid tumours

and one patient had haematological malignancy. All four patients had central venous catheters and were lymphopenic when their symptoms began. All four patients received different regimes of anti-tuberculous treatment for varying durations with 2 patients still on treatment and 2 patients successfully treated without recrudescence of infection.

Conclusions: When the aetiology for febrile immunocompromised children is unclear, suspicion of infections due to non tuberculous mycobacteria should be raised. Currently there is no standard approach to type and duration of treatment in children with cancer and evidence based guidelines are urgently needed.

PO261 SIOP19-0547 | Increase Thrombin Generation Assay in Pediatric Acute Lymphoblastic Leukemia Treated with L-Asparaginase and Corticosteroid

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Background/Objectives: Acute lymphoblastic leukemia (ALL), most common pediatric cancer in Thailand. Thromboembolism found 1.7-36.7% in ALL patients, which were significant cause of ALL mortality. Thrombin generation assays (TGA) is a novel method to evaluate the risk of bleeding and thrombosis by monitoring thrombin concentrate forming in hemostatic process.

To study thrombin generation assay in pediatric ALL whom treated with L-asparaginase and corticosteroid during induction or delayed intensification of Thai national protocol.

Design/Methods: This is a prospective case control study. TGA were measured 2 difference times in all pediatrics ALL patients which on induction or delayed intensification protocol. Blood sample was collected before and after this treatment within 10 days. Monitored Lag-time, Peak of TGA, elevated endogenous thrombin potential (ETP). Thrombophilia patients, Relapsed protocol patients, and poor compliance were excluded.

Results: Fourteen patients (6 males and 8 female) were enrolled which is median age 7.87 years old, 12 cases and 4 cases were B cell and T cell ALL, respectively. Seven cases were collected during induction phase and 7 cases in intensification phase. No thrombosis event was found. Shorter lag-time, higher peak of TGA and increase ETP compared pre and post treatment, p-value: 0.04, < 0.01, 0.01 respectively, correlated with increased thrombosis risk.

Conclusions: TGA is another method to evaluate hypercoagulable stage in pediatric ALL treat with L-asparaginase and corticosteroid and show increased result after treatment. TGA may be use to predicted thrombosis.

PO262 SIOP19-0546 | Fertility Preservation in Pediatric Patients with Hematologic Malignancies

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Background/Objectives: In recent years, infertility after treatment has been attracting attention as an important factor affecting quality of life. The American Society of Clinical Oncology recommends that oncologists should inform patients about the possibility of infertility and fertility preservation prior to gonadotoxic therapy. Thus, we sought to examine the cases in our department with the aim to investigate the state of fertility preservation in patients who have underwent chemotherapy.

Design/Methods: We conducted a retrospective investigation of pediatric patients with hematologic malignancies who were treated in our hospital between January 2005 and December 2018.

Results: A total of 182 patients were identified and studied: 112 had acute lymphoblastic leukemia; 33 acute myeloid leukemia; 19 malignant lymphoma; 7 myelodysplastic syndrome; 6 aplastic anemia; 2 chronic myeloid leukemia; 2 juvenile myelomonocytic leukemia, and 1 transient abnormal myelopoiesis. Fifty-one hematopoietic stem cell transplantation were performed. All patients who received transplantation were provided information for informed consent, including the risk of infertility; however, only 8 patients who were administered chemotherapy alone were provided information regarding infertility. Sperm banking was discussed with 10 male patients, all of whom agreed to sperm cryopreservation. Unfortunately, 2 patients had azoospermia. One female patient underwent ovarian tissue cryopreservation.

Conclusions: Sperm cryopreservation is a technique available for fertility preservation in post-pubertal male patients. Cryopreservation and subsequent transplantation of gonadal tissue may serve as alternative methods in pre-pubertal female patients. Further studies should be required to facilitate combining therapeutic treatment and fertility preservation.

PO263 SIOP19-1264 | Steroid Diabetes Mellitus in Children and Adolescents During Intensive Treatment of Leukemia in the Regional Children Onco-Hematology Center Named After V. Gerein

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Background/Objectives: Among the many complications of treatment, there is steroid diabetes mellitus which is most often seen in patients with already established metabolic syndrome or having burdened heredity.

The aim of the study was to analyze the frequency and clinical features of steroid diabetes in patients with acute lymphoblastic leukemia (ALL) during intensive chemotherapy.

Design/Methods: In a retrospective study for the period from 01/01/1994 to 01/01/2019, 572 children with ALL were treated. For 25 years, the BFM-ALL 90 (M), MB 2002, MB 2008, ALL-Baby, MB 2015 protocols of polychemotherapy were used in the Center for the treatment of ALL. The research group included 16 patients diagnosed steroid diabetes aged from 3 to 17 years $M 7.93 \pm 4.8$. The median of age in patients with ALL in the center was 5.1 ± 2.3 . All programs include one of the steroids in the list of drugs: prednisone, metipred, or dexamethasone.

Results: The complication was rare, it occurred only in 2.8% of patients. There were 12 boys (75%), which is 3 times more than girls - 4 (25%). Steroid diabetes mellitus often manifested itself in anti-relapse treatment (69.23%), that is, in patients with significant predisposition and more often developed on dexamethasone therapy - in 14 (87.5%) patients than in prednisone and medrol - in 1 (6.25%) case; adolescent boys are more prone to this complication of ALL therapy Experts noted the phenotypic similarity of the majority - 13 (81.25%) patients, 15 (0.9%) have relatives who had at least three signs of metabolic syndrome.

Conclusions: Thus, the risk factors for the development of steroid diabetes mellitus in children and adolescents during the period of intensive chemotherapy include: previous long-term therapy, the use of dexamethasone in comparison with other drugs, adolescence and familial metabolic syndrome.

PO264 SIOP19-0127 | Prevalence of Infectious Complications in Children with Cancer

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Background/Objectives: Infections are the most common complications during chemotherapy due to neutropenia causing significant morbidity and mortality. The trends have been changing over time due to use of multi-agent intensive chemotherapy regimens causing severe and prolonged neutropenia leading to life threatening infections from known and emerging organisms. We looked our data to see what complications we get in our patients.

Design/Methods: The data was collected on patients treated in King Fahad Medical City from July 2009 to Dec 2015. Any patient presenting with a fever of 37.8 C on 2 occasions 30 minutes apart or one episode of 38C or positive culture reported in a child with suspected sepsis. Duration of Neutropenia of <7 days as mild, 7-14 days moderate and > 14 days as severe. Patients were screened for fungal infections after 5 days of unresolved fever. The collection of data was from patient files, Hospital Information Management system and patient road maps. Specific forms were used for the collection and then uploaded on spreadsheets.

Results: We found that 86 patients had one episode only while 92 had 2 or more episodes reaching up to 11 episodes in 1 patient. We found positive cultures in 17.3% of episodes with staphylococcus as common gram positive and Klebsiella Pneumoniae as common gram negative bacteria, respiratory viral infections in 13.8% and GI infections in 9%. We found Candida albicans as the most common fungus while other yeasts followed. The episodes were associated with neutropenia of <500 and duration of neutropenia of >7 days in. We had 2 deaths one from recurrent infections with CNS damage and one from Pulmonary infections causing pulmonary haemorrhage.

Conclusions: Neutropenia of <500 and duration of >7 days came out to be significant risk factors for infection across all diseases more so in AML (Acute Myeloid Leukemia).

PO265 SIOP19-0150 | Successful Pain Control of Chemotherapy-Induced Mucositis in Children by Tramadol – A Single-Center Experience

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Background/Objectives: Mucositis is a painful condition. Treatment for moderate-to-severe pain is based on intravenous (IV) morphine and correlate with severe side effects. Tramadol is a weak opioid with a longer half-life than morphine and fewer side effects.

Design/Methods: All admissions to the Pediatric Hemato-Oncology Department due to mucositis between November 2016 and November 2017 were retrospectively analyzed.

Pain intensity had been evaluated using appropriate pain scales. Mucositis had been scored according to the WHO grading system. IV tramadol had been used for a pain numerical rating score (NRS equivalent) >4/10. We retrospectively evaluated if our protocol had effectively achieved a reduction of the NRS equivalent score by 2 points or <6/10 within 24

hours. We analyzed tramadol and strong opioid side effects, correlation between mucositis grade and analgesic treatment, correlation between grade of mucositis and its duration, correlation between duration of neutropenia and the need for morphine treatment.

Results: 34 patients had experienced 54 mucositis episodes. Thirty-four (63%) episodes had received tramadol alone. Fifteen (27%) episodes had required <5 rescue doses of morphine per day. Five (10%) episodes had required IV morphine patient-controlled analgesia. In grade 4 mucositis, 79% of the episodes required additional opioids other than tramadol ($p<0.01$). The grade of mucositis was an independent factor for additional opioid treatment, with 17 times higher risk for grade 4 mucositis compared to grade 2 ($p<0.05$). Mean treatment duration was highest in grade 4 mucositis ($p<0.05$). The use of tramadol was associated with mild side effects. Patients treated with tramadol had shorter mean duration of neutropenia compared to those that needed additional opioids (4.18 days versus 7.4 days, $p<0.05$).

Conclusions: Adequate analgesia had been achieved in 90% of patients using tramadol. This is the first description of the utility and advantages of tramadol in the successful treatment of pain in pediatric patients with chemotherapy-induced mucositis.

PO266 SIOP19-0565 | Adverse Events and Perioperative Complications in Children with Solid Tumor Receiving Sorafenib or Sorafenib Plus Irinotecan

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Background/Objectives: Sorafenib is an oral small molecule inhibitor of multiple kinases controlling tumor growth and angiogenesis. The optimal management of adverse events (AEs) and complications in wound healing after surgical intervention are key to maintaining patients on individual treatment for as long as possible. Here, we analyzed AEs for pediatric patients receiving sorafenib or sorafenib plus irinotecan.

Design/Methods: Between 2012 and 2019, the clinical charts of patients who were treated with sorafenib were retrospectively reviewed in our department. All the patients were orally administered sorafenib, 200 mg/m²/dose, twice daily, continuously in 28-day cycles. Patients with hepatoblastoma who received sorafenib combined with irinotecan 20 mg/m² × 5 days were also included in the analysis. AEs were evaluated by the CTCAE v4.0. In addition, we also examined the time from surgery to the start of chemotherapy in patients undergoing surgery.

Results: We enrolled twelve patients with hepatoblastoma, hepatocellular carcinoma or malignant myoepithelial tumor. The median age at the time of sorafenib initiation was 4.5 years (2–15 years). The median number of sorafenib and sorafenib plus irinotecan treatment cycles was 7 (2–31 cycles) and 7.5 (2–18 cycles), respectively. In patients undergoing surgery, the median duration of sorafenib interruption was 8 days, which was from 1 day before operation to 7 days after operation. There were no anatomical leakage and no wound infection. The most frequent severe AEs (grade 3 or more) were hematologic toxicity (8.5%) and hyperten-

sion (1.5%). Severe palmar-plantar erythrodysesthesia or diarrhea did not appear during any cycles. In three patients who received sorafenib for > 8 courses, either grade 2 hypothyroidism or proteinuria was noted. Growth retardation was most discernible when sorafenib was initiated in the prepubertal period.

Conclusions: Sorafenib and sorafenib plus irinotecan were well tolerated in children. Such sorafenib therapies combined with surgery may be therapeutic options for children with refractory solid tumor.

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